COMMENTS

DEVELOPING, TESTING, AND MARKETING AN AIDS VACCINE: LEGAL CONCERNS FOR MANUFACTURERS

ALISON JOY ARNOLD†

INTRODUCTION

Due to the lack of a national policy for dealing with the AIDS¹ pandemic, individuals within AIDS high risk groups are rapidly becoming society's new health advocates. Occasionally employing confrontational tactics,² these individuals are attempting to

† A.B. 1982, Brown University; M.A. 1988, Wesleyan University; J.D. Candidate 1991, University of Pennsylvania. This Comment is dedicated to my family, in appreciation for their support and encouragement, and to my former colleagues in the pharmaceutical industry who remain undaunted by the obstacles. I am grateful to Scott Burris for his comments on earlier drafts of this manuscript.

¹ Acquired Immune Deficiency Syndrome (AIDS) is a communicable and sexually transmitted disease caused by the human immuno-deficiency virus (HIV). It is the final phase in a continuum characterized by four distinct disease stages: first, an initial infection which often mimics mononucleosis; second, a period of latent, asymptomatic infection; third, persistent, regionalized lymph node enlargement sometimes called AIDS-related Complex (ARC); and finally, the multiple opportunistic infections, neurological impairments, and other clinical presentations that constitute AIDS. See Centers for Disease Control, U.S. Dep't of Health & Human Servs., *Classification System for Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus Infection*, 105 ANNALS INTERNAL MED. 234, 234-35 (1986).

The HIV virus is a retrovirus; it uses an enzyme called reverse transcriptase to introduce its genetic material (ribonucleic acid, or RNA) into the genetic material (deoxyribonucleic acid, or DNA) of a host cell. Initially, the virus is virtually undetectable. Seropositivity (the appearance of viral antibody in the serum) occurs when the altered host cell is properly stimulated by antigens. At that point, the infected host cell's replicatory machinery "sees" both the foreign viral material, as well as its own cellular DNA, and thus produces infected cells. Viral proteins are then synthesized and are subsequently packaged together with viral genome and released, going on to attack additional cells. HIV has a predilection for particular host cell types, namely, T-helper lymphocytes (also called T-4 cells), macrophages, and monocytes. Since the T-helper lymphocytes are responsible for cell-mediated immunity, their destruction by the virus is a critical cellular event in the development of the disease, causing the immunodeficiency which gives AIDS its name. See Fauci, Temin & Martin, *The Scientific Agenda for AIDS*, ISSUES SCI. & TECH., Winter 1988, at 33, 33-35; Mayer, *The Clinical Challenges of AIDS and HIV Infection*, 14 LAW, MED. & HEALTH CARE 281 (1986); Schild & Minor, *Human Immunodeficiency Virus and AIDS: Challenges and Progress*, 335 LANCET 1081, 1081-82 (1990).

² For example, Larry Kramer is the founder of the AIDS Coalition to Unleash

galvanize those within the research, regulatory, and pharmaceutical communities to provide access to AIDS drugs through special distribution programs, and to accelerate AIDS drug and vaccine development.³ If these goals are to be realized, a radical change in the approach taken toward the research, approval, and marketing of new drugs may be required. Speeding up the drug approval process may mean the utilization of patients in high-risk clinical experimentation. Moreover, drug availability and pricing policies may depend on the ability of manufacturers to limit their own liability. The consequences of these issues extend beyond the AIDS epidemic and influence the extent to which the drug development process will be able to respond to disease victims in the future.

As scientific progress towards an AIDS vaccine⁴ begins to generate significant media attention and public interest, it is important to remain aware of the obstacles present in developing a successful vaccine for the prevention of AIDS. Part I of this Comment provides a brief overview of pharmaceutical product development and oversight of this process within the Federal Drug Administration (FDA). Part II analyzes the dilemma the manufacturers face when using human subjects in vaccine testing. Part III discusses liability risks for potential AIDS vaccine manufacturers.⁵

Power (ACT UP). He has described the tactics used by the coalition:

We have protests, which include taking over the opening plenary session of the AIDS conference in Montreal, blocking the Golden Gate Bridge and protesting endlessly at city hall here in New York. We have telephone zaps where we tie up switchboards. We purchased millions of dollars of tickets when Northwest Airlines refused to carry AIDS people as passengers, tickets that weren't paid for, of course.

Simpson, *Using Rage to Fight the Plague*, TIME, Feb. 5, 1990, at 7 (providing additional accounts of confrontational tactics employed by ACT UP).

³ See Marsa, *Phoenix Rising*, OMNI, Dec. 1989, at 51, 54-58.

⁴ Vaccination is a method of inducing immunity by the injection of a suspension of attenuated or killed microorganisms, including viruses.

The classic approach to developing a vaccine is to devise an immunogen that invokes an immune response [including antibody production] that can prevent absolutely the initial infection Some vaccines may be initially infected with a wild-type micro-organism; however, because of vaccine-induced immunity, the person may develop only a subclinical infection. Thus, a vaccine may also be designed to prevent the development of disease once the person is infected. Lastly, once disease is present, [some vaccines] may be used to bolster immunity and prevent the progression of disease.

Fauci, Gallo, Koenig, Salk & Purcell, *Development and Evaluation of a Vaccine for Human Immunodeficiency Virus (HIV) Infection*, 110 ANNALS INTERNAL MED. 373, 373 (1989) [hereinafter *Development*] (footnote omitted).

⁵ See *infra* text following note 68.

These risks are complicated by the courts' failure to establish a uniform way to evaluate high-risk therapeutic products, thereby making it difficult for manufacturers to determine whether they will be immune from strict liability claims.⁶ Part IV discusses possible future solutions for removing the legal barriers to AIDS vaccine development. And finally, this Comment concludes that the successful development and distribution of an AIDS vaccine requires a united effort among manufacturers, lawmakers, and regulators. A safe and effective vaccine can reach the marketplace only if legal obstacles are removed.

As legal strategies are developed to deal with an AIDS vaccine, it must be remembered that bringing this product through development will not be an easy task. Researchers and regulators will have to work overtime, and the obstacles they face should not be discounted.

I. FROM THE LABORATORY TO THE MARKETPLACE: AN OVERVIEW OF PHARMACEUTICAL PRODUCT DEVELOPMENT

To appreciate fully the concerns surrounding the licensing of new vaccines, it is necessary to understand the federal administrative process by which pharmaceutical products move from the laboratory to the marketplace. The following discussion will provide a brief overview of this process.

Pursuant to its statutory mandate under the Federal Food, Drug, and Cosmetic Act (FDCA),⁷ the FDA has promulgated both procedural and substantive regulations for the approval of all drug products.⁸ Vaccines fall within a category of drugs known as

⁶ See *infra* text accompanying notes 84-90.

⁷ 21 U.S.C. §§ 301-93 (1988).

⁸ A "drug" is considered to be any article "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease," or any non-food article intended structurally or functionally to affect the body. 21 U.S.C. § 321(g) (1988).

Under the Federal Food, Drug, and Cosmetic Act, the FDA has the authority "to act as both a public health promoter, by facilitating the approval of important new safe and effective therapies, and as a public health protector, by keeping off or taking off the market drugs not shown to meet safety and efficacy standards." 50 Fed. Reg. 7452, 7452 (1985). The Supreme Court has endorsed the FDA's regulatory authority. See *Weinberger v. Hynson, Wescott & Dunning, Inc.*, 412 U.S. 609 (1973); *Ciba Corp. v. Weinberger*, 412 U.S. 640 (1973); *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973); *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655 (1973).

biologics,⁹ and are subject to licensing provisions under the Public Health Service Act,¹⁰ in addition to FDA drug regulation.

Once the obstacles of preclinical development¹¹ have been

⁹ "Biological product' means any virus, therapeutic serum, toxin, antitoxin, or analogous product applicable to the prevention, treatment or cure of diseases or injuries of man." 21 C.F.R. § 600.3(h) (1990).

¹⁰ 42 U.S.C. §§ 201-300 (1988). The process of licensure is overseen by the Office of Biologics Research and Review, Center for Drugs and Biologics of the FDA. The goal of licensure is to ensure that manufacturing facilities and biologic products "meet standards, designed to insure the continued safety, purity, and potency of such products" 42 U.S.C. § 262(d) (1988); see also 21 U.S.C. §§ 351-52 (1988).

The FDA routinely inspects manufacturing facilities, and is empowered to examine individual vaccine lots in order to ensure compliance with FDA-approved standards for manufacturing and testing. See 21 C.F.R. §§ 600.20, 610.1-.2 (1990); *Berkovitz v. United States*, 486 U.S. 531, 546-47 (1988) (noting that the discretionary nature of FDA vaccine-lot testing does not bar a negligence action for the FDA's failure to ensure regulatory compliance).

¹¹ A number of biomedical factors have complicated efforts to develop an effective AIDS vaccine. First, the usual methods of vaccine development depend on the use of either attenuated virus or inactivated virus. In AIDS research, however, attenuated virus is thought to pose the risk of latent infection, and inactivated virus has had varying results in animal models. See Ada, *Prospects for a Vaccine Against HIV*, 339 NATURE 331 (1989); Liew, *New Aspects of Vaccine Development*, 62 CLINICAL & EXPERIMENTAL IMMUNOLOGY 225 (1985); *Development*, *supra* note 4, at 379 (edited summary of a conference sponsored by the National Institutes of Health).

Second, although a purified HIV subunit (such as a protein from the viral envelope) might be sufficient to generate an immune response, choosing a suitable subunit may pose a number of difficulties. For example, a successful HIV vaccine must perform two separate functions: it must induce the formation of antibodies and also neutralize the infected cells before they reproduce. See Ada, *supra*, at 331 (stating that "the vaccine should induce antibodies that neutralize viral infectivity as well as cytotoxic T lymphocytes").

Third, there are multiple strains of the HIV virus, and therefore, any vaccine developed must be able to protect against all strains and do so for a substantial period of time. See Hahn, Shaw, Taylor, Redfield, Markham, Salahuddin, Wong-Staal, Gallo, Parks & Parks, *Genetic Variation in HTLV-III/LAV Over Time in Patients with AIDS or at Risk for AIDS*, 232 SCI. 1548 (1986).

Finally, both the identification of viable animal models in which to study the disease, and the use of chimpanzees as one such model, have been hampered by several factors. Chimpanzees are an endangered species, expensive, and their use has generated particular concern among animal rights activists. For an overview of the debate concerning the general use of animals in biomedical research, see Cohen, *The Case for the Use of Animals in Biomedical Research*, 315 NEW ENG. J. MED. 865 (1986); Sumner, *Animal Welfare and Animal Rights*, 13 J. MED. & PHIL. 159 (1988); *Transformation of Society's Beliefs is Goal of Animal Rights Movement*, 29 PHYSIOLOGIST 43 (1986) (presentation by William M. Samuels before the Physiology Society).

Until recently, it appeared that the immune responses of chimpanzees challenged with HIV were such that the animals could not be considered suitable for vaccine testing. This no longer appears to be true, and "any AIDS vaccine effort [will probably] pause to consider how the product perform[s] in animals." Garrett, *The Leap to Possibility; Progress Prompts New Optimism for an HIV Vaccine*, *Newsday*, June 10,

overcome and a promising new drug has been identified, and has successfully undergone toxicological testing in animals, the pharmaceutical manufacturer files a "Notice of Claimed Investigational Exemption for a New Drug (IND)" with the FDA.¹² This signals the company's intention to begin clinical testing of the new product, and also begins the FDA's review process.¹³ Following IND submission, the FDA has thirty days to evaluate the application and determine whether safety problems exist.¹⁴ If safety requirements are met, clinical testing in human subjects can begin.¹⁵

Clinical testing in human subjects is conducted in four phases, three of which occur prior to approval for generalized usage and marketing of the product.¹⁶ The first of these phases is consid-

1990, at 5.

Although early pessimism is receding, technical problems continue to retard progress in designing a vaccine that will provide either immunity or a more favorable long term clinical experience for those immunized.

¹² See 21 U.S.C. § 355(i) (1988); 21 C.F.R. § 312.1 (1990).

¹³ Until recently, the FDA was the only regulatory body to grant an investigational exemption, doing so only after determining that a drug's potential benefits justified human testing. See 21 U.S.C. § 355(i) (1988); 21 C.F.R. §§ 50, 56, 312.1 (1990). California has now adopted legislation that will encourage clinical testing of new drugs prior to FDA authorization by providing funding to manufacturers believed to have "a good chance of developing an FDA approved vaccine . . ." CAL. HEALTH & SAFETY CODE § 199.59(b) (West 1990).

¹⁴ "Approval [of the IND] . . . is not an affirmative approval but is merely the absence of an objection registered within the mandatory 30-day waiting period." Halperin, *Research on New Drugs: Balancing the Goals*, 1 CLINICAL RES. PRAC. & DRUG REG. AFF. 325, 332 (1983). Thus, IND approval does not predict FDA endorsement during subsequent steps in the review process. See *id.*

¹⁵ Federal regulations require researchers to obtain the informed consent of subjects before commencing clinical testing. See *infra* text accompanying notes 53-67 (discussing informed consent).

¹⁶ These phases are as follows:

Phase I: The first phase of human testing is directed at determining the safe dosage range for a drug, the ways it is absorbed into the body, and possible levels of toxicity. These tests are usually conducted on 20-80 normal, healthy volunteers.

Phase II: The second phase of human testing is performed on closely monitored patients to learn more about the drug's safety and effectiveness. The number of patients monitored in this phase depends on the nature of the drug but seldom is more than 200. Most Phase II testing is directed at treatment or prevention of a specific disease. Additional animal testing is usually undertaken to gain further safety information. If the tests show the drug may be useful in treating a disease and the long-term animal testing indicates no unwarranted harm, the sponsor [the pharmaceutical company] then proceeds to phase III.

Phase III: This phase involves the most extensive testing. Phase III studies are intended to assess the safety, effectiveness, and most desirable

ered nontherapeutic, while the remaining three phases often provide some therapeutic benefit to the participants.¹⁷

Following the successful completion of Phase III, the pharmaceutical company submits a new drug application (NDA) for FDA approval.¹⁸ The new product is given a chemical and therapeutic classification and submitted to experts in the FDA review disciplines.¹⁹ The FDA then has 180 days to review the application.²⁰ Additional information may be requested from the pharmaceutical company; hence, the total review period occasionally exceeds 180 days. Application approval is based, in principle, upon the existence of a substantial body of evidence supporting the product's effectiveness as well as the demonstrated safety of the product for its intended use.²¹ "[T]his mandate necessitates an evaluation of the relation between benefit and risk . . . , which in turn requires evaluation of the relation between the pharmacologic effect of a [product] and the benefit presumed to derive from this effect."²² The FDA is permitted a certain amount of subjective judgment in

dosage of the drug in treating a specific disease in a large group of patients (usually several hundred to several thousand, depending on the drug). During Phase III, the drug is used the way it would be administered when marketed. Additional testing intended to define more specifically any drug-related adverse effects is also done in Phase III.

Myers & Moore, *The Drug Approval Process and the Information It Provides*, 21 DRUG INTELL. & CLINICAL PHARMACY 821, 822 (1987); see also *Needs for AIDS Research Activities: Hearings Before the Subcomm. on Health and the Environment of the House Comm. on Energy and Commerce*, 100th Cong., 1st & 2d Sess. 167 (1988) (Final report from the AIDS Clinical Trial Advisory Group discussing the establishment and operation of AIDS Treatment Evaluation Groups, developed to increase the clinical trial network for new AIDS therapies); Flieger, *Testing in 'Real People'*, FDA CONSUMER, Nov. 1987, at 11.

¹⁷ Consider the following:

Experimentation involving human research subjects has at least two subcategories: therapeutic and nontherapeutic. Therapeutic experimentation using a human subject may be defined as that experimentation which has as a goal providing a direct benefit (effective medical therapy) to the subject-patient. In contrast, nontherapeutic experimentation is not directed toward providing a benefit to the subject but is concerned with the discovery of data through the research on the human subject.

Whitlock v. Duke Univ., 637 F. Supp. 1463, 1467 (M.D.N.C. 1986), *aff'd*, 829 F.2d 1340 (4th Cir. 1987).

¹⁸ See 21 C.F.R. § 314.50 (1990).

¹⁹ See Myers & Moore, *supra* note 16, at 823.

²⁰ See 21 C.F.R. § 314.100 (1990).

²¹ See 21 C.F.R. § 314.125(b) (1990).

²² Borer, *t-PA and the Principles of Drug Approval*, 317 NEW ENG. J. MED. 1659, 1659-60 (1987).

its evaluation, and as a result conflict often surrounds the approval process.

Once a pharmaceutical product has met FDA requirements and has been granted approval, the manufacturing company may begin marketing and sales.²³ The company, however, is not out of the FDA's jurisdiction. Experimental documentation continues to be accumulated during Phase IV trials,²⁴ and the company is responsible for submitting this information to the FDA in scheduled annual reports for the remaining life of the patent.²⁵ Through its monitoring of the product's marketing experience, the FDA ensures that unfavorable effects are minimized and that labeling reflects any adverse reactions or contraindications.²⁶

Pharmaceutical product development is a long, tedious, and expensive process. A recent survey estimated that development time now averages twelve years, while costs average 231 million U.S. dollars for each new product.²⁷ Since the combined annual revenues generated by all vaccines have fallen to between 200 million²⁸ and 547 million²⁹ U.S. dollars in recent years, an AIDS vaccine could easily take many years to show a profit for the pharmaceutical company. Therapeutic liability,³⁰ existing patent

²³ See 21 C.F.R. § 314.105 (1990).

²⁴ The post-marketing, or Phase IV, clinical trials allow the measurement of variables not adequately assessed during Phase III research. For instance, the regimens and clinical situations studied during Phase III do not always correlate with those in which the product will be utilized after marketing. Also, even the large number of patients involved in Phase III trials are not fully representative of the treatment population—rare yet serious side effects may not be perceived until after marketing. In addition to monitoring safety issues, the pharmaceutical company looks for possible new indications; that is, the discovery of secondary effects which might permit use in a new population. Regulatory approval of such usage would result in increased utilization and higher profits for the company. See Townsend, *Postmarketing Drug Research and Development*, 21 DRUG INTELL. & CLINICAL PHARMACY 134, 134 (1987).

²⁵ The manufacturer must continuously report any adverse reactions or unexpected side effects "whether or not considered drug related . . ." 21 C.F.R. § 310.305(b)(2)-(3) (1990). The FDA also reviews the scientific and medical literature to gather evidence about drug hazards. See 50 Fed. Reg. 7452, 7473 (1985). Failure by the manufacturer to provide experimental documentation "may be grounds . . . for suspending or withdrawing approval of the application." 21 C.F.R. § 310.303(a) (1990).

²⁶ See Myers & Moore, *supra* note 16, at 823.

²⁷ See Rotman, *The Price of Doing R & D Soars*, CHEMICAL WK., June 13, 1990, at 46 (noting a survey conducted at Tufts University).

²⁸ See Garrett, *supra* note 11.

²⁹ See Andrews, *A Major Revival in Research on Vaccines*, N.Y. Times, Aug. 22, 1990, at D7, col. 1.

³⁰ Dr. George Todaro, former president of Oncogen (a subsidiary of Bristol-Myers

life,³¹ and the demographics of AIDS-infected individuals³² are also critical to a company's ability to recoup its initial investment and show a profit. Combined, these factors will have a significant impact on corporate incentives to invest in AIDS vaccine research and development.

Squibb) noted that although Bristol-Myers Squibb "will continue searching for an AIDS vaccine . . . concerns about liability force the company to abandon anything that is not proven 100-percent effective." To that observation Dr. Jonas Salk, "father of the polio vaccine," responded, "[t]here is no one-hundred-percent safe and effective vaccine." Garrett, *The Waiting Game in AIDS Research: Giant Drug Companies Are Watching the Little Guys in the Quest for a Vaccine*, *Newsday*, Sept. 18, 1990, at 1, 5; see also *infra* notes 68-157 and accompanying text.

³¹ In 1984, Congress enacted legislation to address pharmaceutical manufacturers' concern that the long FDA approval process was eroding their 17 year period of market exclusivity (as granted under the federal patent statute, 35 U.S.C. § 154 (1988)). The Drug Price Competition and Patent Term Restoration Act authorized five year extensions for patents of any new drug product that retained a patent life of less than 14 years following FDA approval. See Pub. L. No. 98-417, 98 Stat. 1585, 1599 (1984) (codified at 35 U.S.C. § 156(c)(3) (1988)). For an analysis of this legislation, see Wheaton, *Generic Competition and Pharmaceutical Innovation: The Drug Price Competition and Patent Term Restoration Act of 1984*, 35 CATH. U.L. REV. 433 (1986).

Recognizing that more innovative incentives may be required to spur manufacturer participation in the AIDS vaccine effort,

Harvard University's Dr. Jonathan Mann, former director of the Global Program on AIDS, [has] proposed a patent-incentive program for vaccine development. Under the Mann plan, a company that develops an AIDS vaccine would donate patent rights to an international agency, such as WHO [the World Health Organization]. In exchange, the company would receive a transferable right to a 10-year international patent extension on its most profitable, nonlifesaving drug, such as an acne cream.

Garrett, *supra* note 30, at 5.

³² As has been noted:

The demographics of who is getting AIDS is changing, shifting throughout the world to poorer populations. Vaccine manufacturers know that within 10 years the major purchasers of an AIDS vaccine will be the World Health Organization [WHO] and governments, not individuals. And that means . . . there will be strong pressure to keep costs low.

Garrett, *supra* note 11, at 5.

Further,

Dr. Roy Widdus of WHO's Global Program on AIDS said any vaccine that costs more than \$1 a person would be unaffordable.

When a hepatitis-B vaccine was developed in the United States, it cost \$100 a person. It took 15 years of international pressure to bring that cost to \$1 a person, Widdus said, 'and a lag time like that would be devastating in the case of AIDS.'

Garrett, *supra* note 30, at 5.

II. DILEMMAS FOR MANUFACTURERS DURING CLINICAL DEVELOPMENT: THE USE OF HUMAN SUBJECTS IN AIDS VACCINE TESTING

The technical hurdles associated with preclinical vaccine development have not impeded all progress toward an available HIV vaccine. Preliminary human trials with a vaccine produced by MicroGeneSys, Inc. began in September of 1987,³³ and since that time, testing of additional vaccine candidates has been proceeding in the United States and abroad.³⁴ As the development of an AIDS vaccine moves through the various phases of human testing, manufacturers will be attempting to design clinical protocols that favorably balance harms and benefits to participants. In so doing they will face two challenges: (1) applying the legal precepts of informed consent to potentially vulnerable human subject populations;³⁵ and (2) predicting the liability costs arising from failures to apply these precepts successfully.

The doctrine of informed consent was first articulated in an experimental context³⁶ in response to several cases of egregious

³³ See Fauci & Fischinger, *The Development of an AIDS Vaccine: Progress and Promise*, 103 PUB. HEALTH REP. 230, 234 (1988).

³⁴ See Cherfas, *Hope for AIDS Vaccines*, 246 SCI. 23, 23 (1989) (discussing promising preliminary data presented by the Chiron Corporation describing development of a "safe" vaccine which "induced T-cell immunity" in human volunteers); Cohen, *AIDS Vaccine Conference: Is "More" Better?*, 250 SCI. 369, 369 (1990) (describing the research and development status of AIDS vaccine research being conducted by Applied Biotechnology, Inc., Oncogen British Bio-Technology Group, Biocine, Genentech, Immune Response Corp., Cambridge Bioscience Corp., Connaught Laboratories, Ltd., MicroGeneSys, Inc., Molecular Vaccines, Replican Corp., and Viral Technologies, Inc.); Garrett, *supra* note 30, at 5 ("Ten different [AIDS] vaccine products are in clinical trials, and several more are being tested on animals.").

³⁵ "Human subject" means an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient." 21 C.F.R. § 56.102(21)(e) (1990).

³⁶ The doctrine was developed in medical malpractice law, but has been applied by analogy to clinical experimentation. This analogy is not perfect, however, and the requirements of informed consent may be even *more* compelling under experimental conditions. The salient differences between clinical experimentation and medical treatment have been described as follows:

In the investigator-subject relationship, the primary purpose is to gain knowledge; the direct benefit to the subject may be nil, minor, or even beneficial, but is in any case subsidiary. The investigator may or may not be a physician; the subject may or may not be a patient. . . . In the [investigator-subject relationship,] . . . the main objective is to secure knowledge; in the [physician-patient relationship,] . . . the welfare of the patient is the overriding consideration. . . . [T]he former relationship may be characterized as a scientific alliance

exploitation of clinical subjects.³⁷ Since that time, the doctrine has been widely accepted by the courts, incorporated into federal, state and international codes, and has become a bulwark of legal protection for individual autonomy³⁸ both in and out of the clinical research setting.³⁹

Blumgart, *The Medical Framework for Viewing the Problem of Human Experimentation*, 98 DAEDALUS 248, 255-56 (1969).

³⁷ See, e.g., T. BEAUCHAMP & J. CHILDRESS, PRINCIPLES OF BIOMEDICAL ETHICS 182-83, 276-77 (1979); Brandt, *Racism and Research: The Case of the Tuskegee Syphilis Study*, 8 HASTINGS CENTER REP. 21 (1978) (discussing a 40-year syphilis study which became public in the 1970s, in which black males with the disease were monitored but untreated, despite the availability of effective treatment during the final twenty years of the experiment).

³⁸ For a discussion of patient autonomy, see Shultz, *From Informed Consent to Patient Choice: A New Protected Interest*, 95 YALE L.J. 219, 220 (1985) (concluding that patient preferences generally ought to be controlling over other interests).

³⁹ The informed consent doctrine has been extensively addressed by courts and legislatures. See, e.g., Karp v. Cooley, 493 F.2d 408 (5th Cir. 1974); Mackey v. Procnunier, 477 F.2d 877 (9th Cir. 1973); Canterbury v. Spence, 464 F.2d 772 (D.C. Cir. 1972), cert. denied, 409 U.S. 1064 (1972); Bailey v. Lally, 481 F. Supp. 203 (D. Md. 1979); 21 U.S.C. § 355(a) (1982) (authorizing the FDA to approve any "new drug" experimentation using human subjects which involves interstate commerce); National Research Act of 1974, 42 U.S.C. § 289(a) (1985) (creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research which has authored ethical guidelines for human experimentation resulting in The Belmont Report); ALASKA STAT. § 09.55.556 (1983); CAL. HEALTH & SAFETY CODE §§ 24171-75 (West 1984); DEL. CODE ANN. tit. 18, § 6852 (1989); FLA. STAT. ANN. §§ 458.331(1)(u), 460.413(1)(t), § 768.46 (West 1981, 1986); HAW. REV. STAT. § 671-3 (1985); IDAHO CODE §§ 39-4301-39-4306 (1985); IOWA CODE ANN. § 147.137 (West 1989); KY. REV. STAT. ANN. §§ 304.40-320 (Michie/Bobbs-Merrill 1988); LA. REV. STAT. ANN. § 14:87.2 (West 1986); ME. REV. STAT. ANN. tit. 24, §§ 2905, 2905-A (1990); NEB. REV. STAT. § 44-2816 (1988); NEV. REV. STAT. § 41A.110 (1986); N.H. REV. STAT. ANN. §§ 507-C:1(III), 507-C:2(II) (1983); N.Y. PUB. HEALTH LAW §§ 2440-2446 (McKinney 1985); N.C. GEN. STAT. § 90-21.13 (1985); OHIO REV. CODE ANN. § 2317.54 (Anderson 1981); OR. REV. STAT. § 677.097 (1989); PA. STAT. ANN. tit. 35, §§ 6602-03 (Purdon 1985); R.I. GEN. LAWS § 9-19-32 (1985); UTAH CODE ANN. § 78-14-5 (1987); VT. STAT. ANN. tit. 12, § 1909 (Supp. 1985); VA. CODE ANN. §§ 37.1-234-37.1-241 (1984); WASH. REV. CODE ANN. §§ 7.70.050, 7.70.060 (Supp. 1990); 21 C.F.R. § 50.40-48 (1990) (protections pertaining to clinical investigations involving prisoners as subjects); 45 C.F.R. § 46.301-06 (1990) (additional protections pertaining to biomedical and behavioral research involving prisoners as subjects); *The Nuremberg Code* (1949) (adopted by the United Nations General Assembly on Dec. 11, 1946), reprinted in R. LEVINE, ETHICS AND REGULATION OF CLINICAL RESEARCH app. 3, at 285 (1981); *World Medical Association Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects* (adopted by 18th World Medical Assembly, Helsinki, Finland (1964), revised by 29th World Medical Assembly, Tokyo, Japan (1975)), reprinted in R. LEVINE, *supra*, app. 4, at 287.

Despite the foregoing provisions, recent developments suggest that there are some circumstances in which a waiver of the informed consent requirement can be justified.

Informed consent may embody a number of elements,⁴⁰ but generally requires that a research subject (or her authorized representative) be competent to agree voluntarily to a risk about which she is knowledgeable. Since it is the duty of the sponsor of a clinical trial to effectuate these requirements,⁴¹ lack of informed consent is likely to constitute the major factor leading to manufacturer liability during the course of vaccine trials.⁴²

On December 21, 1990, an interim rule was promulgated by the FDA, amending current informed consent regulations for American military personnel serving in the Persian Gulf. See *Informed Consent for Human Drugs and Biologics; Determination That Informed Consent Is Not Feasible*, 55 Fed. Reg. 52,814 (1990). The new rule allows U.S. troops to be given experimental drugs targeted against the chemical and biological weapons most likely to be deployed in military combat. According to the new provision, these drugs, none of which has yet been approved by the FDA for its proposed use, may be given to soldiers without their consent. See *id.* The new rule requires that the Defense Department request a waiver from the FDA for each drug or biologic sought to be administered. Waivers are to be granted on a case-by-case basis. See *id.*

The Defense Department received such waivers for the use of two drugs, and an unidentified soldier stationed in Saudi Arabia sought to enjoin their application. The District Court for the District of Columbia accepted the FDA justification for the interim rule that "certain military concerns may make obtaining informed consent from military personnel in combat impracticable." *Doe v. Sullivan*, 756 F. Supp. 12, 16 (D.D.C. 1991). The court denied the injunction of the drugs' application based on the military nature of the Defense Department decisions involved, which the court declined to second-guess. *Id.* at 17.

Public debate on the new policy has been vigorous, with opinions sharply divided. Some take a position recognizing both the difficulty of obtaining informed consent in the heat of battle and the need to protect adequately military personnel who could not be excused from their duties if they were able to exercise informed consent. See Gladwell, *Suit Filed to Block Use of Unapproved Drugs on U.S. Troops*, Wash. Post, Jan. 12, 1991, at A22, col. 1. Others question whether war is a sufficient justification for "the loss of normal protections that all citizens should have with respect to experimental drugs." Suplee, *FDA Consents To Use of Unapproved Drugs on U.S. Desert Troops*, Wash. Post, Dec. 22, 1990, at A10, col. 5 (quoting Arthur Caplan, director of the Center for Biomedical Ethics at the University of Minnesota).

⁴⁰ See 21 C.F.R. §§ 50.20-50.48 (1990); 45 C.F.R. § 46.116(a)-(b) (1990) (providing the general requirements for informed consent).

⁴¹ The regulations contain a broad definition of "sponsor," including an individual, pharmaceutical company, governmental agency, academic institution, private organization, or other organization. See 21 C.F.R. § 312.3(b) (1990). Under the regulations, the sponsor's duty to obtain informed consent is clear: "no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative." *Id.* § 50.20.

⁴² See generally Thompson, *Protecting 'Human Guinea Pigs'*, FDA CONSUMER, Dec.-Jan. 1987, at 15 (noting that while the "FDA does not require that subjects be compensated if there is injury or other untoward result . . . in any study that involves more than minimal risk, subjects must be told before they enter the study whether compensation and medical treatment will be provided and what that compensation

Given the manner in which modern courts have dealt with the informed consent issue in medical research, it is likely that breaches of the duty to obtain informed consent during either non-therapeutic or therapeutic research will be actionable under a negligence standard.⁴³ While this standard is lower than the strict liability standard that could exist for vaccine manufacturers who reach the market with their products,⁴⁴ a negligence standard may still be problematic.

First, it may be difficult for manufacturers to determine the appropriate type and amount of information that must be disclosed to subjects in order to meet the knowledge requirement.⁴⁵ Although federal regulations set out the elements of informed consent for federally funded experiments,⁴⁶ the regulations do not preempt applicable state or local laws.⁴⁷ Additionally, not all experiments will be federally funded, and therefore federal

will be or how to obtain information about it").

⁴³ See, e.g., *Cobbs v. Grant*, 8 Cal. 3d 229, 240, 502 P.2d 1, 8, 104 Cal. Rptr. 505, 512 (1972) (noting the trend toward categorizing the failure to obtain informed consent as negligence); *Trogun v. Fruchtman*, 58 Wis. 2d 596, 598-600, 207 N.W.2d 297, 312-13 (1973) (quoting Dean Prosser who observed that actions for the failure to obtain informed consent are properly viewed as negligence actions).

To prevail under a theory of negligence, a plaintiff must prove the existence of four factors: (1) a legal duty of the defendant that must be fulfilled in accordance with an established standard; (2) a breach of that duty; (3) injury, damage, or loss suffered by the plaintiff; and (4) a causal nexus between the defendant's breach of duty, and the injury, damage or loss sustained by the plaintiff. See RESTATEMENT (SECOND) OF TORTS § 4 (1965).

Some courts, however, do still occasionally use other methods of analysis when dealing with these cases. See, e.g., *Spikes v. Heath*, 175 Ga. App. 187, 332 S.E.2d 889 (1985) (applying a fraud standard); *Cardwell v. Bechtol*, 724 S.W.2d 739, 750 (Tenn. 1987) (noting that the failure to provide adequate informed consent "is not negligence but battery").

⁴⁴ See *infra* notes 70-83 and accompanying text.

⁴⁵ The "knowledge" requirement demands more than the mere provision of information—the information provided must be understood. See *Reyes v. Wyeth Laboratories*, 498 F.2d 1264, 1270, cert. denied, 419 U.S. 1096 (1974) (noting that language and educational barriers may have impinged upon the plaintiff's ability to give informed consent); *Corn v. French*, 71 Nev. 280, 284-85, 289 P.2d 173, 175-76 (1955) (recognizing that although the patient had signed a consent form for the procedure, she had failed to understand the meaning of the word "mastectomy"); see also *Rutenberg, Clearer Medical Consent Forms Needed*, UPI, Nov. 18, 1983 (LEXIS, Nexis library, UPI file) (stating that Veterans Administration researchers found that "efforts to protect the rights of research subjects through federal regulations have resulted in . . . [information] but [have not] ensur[ed] that the information is comprehensible, understood, and used").

⁴⁶ See 45 C.F.R. § 46.101(a) (1990); 30 Fed. Reg. 18,914 (1974).

⁴⁷ See 21 C.F.R. § 50.25(c) (1990); 45 C.F.R. § 46.116(c) (1990).

informed consent regulations premised on federal funding may not apply.⁴⁸ Since federal regulations may be neither applicable nor controlling, the knowledge requirement may be significantly determined by statutes that speak to the issue of informed consent and articulate specific disclosure standards. The doctrine of informed consent, as developed with regard to patient procedures generally, indicates that there will be subtle yet significant jurisdictional distinctions as to whether the appropriate standard of disclosure is: (1) information that a reasonable investigator would disclose;⁴⁹ (2) information that a reasonable subject would want to know;⁵⁰ (3) information about which the individual subject involved in testing would wish to be apprised;⁵¹ or (4) information that a reasonable subject with the characteristics of the individual involved in testing would wish to know.⁵²

Second, it may be difficult for manufacturers to satisfy the requirement of voluntariness⁵³ as they attempt to provide legally adequate informed consent to the selected subjects. The selection of subjects has already focused on one of several high-risk populations.⁵⁴ Certain high-risk populations—intravenous drug users, HIV-infected women and men, partners of infected individuals (including prostitutes), and prisoners or mentally incompetent subjects who fall into the foregoing categories—are probably the

⁴⁸ For instance, California has already stimulated the process of AIDS vaccine development by enacting legislation that will permit human trials within the state *without federal authorization*. See *infra* text accompanying notes 196-209.

⁴⁹ See, e.g., *Karp v. Cooley*, 493 F.2d 408, 419 n.11 (5th Cir.) (discussing the majority rule which compels a physician to disclose facts which a reasonable medical practitioner under similar circumstances would have disclosed to her patient regarding the proposed treatment), *cert. denied*, 419 U.S. 845 (1974).

⁵⁰ See, e.g., *Canterbury v. Spence*, 464 F.2d 772, 788 (D.C. Cir.) (finding no duty to disclose dangers of which the person of average sophistication would be aware), *cert. denied*, 409 U.S. 1064 (1972).

⁵¹ See, e.g., *Scott v. Bradford*, 606 P.2d 554, 558 (Okla. 1979) (stating that a physician may withhold disclosure where it would alarm an emotionally upset or apprehensive patient).

⁵² See, e.g., *Fain v. Smith*, 479 So. 2d 1150, 1155 (Ala. 1985) (using the "reasonable person with all of the characteristics of the plaintiff, including his idiosyncracies and religious beliefs").

⁵³ Voluntariness exists when persons are able to "exercis[e] choice about an action free of coercion or undue influence by another person." T. BEAUCHAMP & J. CHILDRESS, *supra* note 37, at 81.

⁵⁴ See Novick, *Clinical Trials with Vulnerable or Disrespected Subjects*, 4 AIDS & PUB. POL'Y J. 125, 129 (1989) (noting that medical scientists involved in planning initial vaccine trials have reportedly suggested that gay men were the appropriate subjects because "their physiology has been altered as a result of their lifestyle and because they will be the first to benefit from an effective vaccine").

least likely to have the capacity to withstand coercion or undue influence.⁵⁵ Many individuals within high-risk, or otherwise suspect subpopulations often lack: (1) access to a public forum where they can voice their grievances; (2) adequate medical knowledge to question the quality⁵⁶ and effects of their experimental treatment; (3) adequate legal knowledge to bring lawsuits seeking compensation for research related injuries; and (4) either the physical⁵⁷ or financial⁵⁸ willpower to resist the temptation to agree to experimentation in exchange for monetary reimbursement or the promise of a "cure."

⁵⁵ See *id.* at 126-28. Scientists also appear to be enthusiastic about recruiting other suspect populations to the vaccine testing effort: Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID), stated that "NIAID hopes especially to enroll more blacks [and] Hispanics, . . . groups [that] . . . have been 'underrepresented' in clinical trials." *Clinical Trials Hotline Open; Patients Sought for Studies*, AIDS POL'Y & LAW, May 17, 1989, at 5; see also Green, *The Transmission of AIDS*, in AIDS AND THE LAW 28, 32, 303 n.38 (H. Dalton & S. Burris eds. 1987) ("A disproportionately high percentage of AIDS patients are black largely because disadvantaged groups are more likely to fall victim to the abuse of drugs.").

⁵⁶ For example, AIDS vaccine trials currently underway are based on the least common strain of the AIDS virus and may be of limited therapeutic value. See Garrett, *supra* note 11, at 5 ("All of the vaccines currently being used on hundreds of human volunteers in the United States are based on a strain of the human immunodeficiency virus called HTLVIIIb. . . . [This strain] is one of the least common of what may be hundreds of AIDS viruses found in nature").

The therapeutic nature of clinical trial Phases II-IV also results in patients' inability to adequately assess the quality of their treatment. Randomized, double-blind, controlled clinical trials (RCCT) will have to be conducted to evaluate the therapy of choice for a uniformly fatal disease. In an RCCT, neither the patient nor the investigator is told whether the patient is receiving a placebo or one of two or more alternate therapy regimens. Patients must be randomly allocated to treatment regimens, in order to correctly attribute pharmacodynamic effects to the vaccine under study. With a disease such as AIDS which appears to be uniformly fatal, grave questions are raised as to the ethical appropriateness of giving a trial group a placebo or a toxic or ineffective control vaccine. Further, since the RCCT may provide the only access to curative therapy, the participation of patients who have no alternatives to a Phase IV trial may be coerced. It would appear that the demands of RCCT's are not easily reconciled with the requirements for informed consent. See generally Levine, *The Apparent Incompatibility Between Informed Consent and Placebo-Controlled Clinical Trials*, 42 CLINICAL PHARMACY & THERAPY 247 (1987); Macklin & Friedland, *Aids Research: The Ethics of Clinical Trials*, 14 LAW MD. & HEALTH CARE 273 (1986).

⁵⁷ The alternatives to participation in research are often nonexistent for critically ill patients. See Scott, *'Freeze' on Drug Testing Feared; Clinical Trials Under Attack on Many Fronts*, L.A. Times, June 12, 1989, at 1, col. 3.

⁵⁸ "There are many reasons why people volunteer to be human guinea pigs for research projects, but money remains the drawing card for many, who can make \$50 or \$60 for giving blood or undergoing painful tests." UPI, Dec. 27, 1982 (LEXIS, Nexis library, UPI file).

Beyond the issue of voluntariness, there are a number of reasons why the use of high-risk subpopulations in nontherapeutic clinical trials may not permit proper characterization of vaccine effects.⁵⁹ Despite these reasons, a number of rationales have been put forth to justify the recruitment of these individuals. One explanation is that male homosexuals "would be one of the top choices to participate in a vaccine trial because of their well-recognized compliance in clinical trials, such as the trial of a vaccine for hepatitis."⁶⁰ Another rationale stems from the concern that despite confidentiality protections, participation in clinical trials may identify volunteers as being at high risk for HIV infection, due to their "lengthy period of interaction with investigators."⁶¹ Ostensibly, the stigma of being identified as an HIV-infected individual is more easily borne by members of subpopulations in which the rates of HIV infection are higher. A third suggestion is that trial data will have greater relevance if there is a chance that participants will engage in high-risk behavior and thereby challenge the vaccine: if the volunteers' immunological profile remained unaffected after continued high-risk behavior, this would serve as striking evidence of a vaccine's efficacy.⁶² Finally, a more suspicious justification may favor the selection of high-risk subpopulations for clinical trials; namely, that less vulnerable individuals are unwilling to assume the risks of participation in AIDS vaccine trials.⁶³ These factors may manipulate the exercise of free

⁵⁹ First, it will be difficult to make safety determinations as to whether an HIV infection that progresses to AIDS is a vaccine-related phenomenon or the result of a latent infection that occurred prior to the onset of the trial. See Wright, *Flying Blind*, 258 SCI. AM. 35, 36 (1988). Second, it may not be relevant to use data generated from high-risk populations to predict the severity of vaccine-associated disease in the general population, since there is a risk that prior infection may have compromised the immune response of a high-risk volunteer. See Novick, *supra* note 54, at 130.

⁶⁰ *Development*, *supra* note 4, at 374 (1989) (citation omitted).

⁶¹ Mariner & Gallo, *Getting to Market: The Scientific and Legal Climate for Developing an AIDS Vaccine*, 15 LAW, MEDICINE & HEALTH CARE 17, 20 (1987).

⁶² See Rothman, *Ethical and Social Issues in the Development of New Drugs and Vaccines*, 63 BULL. N.Y. ACAD. MED. 557, 565 (1987).

⁶³ Until recently, no acceptable animal model, computer model, or in vivo model existed in which to demonstrate the probable efficacy of an AIDS vaccine. See *supra* note 11. This meant that ongoing Phase I testing was being conducted without the rudimentary protections provided by animal safety data. As one investigator rather callously noted:

People will say you shouldn't do a vaccine trial because we haven't shown it's a system that works in the monkeys with SIV or the SCID mice or whatever. I'll ask from now until that happens how many hundreds or

choice by high-risk subpopulations and undermine the legitimacy of their participation as informed volunteers in clinical trials.⁶⁴

As investigators try to appraise the efficacy of the vaccines currently available, "applications for human testing of experimental vaccines are piling up at the FDA"⁶⁵ In designing clinical trial protocols, manufacturers must acknowledge the vulnerability of potential subjects, and determine how to implement safeguards for their protection while still keeping access to trials as equitable as possible.⁶⁶ In light of the risks that volunteers will be asked to

thousands of people will be infected with HIV while we do animal studies What do we lose? If the vaccine is toxic, we made a major mistake, we hurt a lot of people. Well, that's a danger of clinical research. People who volunteer accept that risk—that's what it's all about.

Garrett, *supra* note 11, at 5.

It is noteworthy that even N.I.H. scientists have taken themselves out of the pool of potential experimental subjects:

Despite the rich tradition of scientists' trying new vaccines on themselves . . . N.I.H. scientists conducting the AIDS vaccine experiments have decided against this.

[One researcher] said in an interview that the decision against self-experimentation was not because of any unwillingness on the researchers' part to share the risks they are asking other people to take. Rather, he said they ruled it out in the belief that scientists conducting a human experiment, and thus emotionally involved, could not be objective in giving informed consent on themselves. He cited another reason: some of the researchers might feel pressure from superiors and others to agree to be vaccinated.

Altman, *The Doctor's World; Protecting Volunteers in AIDS Vaccine Test*, N.Y. Times, Aug. 25, 1987, at C1, col. 5.

⁶⁴ Despite these vulnerabilities, it would be incorrect to assume that benefits are nonexistent for individual members of these populations. See Scott, *Medicine; On Trial*, L.A. Times, Oct. 7, 1990, Magazine, at 60 (stating that patients get early access to promising treatments and sophisticated medical care).

⁶⁵ Wright, *supra* note 59, at 36.

⁶⁶ Institutions receiving federal research monies are provided with the limited safeguard of oversight committees, called Institutional Review Boards, or IRB's. An IRB is required by regulation to review all clinical experimentation involving human subjects. See 21 C.F.R. § 56.107 (1990); Scanlon, *Experiment Safeguards; Research review Boards Weigh the Benefits and Risks*, Newsday, Mar. 28, 1989, at 15. But see Rothman, *supra* note 62, at 558 ("[S]everal studies indicate serious weaknesses in institutional review board operations; there are significant variations in the diligence with which boards perform their assignments and in the substantive decisions that they make. . . . [A]n investigator who is dissatisfied or impatient with board decisions at one institution can move his research to another."). Most state statutes, however, do not have an IRB requirement.

One area where IRB's might constructively impact future testing efforts is in expanding access to clinical trials. Inequitable access is not only discriminatory, it may also have a significant impact on the validity of data subsequently accumulated. See Roan, *Sex, Ethnic Bias in Medical Research Raises Questions*, L.A. Times, Aug. 3,

take,⁶⁷ this effort must be made by the manufacturers who stand to profit from their participation.

III. LEGAL ROADBLOCKS IN THE MARKETPLACE: THE IMPOSITION OF TORT LIABILITY ON VACCINE MANUFACTURERS

Despite scrupulous attention to vaccine preparation and testing, manufacturers may still face tort liability exposure once products reach the marketplace. The specter of liability has already forced many manufacturers of childhood vaccines out of the marketplace,⁶⁸ threatening a large sector of society with the risk of preventable diseases. To avoid a similar situation in the AIDS context, vaccine manufacturers must have some degree of insulation from civil tort actions.

A. *Applicable Theories of Liability*

It is most likely that persons seeking compensation from AIDS vaccine manufacturers will advance a legal theory of either strict liability or negligence.⁶⁹ Strict liability is distinguished from negligence in that the former doctrine attaches without proof of fault by the manufacturer.⁷⁰ It does not require that plaintiffs "impugn the conduct of the maker or other seller[,] but [they are] required to impugn the product."⁷¹ The doctrine of strict liability is of continuing vitality in most states.⁷² Underlying its application

1990, at A1, col. 1.

⁶⁷ See Mariner & Gallo, *supra* note 61, at 20 (noting that participation may have detrimental effects on employment, insurance coverage, and social life).

⁶⁸ See *infra* text accompanying note 78.

⁶⁹ Although these are the most likely theories on which a cause of action will be based, manufacturers may also be sued for misrepresentation, misbranding, mispackaging, breach of contract, or under the theories of alternative liability, concert of action, industry-wide liability, or market share liability. For a comprehensive review of medical products liability law, see Maedgen & McCall, *A Survey of Law Regarding the Liability of the Manufacturers and Sellers of Drug Products and Medical Devices*, 18 ST. MARY'S L.J. 395, 397-428 (1986) (explaining the various theories of liability to which manufacturers may be subjected).

⁷⁰ See *supra* note 43 (discussing the four elements that the plaintiff must prove in order to prevail on a negligence theory).

⁷¹ W. PROSSER, D. DOBBS, R. KEETON & D. OWEN, *PROSSER & KEETON ON THE LAW OF TORTS*, § 99, at 695 (5th ed. 1984).

⁷² Most states have adopted some form of the strict liability doctrine as it is set forth in the *Restatement (Second) of Torts*. See *id.* at 694. Section 402A of the *Restatement* provides:

(1) One who sells any product in a defective condition unreasonably dangerous to the user or consumer or to his property is subject to liability

are a number of policy considerations which find their genesis in Judge Traynor's concurring opinion in *Escola v. Coca Cola Bottling Co.*⁷³ First, "manufacturer[s] can anticipate some hazards and guard against the recurrence of others, [whereas] the public cannot."⁷⁴ Second, manufacturers should be deterred from bringing defective products to the marketplace.⁷⁵ Third, manufacturers are best situated to insure against a product's risk and distribute such costs to consumers.⁷⁶

Weighing against strict liability is a fear that the development and production of valuable products will be curtailed if manufacturers find that they are being used as "deep pockets" to compensate victims for all unforeseeable product-related injuries. While urging his colleagues to support the establishment of uniform federal rules for product liability,⁷⁷ one senator noted,

Manufacturers, whose survival depends on narrow margins and, consequently, close control of costs, are confronted with one

for physical harm thereby caused to the ultimate user or consumer, or to his property, if

- a) the seller is engaged in the business of selling such a product, and
- b) it is expected to and does reach the user or consumer without

substantial change in the condition in which it is sold.

(2) The rule stated in Subsection (1) 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.

RESTATEMENT (SECOND) OF TORTS § 402A (1965).

⁷³ 24 Cal. 2d 453, 150 P.2d 436 (1944).

⁷⁴ *Id.* at 462, 150 P.2d at 440-41.

⁷⁵ *See id.*

⁷⁶ *See id.* The Supreme Court of New Jersey has also recognized this argument:

[T]he manufacturers and distributors of defective products can best allocate the costs of the injuries resulting from those products. The premise is that the price of a product should reflect all of its costs, including the cost of injuries caused by the product. This can best be accomplished by imposing liability on the manufacturer and distributors. Those persons can insure against liability and incorporate the cost of the insurance in the price of the product.

Beshada v. Johns-Manville Products Corp., 90 N.J. 191, 205-6, 447 A.2d 539, 547 (1982). But see Berger, *The Impact of Tort Law Development on Insurance: The Availability/Affordability Crisis and Its Potential Solutions*, 37 AM. U.L. REV. 285 (1988) (discussing how the declining predictability of liability assignments in the courts has threatened to obliterate the ability of manufacturers and insurers to spread their risk efficiently).

⁷⁷ *See infra* notes 165-68 and accompanying text.

great unknowable cost: Their liability for legal claims against them. . . .

The rise in product liability costs and the threat of litigation have forced many manufacturers to withdraw useful products from the market and to cancel the research and development of new, innovative and, at times, life-saving products. . . . Lederle Laboratories is now the sole U.S. manufacturer of the DPT vaccine for polio. Merck & Co. is the only producer of the combined measles, mumps and rubella vaccine. All others have left the field due to the threat of product liability lawsuits.⁷⁸

Acknowledging the public's interest in the development and availability of prescription drugs and vaccines, the drafters of section 402A carved out an exception for "unavoidably unsafe" products.⁷⁹ The application of comment k requires that the manufacturer has "properly prepared and marketed and [given] proper warning"⁸⁰ for the product in question. If the manufacturer has satisfied these preconditions, it will be exempt from strict liability, provided the product in question is unavoidably unsafe.⁸¹ Underlying the comment k exemption are two significant policy rationales. First, many products may not be able to be made safe for their intended and ordinary use:

Such a product, properly prepared, and accompanied by proper directions and warnings is not defective, nor is it *unreasonably* dangerous [T]he seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, where 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.⁸²

Second, society's need for certain products is of such magnitude that the manufacturers of those products should not be subject to strict liability, despite the fact that consumers may be injured by the use of their products.⁸³

⁷⁸ 136 CONG. REC. S16,661 (daily ed. Oct. 25, 1990) (statement of Sen. Heinz).

⁷⁹ For an overview of the history of section 402A, see 41 A.L.I. PROC. 349 (1964); Comment, *An Escape from Strict Liability: Pharmaceutical Manufacturers' Responsibility for Drug-related Injuries under Comment k to Section 402A of the Restatement (Second) of Torts*, 23 DUQ. L. REV. 199, 201-02 (1984).

⁸⁰ RESTATEMENT (SECOND) OF TORTS § 402A comment k (1965).

⁸¹ See *id.*

⁸² *Id.*

⁸³ Although this justification is not explicitly set forth in comment k, it is

B. *Judicial Application of Comment k to Pharmaceutical Products*

A majority of jurisdictions have adopted comment k⁸⁴ and have recognized its particular relevance to prescription drugs and vaccines.⁸⁵ However, as one court pointed out, "[s]imple adoption of Comment k does not solve the problems associated with its application."⁸⁶ Indeed, judicial application of comment k has been

exemplified by concerns voiced prior to the drafting of the comment:

During a rather confusing discussion of a draft of what was to become section 402A, a member of the institute proposed that drugs should be exempted from strict liability on the ground that it would be "against the public interest" to apply the doctrine to such products because of "the very serious tendency to stifle medical research and testing." Dean Prosser . . . responded that the problem was a real one, and that he had it in mind in drafting section 402A. A motion to exempt prescription drugs from the section was defeated on the suggestion of Dean Prosser that the problem could be dealt with in the comments to the section.

Brown v. Superior Ct., 44 Cal. 3d 1049, 1058, 751 P.2d 470, 475, 245 Cal. Rptr. 412, 416 (1988) (citations omitted); see also Schwartz, *Unavoidably Unsafe Products: Clarifying the Meaning and Policy Behind Comment k*, 42 WASH. & LEE L. REV. 1139, 1141 ("Society wishes to encourage the manufacture of ethical drugs, and the research and development of new drugs. The imposition of strict liability would stifle these goals.").

⁸⁴ See, e.g., *Brooks v. Medtronic, Inc.*, 750 F.2d 1227, 1230-31 (4th Cir. 1984) (stating that certain products, particularly ethical drugs which often cause unwanted side effects despite careful design and manufacturing, are deemed "unavoidably unsafe," but are not unreasonably dangerous if they are marketed with proper directions for use or include adequate warnings of potential side effects); *Basko v. Sterling Drug, Inc.* 416 F.2d 417, 426 (2d Cir. 1969) (holding that a manufacturer who supplies the public with an "apparently useful and desirable product, attended with a known but apparently reasonable risk" is subject only to the "ordinary negligence concept of duty to warn"); *Stone v. Smith, Kline & French Laboratories*, 447 So. 2d 1301, 1304 (Ala. 1984) (holding that with regard to "unavoidably unsafe," yet properly prepared prescription drugs, the adequacy of the warning determines whether the marketed drug is defective or unreasonably dangerous); *Moore v. Vanderloo*, 386 N.W.2d 108, 117 (Iowa 1986) (requiring proper warnings and directions for use); *Johnson v. American Cyanamid Co.*, 239 Kan. 279, 285-86, 718 P.2d 1318, 1323 (1986) (holding that the mere manufacture of a vaccine will not be actionable on the ground of design defect), *aff'd*, 243 Kan. 291, 758 P.2d. 206 (1988); *Payton v. Abbott Labs*, 386 Mass. 540, 571-72, 437 N.E.2d 171, 189 (1982) (stating that public policy dictates rejecting strict liability in favor of negligence for drug-related injuries).

⁸⁵ See Schwartz, *supra* note 83, at 1141 (stating that "[w]hile comment k could be read to apply to other [nonpharmaceutical] products, it does not really give us any examples or suggest other areas where the policy balancing is precisely the same"). Note that comment k is generally not thought to embrace proprietary drugs. See *Torsiello v. Whitehall Laboratories*, 165 N.J. Super. 311, 321 n.3, 398 A.2d 132, 137 n.3 (1979) (distinguishing aspirin from products that may produce an adverse effect when taken as recommended).

⁸⁶ *Patten v. Lederle Laboratories*, 676 F. Supp. 233, 235 (D. Utah 1987).

inconsistent. Generally, courts have chosen one of two approaches: when faced with evidence that a pharmaceutical product, properly prepared and used according to the manufacturers' directions, resulted in injury to a plaintiff, they have defined the scope of comment k protection in either an expansive or a restrictive manner. An expansive application of the exception grants all prescription drugs the status of "unavoidably unsafe" products, and thereby exempts the manufacturers of all such products from strict liability based on alleged design defects in their products.⁸⁷ A restrictive application of the exception favors greater scrutiny of individual products before determining that a product is "unavoidably unsafe," and evaluates the importance of one or more of three determinants, namely, (1) whether the risk of the product foreseeably outweighs its utility;⁸⁸ (2) whether the product could have been designed in a safer manner;⁸⁹ and (3) whether feasible alternatives for the product exist.⁹⁰ A sampling of recent decisions illustrates both of these trends.

1. Expansive Application of Comment k

*Fellows v. USV Pharmaceutical Corp.*⁹¹ involved a challenge to the manufacturer of Doriden, a prescription drug for insomnia. After reviewing the plaintiff's strict liability claim, the Maryland district court granted immunity to the manufacturer on the basis of the blanket protection provided by comment k.⁹² The court noted that "prescription drugs are not considered unusually dangerous under section 402A, and the manufacturer will not incur liability under that section, unless the manufacturer has failed to provide adequate warnings of the drug's possible dangers."⁹³

Although apparently reaching the same conclusion as the *Fellows* court, the Kansas Supreme Court did not explicitly state its preference for an expansive application of comment k to all

⁸⁷ See *infra* notes 91-111 and accompanying text.

⁸⁸ See *infra* notes 113-32 and accompanying text.

⁸⁹ See *infra* notes 133-35 and accompanying text.

⁹⁰ See *infra* notes 136-41 and accompanying text.

⁹¹ 502 F. Supp. 297 (D. Md. 1980).

⁹² See *id.* at 300.

⁹³ *Id.* At least one of the cases to which the court claimed to have looked for guidance had not read comment k in quite so expansive a fashion. See *infra* text accompanying notes 113-19 (discussing *Reyes v. Wyeth Laboratories, Inc.*, 498 F.2d 1264 (5th Cir.), *cert. denied*, 419 U.S. 1096 (1974)).

pharmaceutical products. In *Johnson v. American Cyanamid Co.*,⁹⁴ the Kansas court secured immunity for a polio vaccine manufacturer by summarily concluding that because the product at issue was "an 'unavoidably unsafe product' that [was] an 'apparently useful and desirable product, attended with a known but apparently reasonable risk' . . . [p]ublic policy require[d] that the mere manufacture of the vaccine not be actionable on the ground of design defect."⁹⁵ While admonishing the trial court for its failure to hear evidence on the issue of the application of comment k "outside the presence of the jury and [making] the determination thereon,"⁹⁶ the supreme court chose not to identify any particular factors that the trial court might have considered in making this determination as a matter of law. This decision has been interpreted as signifying the court's belief that vaccines automatically fall within the scope of comment k's protections.⁹⁷

In *Morris v. Parke, Davis & Co.*,⁹⁸ a California district court rejected the plaintiff's efforts to proceed against manufacturers of the Diphtheria-Pertussis-Tetanus (DPT) vaccine on the basis of strict liability for defective design. In a brief discussion which foreshadowed a later pivotal decision by the Supreme Court of California,⁹⁹ the district court recognized the "automatic application of comment k to vaccine and prescription drug cases, and the resulting foreclosure of design defect strict liability [claims]"¹⁰⁰ Although the court dismissed the plaintiff's design defects claim, it did permit

⁹⁴ 239 Kan. 279, 718 P.2d 1318 (1986).

⁹⁵ See *id.* at 286, 718 P.2d at 1323.

⁹⁶ *Id.*

⁹⁷ See *Patten v. Lederle Laboratories*, 676 F. Supp. 233, 236 (D. Utah 1987) (citing *Johnson* as support for the proposition that "[s]ome courts have taken the view that Comment k applies to all design defect claims involving prescription drugs as a matter of law.") But see *Graham v. Wyeth Laboratories*, 666 F. Supp. 1483, 1494-98 (D. Kan. 1987), *rev'd*, 906 F.2d 1399 (10th Cir. 1990), *cert. denied*, 111 S. Ct. 511 (1990). In *Graham*, the defendant, a manufacturer of the DPT vaccine, argued that based on *Johnson*, Kansas had adopted the expansive application of comment k, and had thereby freed vaccine manufacturers from liability for design defects as a matter of law. The district court rejected this interpretation of *Johnson*, stating that in its view, "the *Johnson* decision is not—nor is it intended to be—so far reaching." *Id.* at 1496. The court of appeals found the *Johnson* opinion "unclear" as to whether "the comment (k) defense precludes a strict liability design defect claim as a matter of law in all cases involving licensed prescription vaccines," and therefore chose to leave the district court's interpretation undisturbed. *Graham*, 906 F.2d at 1406.

⁹⁸ 667 F. Supp. 1332 (C.D. Cal. 1987).

⁹⁹ See *Brown v. Superior Court*, 44 Cal. 3d 1049, 751 P.2d 470, 245 Cal. Rptr. 412 (1988); *infra* text accompanying notes 102-10.

¹⁰⁰ *Morris*, 667 F. Supp. at 1334, n.1.

him to pursue a claim of strict liability for manufacturing defects, noting that comment k did not shield manufacturers from such claims.¹⁰¹

Similarly, in *Brown v. Superior Court*,¹⁰² the Supreme Court of California agreed with an expansive interpretation of comment k that had been articulated in the pretrial rulings of the trial court.¹⁰³ In its appellate review, the supreme court analyzed the purposes for which the comment k exemption was implemented,¹⁰⁴ the alternatives to a blanket immunity approach,¹⁰⁵ and the routine application of comment k in other courts,¹⁰⁶ and concluded that comment k should exempt manufacturers of prescription drugs from strict liability arising from claims alleging the defective design of their products.¹⁰⁷ Although acknowledging the appeal of a more restrictive application of comment k (i.e., one that would seek to evaluate pharmaceutical products on a case-by-case basis),¹⁰⁸ the supreme court recognized that such an application would place manufacturers in a legal quandary,¹⁰⁹ and

¹⁰¹ The court provided a helpful analysis of the distinctions between the two types of defects:

A product has a "manufacturing defect" if and only if the product caused a plaintiff's injury because it deviated from the manufacturer's intended result or from other ostensibly identical units of the same product line.

In contrast, in the case of a design defect the injury producing agent is common to all products of a certain line, and the defect lies in the original design or model. A product has a design defect if and only if: (a) the plaintiff establishes that the product failed to perform as safely as an ordinary consumer would expect when used in an intended or reasonably expected manner, or (b) the plaintiff proves that the product's design proximately caused his injury and the defendant fails to prove that, on balance, the benefits of the challenged design outweigh the risk or danger inherent in such design.

Id. at 1335 (citations and footnotes omitted).

¹⁰² 44 Cal. 3d 1049, 751 P.2d 470, 245 Cal. Rptr. 412 (1988).

¹⁰³ *See id.* at 1055, 751 P.2d at 473, 245 Cal. Rptr. at 415. The trial court "determined that defendants could not be held strictly liable for the alleged defect in DES but only for their failure to warn of known or knowable side effects of the drug." *Id.*

¹⁰⁴ *See id.* at 1058-59, 751 P.2d at 475, 245 Cal. Rptr. at 416-17.

¹⁰⁵ *See id.* at 1060-61, 751 P.2d at 477, 245 Cal. Rptr. at 418.

¹⁰⁶ *See id.* at 1059-60, 751 P.2d at 476, 245 Cal. Rptr. at 417-18.

¹⁰⁷ *See id.* at 1065, 751 P.2d at 480, 245 Cal. Rptr. at 421.

¹⁰⁸ *See id.* at 1067, 751 P.2d at 481, 245 Cal. Rptr. at 423 ("It seems unjust to grant the same protection from liability to those who gave us thalidomide as to the producers of penicillin.").

¹⁰⁹ As the court noted,

A manufacturer's incentive to develop what it might consider a superior product would be diminished if it might be held strictly liable for harmful

would also impede "significant advances in scientific knowledge, discouraging the development of new and improved drugs to combat disease."¹¹⁰

The view that manufacturers of prescription pharmaceuticals should be exempt from strict liability has not been consistently adopted by all courts. The following cases illustrate a divergent trend to remove the protective blanket of immunity from such manufacturers, and instead use a restrictive application of comment k that requires the case-by-case evaluation of pharmaceutical products.

As a review of these cases will indicate, the restrictive application of comment k is often problematic. In addition to the lack of uniformity among courts regarding the factors to be considered in determining whether comment k is applicable, it also may not be clear whether it is the judge or the factfinder who should apply any test that is developed.¹¹¹

side effects because a trial court could decide . . . that in fact another product which was available on the market would have accomplished the same result. Further, the question of the superiority of one drug over another would have to be decided not in the abstract but in reference to the plaintiff, since the advantages of a drug cannot be isolated from the condition of a particular patient. . . . [D]ifferent trial judges might reach different conclusions as to whether the same drug should be measured by strict liability principles, because the determination in each case depends on the evidence as well as the subjective determination of the judge.

Id. at 1067-68, 751 P.2d at 482, 245 Cal. Rptr. at 423.

¹¹⁰ *Id.* at 1066, 751 P.2d at 481, 245 Cal. Rptr. at 422.

¹¹¹ For a discussion of whether the judge or the jury determines comment k applicability, see *Toner v. Lederle Laboratories*, 112 Idaho 328, 732 P.2d 297 (1987) (*infra* note 121); *Senn v. Merrell-Dow Pharmaceuticals, Inc.*, 305 Or. 256, 751 P.2d 215 (1988) (*infra* note 127); *Johnson*, 239 Kan. 279, 718 P.2d 1318 (*supra* text accompanying notes 94-97); *Brown*, 44 Cal. 3d 1049, 751 P.2d 470, 245 Cal. Rptr. 412 (*supra* note 109); see also *Graham v. Wyeth Laboratories*, 906 F.2d 1399 (10th Cir. 1990), *cert. denied*, 111 S. Ct. 511 (1990). Here, the appeals court declined to state that the district court had abused its discretion by not holding a "mini-trial" in order to determine the application of comment k. The court noted that "mini-trials can result in 'undue delay, waste of time, and needless presentation of cumulative evidence.'" *Id.* at 1405 n.10 (quoting *Moe v. Avions Marcel Dassault-Breguet Aviation*, 727 F.2d 917, 935 (10th Cir. 1987)). The lower court had concluded that the comment k assessment was one for the court to make, but one that could be made in the presence of the jury since the evidence "will be the same evidence from which the jury will determine negligence." *Graham*, 666 F. Supp. 1483, 1498 (D. Kan. 1987), *rev'd*, 906 F.2d 1399 (10th Cir. 1990), *cert. denied*, 111 S. Ct. 511 (1990).

2. Restrictive Application of Comment k

In restrictively applying comment k, courts have identified one or more of three requisites that must be established before it can be determined that a product is unavoidably unsafe, and its manufacturer deserving of protection from strict liability design defect claims.¹¹² Each of these will be considered in turn below.

a. *Whether the Risk of the Product Forseeably Outweighs Its Utility*

*Reyes v. Wyeth Laboratories*¹¹³ typifies the early case law developing a risk versus benefit balancing test for the analysis of liability claims involving prescription drugs.¹¹⁴ In *Reyes*, the Fifth Circuit adopted such a test for a manufacturer of the Sabin oral polio vaccine. Although the court recognized the unavoidably unsafe nature of the vaccine, it chose to consider whether the vaccine was "so unsafe that marketing it at all [was] 'unreasonably dangerous per se.'"¹¹⁵ On balance, the court found that the "legitimate public interest in [the vaccine's] availability" outweighed its risks.¹¹⁶

Continuing its risk/benefit analysis, the *Reyes* court also considered whether the vaccine had been "introduced into the stream of commerce without sufficient safeguards."¹¹⁷ Concluding that the manufacturer had not met its duty to warn individual consumers about the risk posed by the vaccine, the court found the this failure "itself present[ed] a 'defect' in the product . . . [that] cause[d] the product to be 'unreasonably dangerous as marketed.'"¹¹⁸ The manufacturer was held strictly liable for this so-called design defect.¹¹⁹

Similarly, in *Toner v. Lederle Laboratories*,¹²⁰ the Idaho Su-

¹¹² See *supra* notes 88-90 and accompanying text.

¹¹³ 498 F.2d 1264 (5th Cir.), *cert. denied*, 419 U.S. 1096 (1974).

¹¹⁴ See also *Davis v. Wyeth Laboratories, Inc.*, 399 F.2d 121 (9th Cir. 1968). This opinion preceded *Reyes* and likewise held that the Sabin oral polio vaccine was an unavoidably unsafe product qualifying for comment k treatment, since "on balance, public interest demands that it be made available notwithstanding its dangerous characteristics." *Id.* at 128. Regardless, the court found the manufacturer strictly liable because it had failed adequately to warn individual consumers of the risks associated with the product. See *id.* at 130-31.

¹¹⁵ *Reyes*, 498 F.2d at 1273.

¹¹⁶ *Id.* at 1274.

¹¹⁷ *Id.* at 1273.

¹¹⁸ *Id.* at 1275.

¹¹⁹ See *id.* at 1277.

¹²⁰ 112 Idaho 328, 732 P.2d 297, *ans. conformed to*, 828 F.2d 510 (9th Cir. 1987),

preme Court clearly contemplated the weighing of a product's risks and benefits prior to making the determination of unavoidable unsafety necessary for comment k application. The court stated that in order for a manufacturer to prevail in securing comment k protection, the judge or the factfinder would have to be apprised of convincing evidence that the product at issue survived a risk/benefit test.¹²¹ Pointing out that comment k refers "to 'some' products which are avoidably unsafe,"¹²² the court refused to grant blanket protection to all pharmaceutical products. Voicing a concern that would later be rationalized by the *Brown* court,¹²³ the Idaho Supreme Court stated that "[i]t does not serve society that an unavoidably unsafe product, which has occasional or fractionous benefit, should enjoy insulation from strict liability in tort when the product's predominant effects are detrimental to individual and

cert. denied, 485 U.S. 942 (1988). For specification of the questions certified to the Idaho Supreme court, see *Toner v. Lederle Laboratories*, 779 F.2d 1429, 1432-33 (9th Cir. 1986). As noted in *Graham v. Wyeth Laboratories*, 666 F. Supp. 1493, 1498 n.6 (D. Kan. 1987), *rev'd*, 906 F.2d 1399 (10th Cir. 1990), *cert. denied*, 111 S. Ct. 511 (1990), "the Idaho court's finding[s] [are]—in effect—the law of the Ninth Circuit." The reversal of the district court was based on evidentiary errors that occurred at trial, including the exclusion of expert testimony concerning causation and the distorted redaction of one exhibit. See *Graham*, 906 F.2d at 1410-11, 1413. The circuit court agreed with the district court's relevant conclusions regarding comment k and preemption. See *id.* at 1405-06.

¹²¹ The court noted that "[c]learly, the comment contemplates a weighing of the benefit of the product against its risk. Obviously, for comment k to apply, the benefit must outweigh the risk. This weighing process should consider the value of the benefit, the seriousness of the risk, and the likelihood of both." *Toner*, 112 Idaho at 337, 732 P.2d at 306 (citations omitted).

The court placed the burden of proving comment k's application on the manufacturer, stating that "comment k is an affirmative defense to a claim based on strict liability." *Id.* at 339, 732 P.2d at 308.

Note that because it was not presented with the issue, the *Toner* court did not address the question of "whether the judge or jury ought to determine the application of comment k to a particular product." *Id.* at 339 n.9, 732 P.2d at 308 n.9. However, the court noted that

[s]ome courts and commentators, emphasizing the factual determinations necessary, leave it to the jury. Others, concerned with the policy implications of the decision, would have the court decide comment k's application as a matter of law.

Either way, the decision of the applicability of comment k pertains only to claims based on defective design, and not to those based on defective manufacture or inadequate warning. The latter two raise questions of fact to be decided by the jury.

Id. (citations omitted); see also Schwartz, *supra* note 83, at 1147-48 (noting that issues underlying comment k are of law and policy, and thus best suited to judicial review).

¹²² *Toner*, 112 Idaho at 339, 732 P.2d at 308.

¹²³ See *supra* note 108 and accompanying text.

public safety."¹²⁴ The court held that based on the best available evidence at the time of product distribution, "the scales must clearly tip in favor of the benefits for comment k to apply."¹²⁵ The comment would be applied on a case-by-case basis, "when the situation calls for it."¹²⁶

In *Senn v. Merrell-Dow Pharmaceuticals, Inc.*,¹²⁷ the Oregon Supreme Court endeavored to resolve some of the uncertainty relating to comment k's application under Oregon law. Although declining to make a determination as to whether the DPT vaccine at issue was unavoidably unsafe, and thereby deserving of comment k protection,¹²⁸ the court noted that such a determination would raise "[i]ssues of the vaccine's efficacy, the degree of risk attending its use, and the extent to which it is in fact 'unavoidably unsafe'. . . ."¹²⁹ Once again an expansive application of comment k was rejected in favor of one which would examine and ostensibly balance the risks and benefits of the manufactured product.

A risk/benefit approach to identifying unavoidably unsafe products was also set out by the Eighth Circuit in *Hill v. Searle Laboratories*.¹³⁰ Evaluating comment k's application to a medical device, the CU-7 copper intrauterine device, the court determined that it was not the intent of the drafters of comment k to "grant all manufacturers of prescription drugs a blanket exception to strict

¹²⁴ *Toner*, 112 Idaho at 337, 732 P.2d at 306 (citations omitted).

¹²⁵ *Id.* at 337, 732 P.2d at 306. The Idaho Supreme Court relied on many of the arguments set forth in *Kearl v. Lederle Laboratories*, 172 Cal. App. 3d 812, 218 Cal. Rptr. 453 (1985). *Kearl* was overruled by the California Supreme Court in *Brown v. Superior Court*, 44 Cal. 3d 1049, 1061, 751 P.2d 470, 477, 245 Cal. Rptr. 412, 418 (1988).

¹²⁶ *Toner*, 112 Idaho at 339, 732 P.2d at 308; *see also* *Patten v. Lederle Laboratories*, 676 F. Supp. 233, 236-37 (D. Utah 1987) (fashioning an application of comment k based on *Toner*, declining to "provide blanket immunity to all prescription drugs," and determining that "the defendant must demonstrate that, weighing the benefits of the product against its risks, it is apparently useful and desirable"); *Feldman v. Lederle Laboratories*, 97 N.J. 429, 447, 479 A.2d 374, 383 (1984) ("Whether a drug is unavoidably unsafe should be decided on a case-by-case basis; we perceive no justification for giving all prescription manufacturers a blanket immunity from strict liability manufacturing and design defect claims under comment k.").

¹²⁷ 305 Or. 256, 751 P.2d 215 (1988), *ans. conformed to*, 850 F.2d 421 (9th Cir. 1988). For certifications to the Oregon Supreme court, *see Senn v. Wyeth Laboratories*, 850 F.2d 611, 613 (9th Cir. 1988).

¹²⁸ *See Senn*, 305 Or. at 263 n.4, 751 P.2d at 218 n.4 ("We agree with the Idaho Supreme Court's statement that 'it is not for a court sitting on appeal to [determine whether a vaccine is entitled to comment k protection]. The determination would require a full evidentiary hearing such as only a trial court can provide.'").

¹²⁹ *Id.* at 263 n.4, 751 P.2d at 219 n.4.

¹³⁰ 884 F.2d 1064 (8th Cir. 1989).

liability."¹³¹ The court preferred to align itself with what it believed were "[t]he better reasoned opinions" that supported a "view that the unavoidably unsafe exception should only apply upon a showing of exceptional social need."¹³²

b. *Whether the Product Could Have Been Designed in a Safer Manner*

In *Toner*,¹³³ the Idaho Supreme Court articulated an additional factor to be considered in determining whether a product was unavoidably unsafe and its manufacturer thereby encompassed under comment k's protection: the inherent risks of the product at issue had to be inescapable. The court explained that this meant that "the design [of the product] must be as safe as the best available testing and research permits."¹³⁴ Presumably the court believed that either the judge or the jury was entitled to review state-of-the-art methodology on a case-by-case basis, and determine whether a product's benefits might have been achieved in another manner.¹³⁵

c. *Whether Feasible Alternatives for the Product Exist*

In *Brochu v. Ortho Pharmaceutical Corp.*,¹³⁶ a non-vaccine case involving the oral contraceptive Ortho-Novum 2, the court affirmed a jury verdict that permitted an expanded reading of the plaintiff's defective design claim. The court reasoned that there was sufficient evidence to support the jury's finding that because a similar, equally effective, and safer contraceptive had been available, the "risk posed by the 100 mcg. pill outweighed whatever advantages, if any, it

¹³¹ *Id.* at 1069.

¹³² *Id.* (citations omitted); see also *Belle Bonfils Memorial Blood Bank v. Hansen*, 665 P.2d 118, 123 (Colo. 1983) (stating that "in order to fall within the comment k exception, not only should an unavoidably unsafe product carry a unique or profound benefit, but that benefit should extend to the vast majority of users of the product").

¹³³ 112 Idaho 328, 732 P.2d 297 (1987).

¹³⁴ *Id.* at 337, 732 P.2d at 306.

¹³⁵ See *Patten v. Lederle Laboratories*, 676 F. Supp. 233, 237 (D. Utah 1987) (restating the proposition discussed in *Toner* that "[c]omment k does not require that sellers be omniscient, but it does hold them to the current state of the art"); *White v. Wyeth Laboratories*, 40 Ohio St. 3d 390, 395, 533 N.E.2d 748, 752 (1988) (citing *Toner* for the proposition that "not all drugs are so perfectly designed that they cannot be made more pure or more safe . . ."). For a discussion of whether such determinations are to be made by the judge or the jury, see *supra* note 121.

¹³⁶ 642 F.2d 652 (1st Cir. 1981).

might have had over [other oral contraceptives with] lower dosages—in other words, that the Ortho-Novum 2 mg. was unreasonably dangerous.”¹³⁷ The existence of an equally effective, safer pill denied the manufacturer of the Ortho-Novum pill comment k protection. The manufacturer was found strictly liable for defective product design.¹³⁸

The plaintiffs in *Toner* argued that a viable fractionated cell DPT vaccine was available, posed a lower risk, and was immunologically superior to the defendant’s whole cell vaccine.¹³⁹ This prompted the Idaho Supreme court to require that in order for comment k to apply, “there must be, at the time of the subject product’s distribution, no feasible alternative design which on balance accomplishes the subject product’s purpose with a lesser risk.”¹⁴⁰ However, the court left room for the exercise of some license in making this determination. It recognized that even if a safer or more effective substitute product were available, it would not necessarily be superior. If a riskier product satisfied broader social utility goals it could survive the “feasible alternative” test.¹⁴¹

¹³⁷ *Id.* at 655 n.4. See generally Comment, *Can a Prescription Drug Be Defectively Designed?*—Brochu v. Ortho Pharmaceutical Corp., 31 DE PAUL L. REV. 247, 260-68 (1981) (discussing the impact of drug design litigation on the pharmaceutical field).

¹³⁸ The manufacturer was also found liable for failing to warn the prescribing physician of risks associated with the product. See *Brochu*, 642 F.2d at 658-59.

¹³⁹ See *Toner v. Lederle Laboratories*, 779 F.2d 1429, 1431 (9th Cir. 1986).

¹⁴⁰ *Toner*, 112 Idaho at 337, 732 P.2d at 306.

¹⁴¹ The court noted:

The evaluation of a purported alternative design and the subject product’s design should consider the magnitude of the subject product’s risk that the alternative avoids, the financial costs of the compared designs, the benefits of the compared designs, and the relative safety of the compared designs, including any new risk that the alternative would pose.

Id. (citations omitted); see also *Ackley v. Wyeth Laboratories, Inc.*, No. 89-3821, slip. op. at 12 (6th Cir. Nov. 26, 1990). In *Ackley*, the court explained that in order to

defeat a claim that a product is unavoidably unsafe, the challenger must show an alternative that is *Pareto-superior*, that is, a product that is *at least* as effective *and* also provides less risk. Appellants cannot state a claim for strict liability merely by showing an alternative that provides an alleged modicum of reduction of risk at the expense of some loss of effectiveness.

Id. (citations omitted).

C. *Application of Comment k to an AIDS Vaccine Design Defect*

Given the diversity of approaches the courts have taken when applying comment k, it is impossible to predict exactly which, if any, of the criteria discussed above will guide individual courts as they determine whether an AIDS vaccine is unavoidably unsafe, and whether the manufacturer will be held strictly liable for injuries caused by this product. If manufacturers can survive the less solicitous, restrictive application of comment k, then theoretically they will be exempt from strict liability for design defects under any analysis.

An AIDS vaccine is likely to satisfy the three conditions which various courts, using the restrictive application, have required for demonstrating the quality of "unavoidable unsafety," the precondition for comment k immunity.¹⁴²

First, an AIDS vaccine should easily satisfy any risk/benefit requirement, since it will provide protection from HIV infection and reduce the incidence of AIDS, a fatal disease for which there is no satisfactory treatment. Because the development and production of an AIDS vaccine are of paramount importance, the interest in vaccine availability is likely to outweigh the policy rationales for imposing strict liability on manufacturers.¹⁴³

In addition, some of the policy rationales may be inapplicable to an AIDS vaccine. For example, it may not be feasible for manufacturers to assess adequately the risks associated with an AIDS vaccine at the time of its distribution, and thus the manufacturer may not be in any better position to insure against or absorb the liability costs certain to be associated with this product if it is subject to a strict liability analysis.¹⁴⁴

Second, it is likely that FDA oversight will facilitate manufacturer compliance with standards sufficient to ensure that vaccines which reach the marketplace embody the safest design known at the time of their distribution. If design defect claims against AIDS manufacturers parallel the cases brought to date against DPT and polio vaccine manufacturers, such claims will be based either on the

¹⁴² See *supra* text accompanying notes 88-90.

¹⁴³ See *supra* notes 77-83 and accompanying text.

¹⁴⁴ As the California Assembly noted, the development costs of a vaccine may not be recoupable for the manufacturer. See CAL. HEALTH & SAFETY CODE § 199.51(a) (West Supp. 1990). In addition, casualty insurers may be reluctant to provide coverage for a product having risks that do not lend themselves to actuarial calculations. See Berger, *supra* note 76, at 288.

premise that a selected combination of vaccines is inappropriate,¹⁴⁵ or that an acellular or fractionated cell vaccine would have been safer than the manufactured product.¹⁴⁶ Unless there is evidence that either of these allegedly unsafe characteristics could have been avoided without eliminating the vaccine's usefulness, it is unlikely that an AIDS vaccine manufacturer will be found to have ignored safer design alternatives. The existence of these allegedly safe characteristics should become apparent to, and be corrected by manufacturers during the course of toxicology studies and carefully constructed clinical trials, and the FDA should become aware of such problems in its evaluations of clinical data.¹⁴⁷ Thus, the vaccine which a manufacturer markets should, with the supervision of the FDA, be of the safest design known at the time of distribution.

Third, although the existence of feasible alternatives may affect marketing decisions by AIDS vaccine manufacturers, with respect to

¹⁴⁵ See *Stromsodt v. Park-Davis & Co.*, 257 F. Supp. 991 (1966), *aff'd*, 411 F.2d 1390 (8th Cir. 1969). This case illustrates the problems that can arise from the use of combination vaccines. In *Stromsodt*, the solution in which four vaccines were combined effected the potency of one vaccine, and ultimately caused injury to the plaintiff. *Id.* at 992-93. The district court implicitly viewed the benefits attendant to use of the combination as insufficient to justify its risk, noting that "[t]his was not a situation where an epidemic existed or where need justified the risk of prematurely marketing [the combination vaccine] since products were already available to the medical profession that satisfactorily accomplished what [the combination vaccine] was designed to do." *Id.* at 996.

¹⁴⁶ See *supra* text accompanying note 139.

¹⁴⁷ In attempting to determine the scope of their liability for design defects, manufacturers may, however, encounter two difficulties somewhat unique to the AIDS vaccine effort.

First, the long period of viral incubation prior to manifestation of the disease means that injured plaintiffs may only be identifiable many years after a vaccine is administered. In design defect litigation brought long after product distribution, a jury will have to harmonize an array of subjective determinations, all based on hindsight, as to which early vaccine designs offered greater safety and efficacy.

Second, difficulties for manufacturers may arise from the secrecy that has been attached to the vaccine research effort. See Foreman, *Secrecy in AIDS Research*, Boston Globe, Apr. 13, 1987, at 43, col. 1. One result of this secrecy is unwitting exposure to future liability if evidence of the experience attendant to particular vaccine designs is selectively distributed among scientists and physicians. As has been noted,

[m]anufacturers are deemed to know whatever information is available in the scientific community. This means that they may not avoid liability by neglecting to keep up with the state of research. At the same time, it does not require them to know the unknowable. Thus the information for which they are likely to be held responsible should be limited to that available in the literature and presented at scientific meetings.

Mariner & Gallo, *supra* note 61, at 23.

pricing strategies or target groups,¹⁴⁸ it seems unlikely to cause every potential manufacturer to withdraw from the market altogether. Until regulatory approval is granted for the marketing of at least two AIDS vaccines, alternative concerns are truly speculative; the superiority of a single vaccine obviously cannot be determined in the abstract.

D. *Comment k and the Manufacturer's Duty to Warn*

A final legal issue for manufacturers concerns the scope of their duty to warn under comment k.¹⁴⁹ Case law¹⁵⁰ and legal com-

¹⁴⁸ For example, liability problems would probably be avoided if a manufacturer produced a vaccine that showed occasional adverse effects when administered to an elderly population, but was the only effective vaccine for children.

¹⁴⁹ Even when it has been established that a product is unavoidably unsafe, a manufacturer may still not be entitled to the comment k exemption if it failed to warn of known risks associated with the product. Under comment k, the failure to warn analysis is a negligence-based inquiry. As such, it differs slightly from the manner in which failure to warn is reviewed under common law strict liability standards. This distinction was clarified by the California Supreme Court in *Brown v. Superior Court*, 44 Cal. 3d 1049, 1059 n.4, 751 P.2d 470, 476 n.4, 245 Cal. Rptr. 412, 417 n.4 (1988):

The test stated in comment k is to be distinguished from strict liability for failure to warn. Although both concepts identify failure to warn as the basis of liability, comment k imposes liability only if the manufacturer knew or should have known of the defect at the time the product was sold or distributed. Under strict liability, the reason why the warning was not issued is irrelevant, and the manufacturer is liable even if it neither knew nor could have known of the defect about which the warning was required. Thus, comment k, by focusing on the blameworthiness of the manufacturer, sets forth a test which sounds in negligence, while imposition of liability for failure to warn without regard to the reason for such failure is consistent with strict liability since it asks only whether the product that caused injury contained a defect.

Id. (citations omitted); *see also* *DeLuryea v. Winthrop Laboratories*, 697 F.2d 222, 229 (8th Cir. 1983) ("Under a negligence theory the issue is whether the defendant exercised due care in formulating and updating the warning, while under a strict liability theory the issue is whether the lack of a proper warning made the product unreasonably dangerous." (quoting *Werner v. Upjohn Co.*, 628 F.2d 848, 858 (4th Cir. 1980))).

¹⁵⁰ *See, e.g.,* *Woodill v. Parke Davis & Co.*, 79 Ill. 2d 26, 37, 402 N.E.2d 194, 199 (1980) ("[H]old[ing] a manufacturer liable for failure to warn of a danger of which it would be impossible to know based on the present state of human knowledge would make the manufacturer the virtual insurer of the product . . ."); *see also* *Tatum v. Schering Corp.*, 795 F.2d 925, 926 (11th Cir. 1986) (recognizing that "[b]ecause ethical drugs are considered unavoidably unsafe products, they are defective only when not accompanied by an adequate warning" (citation omitted)); *Reyes v. Wyeth Laboratories*, 498 F.2d 1264, 1274-75 (5th Cir. 1974) (requiring unreasonably dangerous products to carry a sufficient warning); *Feldman v. Lederle Laboratories*,

mentary¹⁵¹ suggest that the sufficiency of a manufacturer's warnings depends on whether it reflects the manufacturer's knowledge of the risks associated with the product at the time of distribution. This view is consistent with Comment j of the Restatement (Second) of Torts § 402A, which limits a manufacturer's duty to warn to situations in which it "has knowledge, or by the application of reasonable, developed human skill and foresight should have knowledge of . . . the danger."¹⁵² Based on this interpretation, AIDS vaccine manufacturers should be absolved of strict liability for failure to warn of unforeseeable risks.

In warning of foreseeable risks, manufacturers may not be responsible for warning consumers directly due to the protections of the "learned intermediary" doctrine.¹⁵³ If it is foreseeable, however, that the vaccine will be administered without the intervention of a physician, or if the manufacturer fails to warn properly the physicians serving as intermediaries, the doctrine will not protect

97 N.J. 429, 453, 479 A.2d 374, 387 (1984) (imputing knowledge of "reliable information generally available or reasonably obtainable in the industry or in the particular field involved").

¹⁵¹ See, e.g., Kidwell, *The Duty to Warn: A Description of the Model of Decision*, 53 TEX. L. REV. 1375, 1395 (1975) ("Only when the risk of damage becomes foreseeable, because of an advance in the body of relevant knowledge, does a duty to warn attach."); Comment, *Requiring Omniscience: The Duty to Warn of Scientifically Undiscoverable Product Defects*, 71 GEO. L.J. 1635, 1642 (1983) (arguing that courts have retained a requirement of foreseeability of risk before manufacturers are required to warn in § 402A cases to avoid requiring "a product manufacturer to warn of defects that were scientifically undiscoverable at the time the product was marketed").

¹⁵² RESTATEMENT (SECOND) OF TORTS § 402A comment j (1965).

¹⁵³ First adopted in *Sterling Drug, Inc. v. Cornish*, 370 F.2d 82, 85 (8th Cir. 1966), the learned intermediary doctrine holds that the manufacturer satisfies its duty to warn if makes "reasonable efforts" to warn doctors of the possibility of side effects. See *id.* It is based on the rationale that

[p]rescription drugs are likely to be complex medicines, esoteric in formula and varied in effect. As a medical expert, the prescribing physician can take into account the propensities of the drug, as well as the susceptibilities of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individualized medical judgment bottomed on a knowledge of both patient and palliative. Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a "learned intermediary" between manufacturer and consumer.

Reyes, 498 F.2d at 1276; see also Comment, *The Impact of Product Liability Law on the Development of a Vaccine against the AIDS Virus*, 55 U. CHI. L. REV. 943, 957-61 (1988) (discussing the application of the learned intermediary doctrine to AIDS vaccine manufacturers).

against liability.¹⁵⁴ In addition, in order to remain insulated from liability, manufacturers must warn of product risks in a manner consistent within the industry.¹⁵⁵ Finally, evidence of a failure to warn which rises to the level of "malice, wantonness, or reckless indifference from which malice could be inferred" may support the imposition of punitive damages on the manufacturer.¹⁵⁶

In summary, although the tort law falls short of completely protecting potential vaccine manufacturers from strict liability, the extent of their liability should be minimized by the critical need for their products. Once a broad range of AIDS vaccines becomes available, it is less clear, however, whether all such vaccines will meet the unavoidably unsafe standard. More rigorous risk-utility evaluations will occur as each successive vaccine becomes available. Legislative intervention may be required to encourage manufacturers to enter the market.¹⁵⁷

¹⁵⁴ See *Reyes*, 498 F.2d at 1276; *Givens v. Lederle*, 556 F.2d 1341 (5th Cir. 1977). *Givens* is particularly interesting because it points out how broad the scope of a "proper warning" can become. The court determined that, although the manufacturer had not misrepresented the safety of its oral polio vaccine to the administering physician, the product warning trivialized the risk because the physician had not felt sufficiently compelled to disclose the one-in-three million chance of injury to his patient. See *id.* at 1345.

¹⁵⁵ See *Tatum*, 795 F.2d at 928 (recognizing that although the defendant had revised its package insert in response to an FDA directive, "no letters were written to physicians and no bulletins [were] sent to [the manufacturer's] detailmen, nor were detailmen told to bring the matter to the attention of physicians"). The court regarded the manufacturer's "method of calling attention to a change in warning indicating a higher risk of serious adverse reaction than previously described" as being "inconsistent with the practice of other drug manufacturers." *Id.* Note, however, that because the standard of liability for failure to warn is negligence, remedial changes in warning literature will be excluded under the rules of evidence. See *Deluryea v. Wintrop Laboratories*, 697 F.2d 222, 229 (8th Cir. 1983) (stating that Rule 407 of the Federal Rules of Evidence "requires exclusion of evidence of subsequent remedial changes in [a manufacturer's] warning literature").

¹⁵⁶ *Deluryea*, 697 F.2d at 231 (citing *Hoffman v. Sterling Drugs*, 485 F.2d 132 (3d Cir. 1973)).

¹⁵⁷ As noted *supra* text accompanying notes 80-81 & 101, manufacturers will not be immune from strict liability claims based on manufacturing defects associated with their products. For an excellent discussion of the manner in which various liability rules impact on the risks associated with the manufacture of pharmaceutical products, see generally Ausness, *Unavoidably Unsafe Products and Strict Products Liability: What Liability Rule Should be Applied to the Sellers of Pharmaceutical Products?*, 78 KY. L.J. 705 (1989-90).

IV. FUTURE SOLUTIONS FOR AIDS VACCINE MANUFACTURERS:
FEDERAL AND STATE LEGISLATIVE EFFORTS AND
THE APPLICABILITY OF THE FEDERAL
PREEMPTION DOCTRINE

A. *Federal Legislative Efforts*

Federal legislation may ultimately be used to achieve uniform vaccine liability standards that strike a balance between the policy objectives of adequately protecting consumers and encouraging the manufacture of socially desirable products. Two recent pieces of legislation may serve as models for future legislative development at the federal level.

1. The National Childhood Vaccine Injury Act

The federal government's most recent activity in legislative vaccine regulation consists of the creation of the National Vaccine Program (NVP) as mandated by the National Childhood Vaccine Injury Act (NCVI).¹⁵⁸ The stated purpose of the NCVI is "to achieve optimal prevention of human infectious diseases through immunization and . . . optimal prevention against adverse reactions to vaccines."¹⁵⁹ Another program created by the NCVI is the National Vaccine Injury Compensation Program,¹⁶⁰ which was designed to provide a "no-fault" compensation scheme for those injured by any of the vaccines required by law for entrance to public school (vaccines for childhood infectious diseases such as iphtheria and tetanus). Although the legislation directed that tort law would provide a secondary remedy for the victims of vaccine-related injuries, it stipulated that such persons must seek compensation¹⁶¹ through channels specified in the legislation prior to filing

¹⁵⁸ 42 U.S.C. §§ 300aa-1 to 300aa-34 (1988).

¹⁵⁹ *Id.* § 300aa-1.

¹⁶⁰ *See id.* § 300aa-10(a).

¹⁶¹ The compensation scheme is funded by revenues generated from an excise tax on vaccine sales between January 1, 1988 and December 31, 1992. *See* 26 U.S.C. §§ 4131-32 (1988). The adequacy of the compensation scheme necessarily requires accurate estimates of the number and amount of future claims. Recognizing this, the legislation provides for termination of awards if the anticipated amount is exceeded in a given period. *See* 42 U.S.C. § 300aa-34 (1988). Once the federal program becomes insolvent, civil tort claims become the only avenue of redress for victims. *See id.*

suit against the vaccine manufacturer.¹⁶² Manufacturers must provide vaccines with warnings detailing the risks.

This program appears to have decreased the number of lawsuits filed against manufacturers, but it is too early to know whether the initial trend will continue.¹⁶³ It is also unclear whether the program can be expanded to include AIDS vaccines. Two commentators take a rather pessimistic look at the potential for the NCVI to offer protection in the AIDS context:

The inclusion of a new, elective vaccine would require acceptance of a much broader principle of social responsibility for any vaccine-related injury. There is also a practical obstacle to extending the NCVI act to cover AIDS vaccines. In order to simplify the process of determining eligibility for compensation, the act presumes that certain injuries have been caused by the vaccine. It will . . . be virtually impossible to identify . . . the times of onset in order to establish a credible schedule of compensable injuries before any AIDS vaccine is tested or distributed.¹⁶⁴

2. The Product Liability Reform Act

Additional federal legislative efforts may take place though the passage of some form of a uniform products liability act.¹⁶⁵ One such effort, the Products Liability Reform Act, is currently under review in the Senate.¹⁶⁶ As it currently stands, this bill will permit drug manufacturers to use FDA approval of a drug as an absolute defense against punitive damages, as long as the manufacturer has not committed fraud during the approval process.¹⁶⁷ However, because the legislation does not include any provisions allowing

¹⁶² All claims are handled by the United States Claims Court. See United States Claims Court, General Order No. 23, 16 Cl. Ct. XXI (Jan 25, 1989) (rules for claims processing); 42 U.S.C. § 300aa-21 (1988). For a discussion of the policy rationale behind Congress's decision not to eliminate redress through the tort system, see Schwartz & Mahshagian, *National Childhood Vaccine Injury Act of 1986: An Ad Hoc Remedy or a Window for the Future?*, 48 OHIO ST. L.J. 387, 395 (1987).

¹⁶³ See Hinman, *DTP Vaccine Litigation Update*, 142 AM. J. DISEASES CHILD 1275 (1988).

¹⁶⁴ Mariner & Gallo, *supra* note 61, at 24.

¹⁶⁵ Models for such efforts may be found in the Department of Commerce Model Uniform Product Liability Act, reprinted in 44 Fed. Reg. 62,714 (1979).

¹⁶⁶ See S. 1400, 101st Cong., 1st Sess., 135 CONG. REC. S8,725-31 (1989); see also S. REP. NO. 356, 101st Cong., 2d Sess. (1990) [hereinafter REPORT]; Gastel, *Product Liability Tort Reform*, INS. INFO. INST., August 1990 (LEXIS, Nexis library, IIRPTS file). For a justification of the legislation, see *supra* text accompanying note 78.

¹⁶⁷ See S. 1400, *supra* note 166, § 303(c), 135 CONG. REC. at S8,727; REPORT, *supra* note 166, at 39.

compliance with FDA standards to create a presumption of product safety,¹⁶⁸ it is only a partial solution. Products designed to FDA standards will still not be "liability-proof," and manufacturers have yet to obtain a yardstick by which to predict their ultimate exposure level. It will be interesting to see what other protections the federal government will be willing to offer drug manufacturers, and whether such protections will solve the liability crisis facing AIDS vaccine manufacturers, or instead create problems of their own.¹⁶⁹

B. *Applicability of the Federal Preemption Doctrine*

Although it has not been successfully argued to date,¹⁷⁰ another theory may eventually assist vaccine manufacturers in their attempts to define the boundaries of potential AIDS vaccine liability: the federal preemption doctrine could limit the liability of manufacturers sued for alleged improper vaccine design, testing, and labeling, or for any other activities that have been sanctioned by the FDA.

The doctrine of federal preemption is rooted in the supremacy clause,¹⁷¹ and it serves to define the boundaries of power between the federal government and the states. Federal preemption of state law occurs when the spheres of state and federal sovereignty intersect to the degree that the autonomy of the state, and its power as a regulatory body must be displaced. Preemption may either be "express,"¹⁷² where an activity is explicitly regulated in the language of a federal statute or regulation, or it may be "implied,"¹⁷³

¹⁶⁸ Such statutes have been enacted at the state level. See *infra* note 187.

¹⁶⁹ "Although congressional leaders said at the time that the swine flu case would not be a precedent for future mass immunization programs . . . it may nevertheless be a relevant precedent for an AIDS vaccine." Weisburd, *AIDS Vaccines: The Problems of Human Testing*, 131 SCI. NEWS 329, 330-31 (1987) (quoting Richard M. Cooper, a Washington attorney, at an NIH workshop).

¹⁷⁰ See *infra* notes 184-85.

¹⁷¹ U.S. CONST. art. VI, cl. 2. "This Constitution, and the laws of the United States which shall be made in pursuance thereof . . . shall be the Supreme law of the Land; and the Judges in every State shall be bound thereby, anything in the Constitution or laws of any state to the contrary notwithstanding." *Id.*

¹⁷² See *Pacific Gas & Elec. Co. v. State Energy Resources Conservation & Dev. Comm.*, 461 U.S. 190, 203 (1983) (noting Congress's ability to "pre-empt state authority by so stating, in express terms"); see also *Fidelity Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 152-53 (1982); *Jones v. Rath Packing Co.*, 430 U.S. 519, 525 (1977).

¹⁷³ See generally *Hillsborough County v. Automated Medical Laboratories*, 471 U.S. 707, 713 (1985) (reviewing several types of implied preemption).

where (1) state law directly conflicts with federal requirements;¹⁷⁴ (2) the federal regulatory scheme is so comprehensive that it can be assumed to be controlling;¹⁷⁵ (3) public policy rationales support an inference of preemption;¹⁷⁶ (4) a review of the legislative history of a federal statute or regulation favors a finding of preemption;¹⁷⁷ or (5) the federal government has made a conscious decision that a particular activity not be regulated.¹⁷⁸ The

¹⁷⁴ As the Supreme Court stated in *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 248 (1984):

If Congress has not entirely displaced state regulation over the matter in question, state law is still preempted to the extent it actually conflicts with federal law, that is, when it is impossible to comply with both state and federal law . . . or where the state law stands as an obstacle to the accomplishment of the full purposes and objectives of Congress.

Id. (citations omitted); *see also* *Michigan Canners & Freezers Ass'n, Inc. v. Agricultural Mktg. & Bargaining Bd.*, 467 U.S. 461, 469 (1984) (stating that "if Congress has not displaced state regulation entirely, it may nonetheless pre-empt state law to the extent that the state law actually conflicts with federal law").

¹⁷⁵ This would be the case if "[t]he scheme of federal regulation [is] so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it," or "the Act of Congress . . . touch[es] a field in which the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject," or finally, if "the object sought to be obtained by federal law and the character of obligations imposed by it . . . reveal the same purpose." *Fidelity*, 458 U.S. at 153 (quoting *Rice v. Sante Fe Elevator Corp.*, 331 U.S. 218, 230 (1947)); *see also* *Howard v. Uniroyal, Inc.*, 719 F.2d 1552, 1559 (11th Cir. 1983) ("The detail and precision with which Congress provided the means for the enforcement of the affirmative action clause makes it reasonable to infer that Congress left no room in section 503(b) for state contract actions to supplement it.").

¹⁷⁶ One such policy-related goal might be the maintenance of uniformity among the states. *See Transcontinental Gas Pipe Line Corp. v. State Oil & Gas Bd.*, 474 U.S. 409, 423 (1986) (holding that state regulation of interstate pipelines "disturbs the uniformity of the federal scheme"); *Chicago & N.W. Transp. Co. v. Kalo Brick & Tile Co.*, 450 U.S. 311, 326 (1981) ("A system under which each state could through its courts, impose on railroad carriers its own version of reasonable service requirements could hardly be more at odds with the uniformity contemplated by Congress in enacting the Interstate Commerce Act."); Note, *Pre-emption as a Preferential Ground: A New Canon of Construction*, 12 STAN. L. REV. 208, 215-16 (1959) ("When federal action is inspired by a desire to avoid multiple and conflicting state regulation . . . the context strongly suggests that the state should not be allowed to continue to govern matters subject to federal regulation.").

¹⁷⁷ *See Northern States Power Co. v. Minnesota*, 447 F.2d 1143, 1146 (8th Cir. 1971), *aff'd*, 405 U.S. 1035 (1972). *But see* *International Paper Co. v. Ouellette*, 479 U.S. 481, 493 (1987) ("We resort to legislative materials only when the congressional mandate is unclear on its face." (citation omitted)).

¹⁷⁸ *See Marshall v. Burlington Northern, Inc.*, 720 F.2d 1149, 1154 (9th Cir. 1983) (stating that "where the [Federal Railroad Administration] has rejected the requirement of strobe or oscillating [warning] lights, a state may not require them"); *Bessemer and Lake Erie R.R. Co. v. Pennsylvania Pub. Util. Comm'n*, 430 Pa. 339, 344, 243 A.2d 358, 360 (stating that "it is no longer open to the states to decide that

Supreme Court has recognized that federal regulations have "no less preemptive effect than federal statutes."¹⁷⁹ The Court has also conceded that state common law tort claims may have regulatory effects¹⁸⁰ and may also be subject to preemption,¹⁸¹ although the Court has been reluctant to recognize preemption in the fields of health and safety.¹⁸²

In the context of AIDS vaccine regulation, the key question with respect to preemption will be whether this doctrine can be inferred from the extent of federal involvement¹⁸³ or the scope of federal interests in uniform regulation or in the availability of this product. Unfortunately, in asking courts to recognize a preemption argument, manufacturers will face a judicial environment that has not been particularly hospitable. With a few exceptions,¹⁸⁴ the courts that have addressed the preemption issue¹⁸⁵ appear disinclined to

federal protections are inadequate and that additional safety measures must be taken"), *cert. denied*, 393 U.S. 959 (1968).

¹⁷⁹ *Fidelity*, 458 U.S. at 153.

¹⁸⁰ See *Sperry v. Florida*, 373 U.S. 379, 403 (1963) ("The authority of Congress is no less when the state power which it displaces would otherwise have been exercised by the state judiciary rather than by the state legislature.").

¹⁸¹ See *San Diego Bldg. Trades Council v. Garmon*, 359 U.S. 236, 247 (1959) ("The obligation to pay compensation can be, indeed is designed to be, a potent method of governing conduct and controlling policy. Even the States' salutary effort to redress private wrongs or grant compensation for past harm cannot be exerted to regulate activities that are potentially subject to the exclusive federal regulatory scheme.").

¹⁸² See *Hillsborough*, 471 U.S. at 718 ("Given the presumption that state and local regulation related to matters of health and safety can normally coexist with federal regulations, we will seldom infer, solely from the comprehensiveness of federal regulations, an intent to pre-empt in its entirety a field related to health and safety.").

¹⁸³ Under either the Food Drug and Cosmetic Act (FDCA), see *supra* text accompanying note 7, or the Public Health Services Act (PHSA), see *supra* note 10.

¹⁸⁴ See, e.g., *Hurley v. Lederle Laboratories*, 863 F.2d 1173 (5th Cir. 1988). Although the circuit court's decision reversed a lower court decision that had fully embraced the preemption argument, the appeals court did recognize that with respect to the adequacy of the product warning, the manufacturer had a compelling argument for preemption:

It would be patently inconsistent for a state then to hold the manufacturer liable for including that precise warning when the manufacturer would otherwise be liable for *not* including it. Thus assuming that the FDA has processed all the relevant and available information in arriving at the prescribed warning, its decision as to the proper wording must preempt by implication that of a state.

Id. at 1179.

¹⁸⁵ See *Abbot v. American Cyanamid Co.*, 844 F.2d 1108, 1112-13 (4th Cir. 1988) (rejecting the arguments that the pervasive nature of the FDCA, PHSA and NCVIA were indicative of congressional intent to preempt and that public health policy would be frustrated by allowing state tort claims against DPT vaccine manufacturers), *cert. denied*, 488 U.S. 908 (1988); *Tarallo v. Searle Pharmaceutical*, 704 F. Supp. 653, 658-

embrace the notion that the purposes of the FDCA or the PHSA are frustrated by permitting plaintiffs to obtain state common law tort remedies from manufacturers. The opinions of commentators¹⁸⁶ seem mixed, and only a few state legislatures¹⁸⁷ have specifically considered either (1) the evidentiary weight to be given to manufacturers' regulatory compliance; or (2) the issue of preemption in a product liability context.

Because the language of FDCA and PHSA do not expressly preempt state law, manufacturers' claims for preemption have been based on a notion that the pervasiveness of federal regulations and the public interests in product availability and uniform regulation of drug labeling support a finding of preemption. Although later reversed, the district court decision in *Hurley v. Lederle Laboratories*¹⁸⁸ provides a succinct summary of the pervasiveness argument with respect to drug labeling:

60 (D.S.C. 1988) (refusing to infer preemption from the alleged comprehensiveness of federal regulations); *Graham v. Wyeth Laboratories*, 666 F. Supp. 1483, 1493 (D. Kan. 1987) (disallowing manufacturer immunity from state tort claims because although "Congress intends vaccines to be at least as uniformly safe as the FDA regulations require, there has never been a congressional intent that innocent victims of adverse reactions should be precluded from being compensated or from demonstrating that the vaccines could be even safer"); see also *Hurley*, 863 F.2d at 1176 n.2 (providing an exhaustive listing of the numerous district court opinions that have found against preemption and three state court opinions that have found for preemption).

¹⁸⁶ See, e.g., Landen, *Federal Preemption and the Drug Industry: Can Courts Co-Regulate?*, 43 FOOD DRUG COSM. L.J. 85, 121 (1988) (favoring preemption and stating that "federal preemption is fully warranted by the federal drug regulatory scheme today"); Note, *A Question of Competence: The Judicial Role in the Regulation of Pharmaceuticals*, 103 HARV. L. REV. 773, 792-93 (1990) (favoring limited preemption and noting that "the judiciary should defer to the institutional superiority of the FDA, and concentrate on ensuring that the FDA has arrived at a reasoned determination based on sufficient information"); Note, *Tort Liability for DPT Vaccine Injury and the Preemption Doctrine*, 22 IND. L. REV. 655, 705 (1989) (favoring preemption and arguing that "[p]reemption of design defect claims would help to alleviate the crisis in vaccine litigation and foster the national objective to prevent the spread of pertussis disease."); Comment, *Federal Preemption and the FDA: What Does Congress Want?*, 59 U. CIN. L. REV. 263, 283 (1989) (disapproving of preemption: "Blanket immunity to drug manufacturers can work to the detriment of injured plaintiffs and has far too serious consequences to be considered by the courts without an express indication that such situations are acceptable to Congress.").

¹⁸⁷ See, e.g., ARK. STAT. ANN. § 16-116-105 (1987); KAN. STAT. ANN. § 60-3304(a) (1983); TENN. CODE ANN. § 29-28-104 (1980) (recognizing that a manufacturer's or supplier's compliance with governmental regulations constitutes either evidence or a rebuttable presumption that a product is not unreasonably dangerous).

¹⁸⁸ 651 F. Supp. 993 (E.D. Tex. 1986), *rev'd*, 863 F.2d 1173 (5th Cir. 1988).

[T]he comprehensiveness of the FDA regulation as to DPT labeling evidence a preemptive intent to occupy the field and precludes state regulation.

... The contents and wording of these product inserts are extensively regulated and controlled by the FDA. Furthermore, the language in the product insert cannot be used or changed without prior FDA approval. Thus, the comprehensive nature of the FDA regulations evidences preemptive intent to establish implied preemption as to the labeling/warning of DPT in the present case.¹⁸⁹

The public's interest in a uniform regulatory scheme has been addressed on several occasions by the FDA.¹⁹⁰ Concerns that manufacturer liability for common law tort claims may have regulatory consequences that ultimately deny consumers access to important products have also been discussed in many contexts.¹⁹¹

It appears that most courts, believing that the federal regulations establish only minimum regulatory standards,¹⁹² will reject manufacturers' preemption arguments. Choosing to minimize the effect that denying preemption will have on undermining the federal regulatory scheme,¹⁹³ they will instead focus upon their reluctance to deprive injured plaintiffs of a civil remedy.¹⁹⁴ This attitude will force AIDS vaccine manufacturers who wish to make the preemption argument to decide whether to seek review of their preemption claims by the Supreme Court. As this is a forum in which the presumption against federal preemption has consistently been recognized, manufacturers are not likely to be successful.¹⁹⁵

¹⁸⁹ *Id.* at 999 (footnote omitted).

¹⁹⁰ See 51 Fed. Reg. 8181 (1986) (noting that conflicting state requirements "would interfere with the accomplishment of the FDA's objective to bring consistency and uniformity to the marketplace"); 50 Fed. Reg. 51403 (1985) (noting that the FDA seeks to further a "well-established policy of promoting uniformity in the area [of drug labeling]").

¹⁹¹ See *supra* notes 78, 83 & 110 and accompanying text.

¹⁹² See *Abbot*, 844 F.2d at 113; *Kociemba v. G.D. Searle & Co.*, 680 F. Supp. 1293, 1299 (D. Minn. 1988).

¹⁹³ Courts have specifically downplayed the importance of maintaining uniformity in the regulatory scheme. See *Graham*, 666 F. Supp. at 1493 (urging that "[u]niformity is a goal to be achieved in the interest of more fully protecting citizens from unsafe products—it is *not* to be achieved by sacrificing public health").

¹⁹⁴ See *Abbot*, 844 F.2d at 1112 (noting that since no federal remedy exists, the presumption against preemption is greater); *Wack v. Lederle Laboratories*, 666 F. Supp. 123, 127-28 (N.D. Ohio 1987) ("The Court is also reluctant to hold implied preemption applies to the plaintiffs' design defect, inadequate warnings and punitive damage claims because such action would effectively deprive the plaintiffs of any civil remedy.").

¹⁹⁵ "[F]ederal regulation of a field of commerce should not be deemed preemptive

C. State Legislative Efforts: The California Model

In 1986, after determining that potential AIDS vaccine manufacturers needed incentives to bring their products to market, the California Assembly enacted legislation that would eventually provide assistance in both the clinical testing and the marketing phases of vaccine development. This legislation may serve as a model for other states hoping successfully to mobilize manufacturers in the AIDS vaccine effort.

The California legislation attempted to facilitate vaccine development in a number of ways.¹⁹⁶ First, it gave a state regulatory body, the Food and Drug Branch (FDB) of the California Department of Health Services, the necessary resources to oversee clinical testing by up to three vaccine manufacturers once approval by either the federal FDA or FDB¹⁹⁷ had been granted.¹⁹⁸ Sec-

of state regulatory power in the absence of persuasive reasons—either that the nature of the regulated subject matter permits no other conclusion, or that the Congress has unmistakably so ordained.” *Florida Lime*, 373 U.S. at 142; see also *supra* note 182.

¹⁹⁶ See CAL. HEALTH & SAFETY CODE § 199.45(o) (West Supp. 1990).

¹⁹⁷ See *id.* § 199.57(a). The legislative findings that prefaced the 1987 amendments to California’s AIDS programs laws are instructive in detailing the legislature’s motivation for permitting parallel state regulation of AIDS vaccine clinical trials:

(a) California has a strong interest in facilitating and expediting the clinical testing of AIDS drugs. At the same time, California has an interest in ensuring that such testing is performed only under carefully considered, developed and recognized medical protocols.

(b) The State Department of Health Services already has the authority to approve new drug applications pursuant to Section 26670 of the Health and Safety Code and to permit investigational use of new drugs by qualified investigators pursuant to Section 26674 of the Health and Safety Code where the drug is manufactured and used only within the state.

(c) To facilitate and expedite the development of AIDS drugs, California manufacturers who are developing AIDS drugs should be offered the alternative of applying to the State Department of Health Services for permission to conduct clinical trials and for approval of new drug applications.

(d) The Department of Health Services has adopted the regulations of the federal Food and Drug Administration (FDA) to implement Sections 26670 to 26680, inclusive, of the Health and Safety Code. As much as possible, the protocols for investigating new drugs under Section 26679 of the Health and Safety Code shall be similar to those approved by the FDA, so that the data acquired in such investigations may also be submitted to the FDA under Section 505(i) of the federal Food and Drug Act (21 U.S.C. § 355(i)).

(e) It is the intent of the Legislature that the procedures in Sections 26670 to 26680, inclusive, of the Health and Safety Code be utilized to supplement federal procedures to the maximum extent possible under federal law to facilitate the development and testing of AIDS-related drugs and that they

ond, the statute: (1) appropriated research monies for the subsidization of AIDS clinical vaccine trials; (2) created an AIDS Vaccine Victims Compensation Fund (the fund);¹⁹⁹ and (3) guaranteed that if fewer than 500,000 units of vaccine were sold, the state would purchase the difference between the actual number sold and 500,000 units of vaccine at a maximum price of \$20 per unit.²⁰⁰ Although early versions of the statute specifically addressed the issue of potential manufacturer liability, codifying a restrictive application of comment k,²⁰¹ this portion of the statute has since been repealed.²⁰² The legislature has instead created an AIDS Vaccine Injury Compensation Policy Review Task Force (the task force)²⁰³ to study and make recommendations on the process of compensating victims through the fund, the procedures for operation of the fund, the method and amount of manufacturer payment into the fund, and "the procedural relationship between a

be utilized, to the extent feasible, in cooperation with the FDA.

Id. historical and statutory notes.

¹⁹⁸ *See id.* § 199.47(e).

¹⁹⁹ Unlike the federal scheme, individuals do not have to go through the state compensation program before seeking a remedy directly from the manufacturer. This may prove to be problematic since individuals are not deterred from suing manufacturers, but will instead bring their claims in the forum likely to award the greatest compensation.

²⁰⁰ *See id.* § 199.51.

²⁰¹ The standards for manufacturer liability were those set out in *Kearl v. Lederle Laboratories*, 172 Cal. App. 3d 812, 218 Cal. Rptr. 453 (1985). *See supra* text accompanying notes 88-90, and 112-141 (discussing the restrictive application of comment k).

²⁰² Section 199.49 was repealed by 1988 Cal. Stat. ch. 1555, § 3.

²⁰³ CAL. HEALTH & SAFETY CODE § 199.50(n)(1)-(5) (West Supp. 1990). The composition of the 14 member task force is as follows:

10 members appointed by the Governor, of which two shall be from a list provided by the California Trial Lawyers Association, one from the State Department of Health Services, the Director of Finance, one unspecified member, and one attorney with experience and expertise in products liability and negligence defense work, two representing recognized groups which represent victims of vaccine induced injuries or AIDS victims, or both, and two representing manufacturers actively engaged in developing an AIDS vaccine. In addition four Members of the Legislature or their designees shall be appointed to the task force, two of which shall be appointed by the Speaker of the Assembly and two of which shall be appointed by the Senate Rules Committee. The chairperson of the task force shall be appointed by the Governor from the membership of the task force.

Id.

potential victim's claim through the fund and a court claim made against the manufacturer."²⁰⁴

Given the broad spectrum of interests represented on the task force, there is no reason to expect that any future recommendations made to the legislature with respect to manufacturer liability will be unduly burdensome. Presumably the broad protections established by the California Supreme Court in *Brown v. Superior Court*²⁰⁵ will guide legislative action in this area. In addition, the other guarantees of this statute, in particular the provision establishing an insured market for potential vaccine products, will certainly serve as direct incentives for manufacturers: "By guaranteeing a minimum market, California will enable manufacturers to spread their fixed costs over a greater number of units, thus lowering the average cost per unit."²⁰⁶

It is too early to know whether the California statute will speed development, limit manufacturer liability, and enable consumers to have access to a beneficial vaccine, or will put California on a collision course with the FDA. So far, the FDA has indicated that it will accept California trial data, yet in truth, the FDA may not be enamored of sharing responsibility with the states. In describing the FDA's position on the aggressive approach by California, one FDA employee noted that "sponsors would suffer, perhaps, from not having FDA input at an earlier stage."²⁰⁷ Another noted that "[t]here is a point to be gained through a more coordinated approach to the entire effort."²⁰⁸ Although it does not appear that the FDA is overly enthusiastic about working with the states in their vaccine efforts,²⁰⁹ it is heartening to see that concern over

²⁰⁴ *Id.* § 199.50(n)(4).

²⁰⁵ 44 Cal. 3d 1049, 751 P.2d 470, 245 Cal. Rptr. 412; see also *supra* notes 102-110 and accompanying text.

²⁰⁶ Comment, *supra* note 153, at 963.

²⁰⁷ Okie, *California Seizes Initiative in Drug Testing; State's Aggressive Approach to Trials of AIDS Vaccines Has FDA Looking Over Its Shoulder*, Wash. Post, Apr. 10, 1990, at A21, col. 1 (quoting Janet Woodcock, director of the FDA division that approves studies of AIDS vaccines).

²⁰⁸ *Id.* (quoting Wayne Koff, chief of the vaccine research development branch at the National Institute of Allergy and Infectious Diseases).

²⁰⁹ The FDA is not alone in voicing lukewarm enthusiasm for special legislative efforts to improve prospects for an AIDS vaccine. At least two commentators have criticized such efforts on ethical grounds. See Mariner & Gallo, *supra* note 61, at 24 ("Is it fair to limit the liability of those who produce AIDS vaccines when manufacturers of other products are not protected? Is it fair to help those injured by AIDS vaccines when those with the disease itself receive no special help?").

the AIDS crisis has been persuasive enough to encourage attempts at improving the prospects for a vaccine.

CONCLUSION

The eventual success of efforts to develop an AIDS vaccine will require greater awareness by investigators of the problems associated with the use of human subjects in clinical testing. These problems are made all the more significant by the immense public pressure for progress on AIDS research—pressure that may give rise to human exploitation in the rush to bring a vaccine to the marketplace. Successful vaccine development may also require legislative intervention or greater judicial protection to ensure that the marketplace remains hospitable to manufacturers.

A united effort must be made by manufacturers, regulators, and other interested parties to streamline the process of vaccine development so that a safe and effective product can reach the marketplace quickly.