

ARTICLES

EMERGING PRODUCT LIABILITY ISSUES IN BIOTECHNOLOGY

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INTRODUCTION

Biotechnology is a new technology capable of much good for humankind.¹ Although it should not be feared,² biotechnology is still unfamiliar, even frightening to some.³ One thoughtful commentator

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1. For ease of reference, products manufactured using biotechnological methods will be referred to as "biotech products," "biotech drugs," or "biotech vaccines." Those products made using processes not involving biotechnology will be referred to as "conventional products," "conventional drugs," or "conventional vaccines." These references are not intended to imply that there are necessarily any significant differences in the products themselves.

2. See O'Reilly, *Biotechnology Meets Products Liability: Problems Beyond The State of the Art*, 24 Hous. L. Rev. 451, 460-61, 477-478 (1987).

3. See *id.* at 461-463 and 477-478 (discussing the risks of juror misunderstanding and technology phobia). Issues including those posed by the fictitious "Rutabaga That Ate Pittsburgh" or the real "ice-minus bacteria" are subjects of intense public scrutiny and many publications. See, e.g., Foundation on Economic Trends v. Heckler, 756 F.2d 143 (D.C. Cir. 1985) (ice-minus bacteria); OFFICE OF TECHNOLOGY ASSESSMENT, NEW DEVELOP-

views the risk of product liability as potentially greater for biotech products than for conventional products.⁴ We believe that ample policy reasons exist for not exposing biotech products to a greater risk of product liability and that fears about such products are unfounded.

In this article, we address the question of product liability for biotech drugs. We examine a path-breaking recent decision of the Supreme Court of California that limits strict product liability for a conventionally produced drug⁵ and conclude that it should apply with equal force to biotech drugs. Part I illustrates two hypothetical situations involving biotech products that raise product liability issues which could be confronted by emerging companies. Part II presents an introduction to biotechnology as applied to pharmaceutical products. A better understanding of the technology itself should help one to understand why products manufactured with this technology will ordinarily not have any greater product liability risk than products manufactured conventionally in the pharmaceutical industry. Part III summarizes briefly the federal regulatory structure for biotech drugs and identifies issues excluded from this article because of extensive analysis elsewhere. With the foregoing background, Part IV reviews the most recent statement of product liability law in California, *Brown v. Superior Court*,⁶ to test how issues involving biotech manufactured products might be resolved. Finally Part V examines several emerging product liability issues for pharmaceuticals made using biotechnological processes and discusses the role of courts in addressing these issues.

I. TWO ILLUSTRATIVE CASES

The two following hypothetical cases illustrate the kinds of problems we believe a biotech pharmaceutical company may experience. The first case, involving a recombinantly produced vaccine against AIDS, illustrates the problems of a manufacturer whose technology has enabled it to produce a drug for which there is such demand that unusual

MENTS IN BIOTECHNOLOGY, Part 3, Field-Testing Engineered Organisms: Genetic and Ecological Issues, U.S. Cong., PUB. NO. OTA-BA-350 (1988); Deatherage, *Scientific Uncertainty in Regulating Deliberate Release of Genetically Engineered Organisms: Substantive Judicial Review and Institutional Alternatives*, 11 HARV. ENVTL. L. REV. 203 (1987); Note, *The Rutabaga That Ate Pittsburgh: Federal Regulation of Free Release Biotechnology*, 72 VA. L. REV. 1529 (1986); Note, *The EPA and Biotechnology Regulation: Coping with Scientific Uncertainty*, 95 YALE L. J. 553 (1986). Given the attention such issues command elsewhere, this article concentrates on the rarely discussed but emerging issues of product liability regarding human pharmaceuticals.

4. See O'Reilly, *supra* note 2 *passim*.

5. *Brown v. Superior Court*, 44 Cal. 3d 1049, 751 P.2d 470, 245 Cal. Rptr. 412 (1988) (product liability suit by the daughters of women who used DES while pregnant).

6. *Id.*

procedures are employed to make it available more quickly than would ordinarily occur. The second case presents the dilemma of a manufacturer who has accepted the assistance of a government agency in testing its drug but then is unable to obtain complete and timely information concerning the results of the agency's testing. After describing each case, we will discuss its significant aspects.

We are not aware of any reported cases that involve product liability for prescription drugs or vaccines produced by biotechnology. Given expanded marketing and distribution of products, it is only a matter of time before such drugs are tested by product liability litigation.

A. Vaccine Case

1. FACTS

Manufacturer Inc. ("Manufacturer"), using recombinant DNA techniques, succeeds in developing a vaccine that shows promise of providing protection against the acquired immunodeficiency syndrome ("AIDS"). Manufacturer confers with the Food & Drug Administration ("FDA") on the proper design for human clinical testing to determine whether the vaccine is safe and effective. After extensive discussions, the FDA submits Manufacturer's clinical testing plan to an Advisory Committee of experts from the appropriate medical and scientific disciplines. After a public meeting, encompassing extensive comments of numerous public interest groups, the Advisory Committee recommends to the FDA that Manufacturer's clinical testing plan, based on contemporary medical and scientific knowledge, is reasonable and appropriate, particularly in light of the current AIDS epidemic that the Committee finds to constitute a critical public health hazard.

Based on the advice and findings of the Committee, the FDA promptly authorizes Manufacturer to begin testing the vaccine in human subjects. The plan provides for administration of the vaccine to normal adults who have been determined not to have been exposed to the human immunodeficiency virus ("HIV"), using several state-of-the-art analytical methods. The clinical testing is conducted with several hundred patients over a period of three years, 1989, 1990 and 1991. Clinical tests for vaccines for other viral diseases are typically conducted in populations of at least twice the number of patients and for periods of about 7 years; hence, clinical testing normally would have a wider range and would continue through 1995. In its letter to Manufacturer authorizing the clinical testing, the FDA approves the finding of the Advisory Committee that less extensive testing in this case is justified not merely

because of the apparent safety of the vaccine but also because of the urgency of the AIDS epidemic.

In 1992, at the conclusion of the clinical testing program, Manufacturer submits three years of data to the FDA and requests authority to produce and market the vaccine. The FDA reconvenes the Advisory Committee, which also reviews the data and holds a public meeting. Departing from the usual practice, Manufacturer consents to making public its clinical results so that interested parties may submit comments to the Advisory Committee. The only adverse side effect observed during the testing is a slight rash and fever among less than 1% of those tested. Only 10% of those receiving the vaccine develop AIDS during the three-year testing period. In contrast, 60% of those from an equivalent group not receiving the vaccine develop AIDS during the test period. By the end of 1992, AIDS has spread to a significant proportion of the population in groups that had not been foreseen at high risk. Meanwhile there is no other vaccine or alternative treatment yet developed, although several promising development programs are underway.

In 1993, after nearly 12 months of review, the Advisory Committee recommends and the FDA grants approval for Manufacturer to produce and market the vaccine under a label carrying warnings only against mild rash and fever. At the same time, the U.S. Surgeon General, the American Medical Association, and the National Institutes of Health jointly issue a recommendation that all persons between the ages of 10 and 75 who are in good health receive the vaccine. In response, Congress creates a national vaccination program leading to an authorization of public (government) purchase of sufficient vaccine from Manufacturer to vaccinate 200 million people. The vaccine will be made available without charge through private health care providers, the armed services, public health agencies, and government clinics established all over the country. It is estimated that approximately 50 million people per year will be vaccinated. Manufacturer agrees to provide the vaccine at a price which it estimates will return a profit of \$1 per vaccination.

In 1994, the second year of the vaccination program, participants in the clinical testing who were vaccinated in 1989 begin reporting adverse reactions that prompt further study. It becomes evident that the antibodies produced in response to the vaccine, although generally effective in preventing AIDS, also suppress certain other antibodies normally conferring protection against common viral and bacterial infections. By the end of 1996, approximately 30% of those vaccinated in 1989 and 1990 develop a variety of viral and bacterial diseases which range in severity from mild rashes and fever to conditions similar to

AIDS itself. During 1995, 1996, and 1997, cases of death, paralysis and other severe conditions are reported in nearly one hundred persons who received the vaccine during the clinical testing program. In 1997, a class action is filed against Manufacturer in federal district court on behalf of all those who have received the vaccine. The plaintiffs allege failure to comply with the requirements of the Food, Drug and Cosmetic Act, breach of warranty, and strict products liability. At the trial, experts testify that the side effects would have been discovered had the usual standard of vaccine testing been followed.

2. DISCUSSION

As illustrated by this case, biotechnology is often able to address significant societal problems not easily solved by conventional techniques; many of the young emerging biotechnology companies could face the type of situation presented in this hypothetical.

The facts suggest that the manufacturer has done all it reasonably can to determine the safety of its product. The FDA's review process is also a thorough one, going to extraordinary lengths⁷ to involve the best scientific and medical opinion available. The FDA review process normally involves a balancing of the risk presented by a drug against its benefit.⁸ In this example, the FDA is presented as requiring less extensive clinical trials than with a conventional vaccine as a result of this balancing process.

In the opinion of the "experts," the risk of harm from the vaccine appears small, particularly in light of the urgent need. With the information available to it the manufacturer provides appropriate warnings. Less extensive testing produces a smaller data base of experience than is usually the case, a situation which is worsened here because the product is provided to an unusually large population. In this kind of situation, it is predictable that there will be some unanticipated side effects from the vaccine, but the nature and severity of these side effects would not be foreseeable. In retrospect, it becomes apparent that if "normal" testing had been conducted, the particular side effect would more likely have turned up. Unfortunately, the previously unrevealed side effect is severe, likely to result in claims for substantial damages.

7. In this hypothetical, the FDA has gone to unrealistic lengths, but we present them in this way to eliminate the issue of inadequate FDA review as an indirect cause of injury.

8. H. GRABOWSKI & J. VERNON, THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS 9-10 (American Enterprise Institute for Public Policy Research, 1983). In the authors' experience, the balancing process includes consideration of the severity of the illness and the availability of alternative therapy.

This example presents a likely dilemma for a biotechnology company. The biotech vaccine presents a significant product liability risk. However, the actual risk is not the one which might have been expected. Generally, the risk of vaccines is that the vaccine will cause the disease against which protection is sought.⁹ In this hypothetical situation, people were not injured by getting AIDS from the biotech vaccine. Instead, the risk of causing unknown, life threatening side effects was increased by rushing the product to market in order to address an urgent societal need.

The real issue is who should pay for the injuries? Should the manufacturer? Although it did not fulfill the normally required standards for FDA approval, it did a reasonable job under the circumstances. Should the individuals (or their insurance companies) bear the cost alone? They surely were guilty of no wrong and were unable to influence the development and review process on which they should have been able to rely. Perhaps society as a whole should bear the burden. After all, the government decided to relax the stringent FDA clinical testing requirements for this vaccine, and, without such governmental intervention, the manufacturer would have waited for more extensive clinical data, and thus decreased the risk of liability.

In one sense the issues raised by this case have nothing to do with biotechnology. Any vaccine that holds promise in preventing AIDS, regardless of the technology used to produce it, would likely be dealt with by the FDA in the same manner as here. An insufficient amount of clinical data here prevented a determination of the vaccine's side effects. The inadequacy of the data resulted from the abnormally short testing program rather than from the vaccine's method of manufacture. The special relevance of the case to biotechnology is that biotech pharmaceutical companies are more likely than conventional pharmaceutical companies to confront these issues because biotechnology promises treatment of important diseases that conventional technologies have thus far not been able to address. Any technology that can produce important new therapies would confront these issues. Biotechnology just happens to be more capable of producing these therapies.

9. See *infra* notes 33-35.

B. Unreported Third Party Reactions

1. FACTS

Sponsor Inc. ("Sponsor") uses recombinant DNA techniques to produce a naturally occurring cholesterol dissolving protein ("CDP") that is produced in small quantities in the bodies of normal healthy people. CDP shows promise as a treatment for arterial sclerosis.

Sponsor receives FDA permission to begin clinical testing of CDP. Because of CDP's potential for improving the health of aging officers, the Joint Chiefs of Staff direct the U.S. Army to conduct clinical tests with Army officers, many of whom suffer from arterial sclerosis attributable to the Army diet.

CDP would be Sponsor's first product. Concerns in the financial community over the economic effects of products liability on the recombinant DNA industry have severely limited the capital available to Sponsor for product development. Hence, Sponsor agrees to supply the Army with CDP for testing at Army hospitals in the hope that sufficient evidence to support approval will thereby ensue more quickly than from the sole efforts of Sponsor. The Army then designs its own clinical testing program and obtains FDA approval to begin an independent testing program. Because of Army regulations and undisclosed matters of national security, the Army refuses to provide Sponsor with its clinical test results before they are made publicly available.

During its first year of clinical testing, Sponsor treats 500 patients in 10 major university hospitals around the country and observes no significant side effects. In these tests, CDP shows remarkable effectiveness at dissolving cholesterol.

During Army's first year of clinical testing, 2 of 10 officers treated in one Army hospital and 3 of 40 in another Army hospital die. In each case, pursuant to the Army's test protocol, the patient received a dose 10% higher than that which Sponsor administered to its patients. In each Army case, death is attributable to kidney failure. Weakened by years of Army beans, the patients' kidneys were unable to process the abnormally large amount of cholesterol dislodged by the CDP. Rumors of these deaths reach Sponsor, but the Army refuses to confirm or deny the rumors or to provide Sponsor with any information.

In the second year of clinical testing, a doctor at a hospital participating in Sponsor's clinical trial treats a retired Army nurse, now head of nursing for a major private hospital. The nurse dies as a result of kidney failure shortly after receiving CDP. The nurse's surviving spouse (a disabled veteran) and six children bring an action against Sponsor alleging, *inter alia*, that Sponsor's failure to include a warning of the possible side

effect in the instructions to physicians led to physicians' failure to warn of the possible side effect when obtaining informed consent, and hence, is a proximate cause of death. Plaintiffs invoke strict products liability as well as a violation of FDA regulations.

2. DISCUSSION

The second illustration presents a major new therapy for a life threatening condition. Because the barriers to entry for a new pharmaceutical company are great, it may be tempted to embrace opportunities promising the possibility of cheaper, quicker clinical trials. However, doing so causes Sponsor to lose control of its clinical trials, something a pharmaceutical company normally would be unwilling to do. Thus, the product liability problem encountered by Sponsor results not from the technology itself but from the business and economic factors faced by biotech companies such as Sponsor. Limited experience and capital led to Sponsor's difficulties. Product liability resulting from such factors is of just as much concern to a biotech company but does not arise from the technology.

Perhaps Sponsor did not realize the Army would not provide it the information or would not provide additional warnings as it gained experience with CDP.¹⁰ Perhaps it assumed the Army would follow Sponsor's clinical trial design. Perhaps the contractual issues were not dealt with effectively because the collaboration was established on a doctor-to-doctor basis rather than with the "interference" of lawyers.

Sponsor's own clinical tests established the drug's apparent safety. The side effect identified in the Army's clinical tests was unknown and, arguably, unknowable to Sponsor. Sponsor was unable to follow up on the rumors it heard because the Army refused to cooperate. The Army's experience occurred under special circumstances that Sponsor could not have anticipated and that would make unlikely a more determined pursuit of the rumor. Query whether Sponsor discharged its duty of inquiry.

The plaintiff is likely to be particularly appealing to a jury. The case presents the risk of significant potential consequential damages being assessed against Sponsor.

10. In the experience of the authors, a pharmaceutical company generally does not control the content of the informed consent used by the physicians participating in its clinical trials. Although a review board at the hospital where the clinical trials are conducted examines and approves the informed consent to be used, the pharmaceutical company does not necessarily have a great deal of control. Hence, even if the company believes additional warnings are appropriate in the informed consent form, it cannot be assured that the hospital will agree.

II. BIOTECHNOLOGY

A. The Industry¹¹

Biotechnology is not a business even though the term is often used in that way. It is a means of making products. The businesses employing biotechnology are generally organized in traditional ways. The term "biotechnology" may be defined as the use of living organisms to make commercial products.¹² These uses fall into several business categories, including human health care, veterinary medicine, plant agriculture, and others.

The production of naturally occurring human proteins for therapeutic uses was the earliest, and remains the most important, application of biotechnology.¹³ The FDA has approved human growth hormone (normally secreted in humans by the pituitary gland) to treat dwarfism as well as insulin to treat diabetes.¹⁴ Interferons and other lymphokines (protein components of the immune system) as well as monoclonal antibodies that attack specific tumor cells are being developed to combat cancer. Tissue plasminogen activator, which occurs in small amounts in the blood stream, dissolves blood clots and has been approved by the FDA for treatment of myocardial infarctions (heart attacks).¹⁵

Biotechnology is also well suited for the development of vaccines. Vaccines are useful in the prevention of disease by stimulating the body to produce antibodies against the disease. Using recombinant DNA methods, vaccines can be produced that consist only of the immunologically active portion of a pathogenic microorganism or virus, free of the risks of traditional vaccines, which use a weakened or killed form of the pathogen itself.¹⁶

11. This section draws extensively from a pamphlet, INDUSTRIAL BIOTECHNOLOGY ASSOCIATION, WHAT IS BIOTECHNOLOGY? (1984). The authors gratefully acknowledge the assistance and contributions to this part by Sean Johnston (Ph.D. in Molecular Biology, UCLA), a third-year student at Stanford Law School and Edward Hurwitz (B.S. in Biochemistry, Cornell) a third-year student at Boalt Hall, University of California, Berkeley.

12. INDUSTRIAL BIOTECHNOLOGY ASSOCIATION, U.S. BIOTECHNOLOGY: MEETING THE GLOBAL CHALLENGE 2 (1988).

13. See OFFICE OF TECHNOLOGY ASSESSMENT, COMMERCIAL BIOTECHNOLOGY: AN INTERNATIONAL ANALYSIS, U.S. Cong., Pub. No. OTA-BA-218, at 3, 19 (1984).

14. FDA OKs Genentech's HGH; Methionine-Free Forms Loom, McGraw-Hill's Biotechnology Newswatch, Nov. 4, 1985, at 2; As Lilly's Synthetic Insulin Gets FDA OK, Novo, Biogen Join to Clone Their Own, McGraw-Hill's Biotechnology Newswatch, Nov. 15, 1982, at 2.

15. Genentech Stock Rises as FDA Approves Activase, Firm's Recombinant TPA, McGraw-Hill's Biotechnology Newswatch, November 16, 1987, at 1.

16. See WHAT IS BIOTECHNOLOGY?, *supra* note 11, at 12.

Recombinant DNA techniques¹⁷ have widespread application in clinical assays and diagnostic products,¹⁸ including products to detect genetic defects.¹⁹ Many of the same techniques used in human health care are being applied to veterinary medicine.²⁰ Although the application of biotechnology to plant agriculture has proceeded more slowly than in other areas,²¹ recent breakthroughs in plant biotechnology allow modifications of plants to increase crop yield, improve crop quality or reduce production costs.²² In addition, biotechnology is important in a variety of other fields.²³

17. DNA, or deoxyribonucleic acid, and "recombinant DNA techniques" are described in detail in part IIB, *infra*.

18. For example, restriction enzymes that make cuts in DNA at specific sites serve to analyze the DNA from human cells and thus identify gene defects that result in specific inherited diseases. Synthetic DNA sequences are used as "probes" to identify and isolate specific genes contained within clinical samples.

19. One technique, Restriction Fragment Length Polymorphism ("RFLP") analysis uses restriction enzymes (proteins that cleave DNA only at specific sequences) to cut DNA obtained from human cells. These fragments are then separated by size using electrophoresis, the smallest DNA bands migrating closest to the positive pole of an applied current. Utilizing the chemical property that complementary DNA sequences will attach ("hybridize") to each other, a DNA probe (a gene segment with a radioactive isotope incorporated into it) is incubated with the filter containing the electrophoresed restriction fragments. Banding patterns from the test subject that differ from the healthy individual's indicate a genetic mutation that may be responsible for a well-known disease.

Sickle cell anemia and Huntington's disease are two examples of diseases that are now detectable using RFLPs. *See WHAT IS BIOTECHNOLOGY?*, *supra* note 11, at 10.

An entire class of diagnostic products now exist that use monoclonal antibodies. These antibodies, which have either a radioactive or fluorescent particle attached, react with one and only one particular antigen. When the monoclonal antibody reaches its target, it attaches, and an accumulation of the antigen-antibody complexes allows detection by a doctor. Hepatitis B, cancer tumors, and HIV infection that can lead to AIDS are a few examples of the diseases now detectable by monoclonal antibodies.

20. Products are being developed that increase meat or milk production, augment feed efficiency in farm animals, or confer livestock with other economically desirable characteristics via the transfer of selected genes into embryos. *See WHAT IS BIOTECHNOLOGY?*, *supra* note 11, at 12.

21. This may have occurred because less has been known of the biology of plants than of animals or microorganisms such as bacteria or yeast.

22. For example, certain changes can improve plant resistance to disease or pests. Improved plant resistance reduces the need to apply chemical pesticides. Other changes result in improvement of the protein content of seeds used as nutrition for people or animals. Still others can induce crops to make their own natural fertilizers.

23. Lower cost processes are being developed for production of amino acids, industrial enzymes and vitamins. Microorganisms have been adapted for degradation of solid waste and the treatment of waste water. Mineral recovery can be enhanced by use of microorganisms which will dissolve and absorb minerals from ore-containing rock. Recovery of oil is enhanced by use of microorganisms that secrete a substance which forces oil out of oil-bearing rock. There are substantial developments in biomass reactors: microorganisms therein can now produce enzymes that degrade plant materials such as cornstalks or wood chips and thus facilitate conversion of the biomass into energy.

B. The Technology²⁴

Biotechnology is principally a new manufacturing method. As such, it is subject to the same problems of quality control as any other manufacturing method. Aside from these, however, there are no inherent risks for products made using the technology.²⁵ Concerns to the contrary probably exist because of a lack of understanding of the technology.

The term "recombinant DNA" has been defined simply as a method for combining genes.²⁶ Recombinant DNA technology makes it possible for researchers to change the genetic instructions of a living cell in order to produce desirable proteins or other biological macromolecules in large quantities. These changes in instructions are inherited by each succeeding generation of the cell.²⁷

Each living cell contains in its DNA all the information needed to make the organism and carry on its functions, including complete instructions on what proteins to produce. The cell also contains the cellular "machinery" to make the proteins called for by these instructions.²⁸

DNA is a duplex molecule -- a so-called "double helix" -- formed by the joining of two nucleic acid polymers. Each nucleic acid polymer, or "strand", of the DNA molecule is assembled from chemical building blocks called nucleotides.²⁹ It is the specific sequence of nucleotide bases along a strand of DNA that encodes the information needed to produce a protein. A cell's protein synthesis machinery "reads" the sequence of nucleotide bases in groups of three, called "codons." Each of the 64 possible codons (which constitute all the possible combinations of triplet base sequences) corresponds to a particular amino acid or acts as a signal to start or stop protein synthesis.

24. For basic references, see 1 & 2 J. WATSON, N. HOPKINS, J. ROBERTS, J. STEITZ & A. WEINER, MOLECULAR BIOLOGY OF THE GENE (4th ed. 1987); J. WATSON, J. TOOZE & D. KURTZ, RECOMBINANT DNA - A SHORT COURSE (1983); Singer, *Genetics and the Law: A Scientist's View*, 3 YALE L. & POL'Y REV. 315 (1985).

25. See WHAT IS BIOTECHNOLOGY?, *supra* note 11, at 17.

26. U.S. BIOTECHNOLOGY: MEETING THE GLOBAL CHALLENGES, *supra* note 12, at 2.

27. A very few simple organisms such as bacteria and the blue-green algae are composed of simple cells in which all the DNA is distributed inside the cell. These are known as prokaryotic cells. In higher organisms, such as man, within each cell the DNA is contained in a separate inner cellular mass called the nucleus. These are known as eukaryotic cells.

28. The cellular machinery is itself composed of proteins that are encoded by DNA. Once the cell is completely developed, the amount and timing of protein production are regulated both by a variety of interactions within the cell (such as protein/DNA or DNA/DNA interactions) and by noncellular stimuli (such as heat or salt concentrations).

29. Each nucleotide contains a phosphate group linked to a sugar molecule, which, in turn, is joined to one of the following four chemicals: adenine (A), thymine (T), guanine (G), or cytosine (C). These four chemicals are called "nucleotide bases."

Amino acids are the building blocks for the proteins, which, in turn, are the basic units of biological processes and materials. The number and sequence of amino acids helps determine the size and shape of each protein.³⁰

A gene is therefore defined as a particular sequence of nucleotide bases, recognized by the cell's protein synthesis machinery as triplet codons. The sequence of codons in turn specifies the sequence of amino acids for a certain protein. Recombinant DNA techniques³¹ involve the steps of excising a gene from the DNA of one cell or organism, such as the gene for insulin from a human cell, and transferring that gene in a functional form to another cell or organism, such as a bacterium. Desirable genetic constructs are thereby created that have never before existed in nature.

C. Advantages of Biotechnology

Biotechnology permits the large-scale production of proteins that have beneficial uses but occur in only minute quantities in nature. In addition, the production of protein pharmaceuticals by biotechnological processes may have other significant advantages over preparations of such products that are obtained from natural sources. As the following discussion illustrates, in some situations, products of biotechnology may actually be safer than equivalent products made using conventional technology.

30. Some proteins are enzymes (agents that are essential to chemical reactions). Others are structural proteins that build cells and tissues. Still others are the hormones that regulate many of an organism's functions.

31. The term "biotechnology" is broader than recombinant DNA techniques.

Monoclonal antibody technology is also important. Antibodies are proteins produced by the body's immune system to defend against foreign substances. Antibodies have a quality called "specificity" because they are produced in response to a particular foreign agent (bacteria, virus, or other substance). They will subsequently interact only with that particular agent. There are now techniques that enable a cell to continuously produce a particular antibody in large quantities. Such cells are called "hybridomas." The antibodies they produce are called "monoclonal antibodies." As described above, monoclonal antibodies have proven useful both as therapeutics and as diagnostic reagents.

Biological process technology is necessary in order to actually make useful proteins in commercial quantities. Microorganisms, such as bacteria or yeast that have been genetically modified to produce a helpful protein, are grown in fermenters containing special nutrients necessary for the cells' growth. Temperature, pressure, and acidity must be meticulously controlled so that the microorganisms grow and reproduce. After a time, the microorganisms begin to produce the sought-for protein. When that phase is completed, the microorganisms may be harvested from the fermenters. In any event, the protein must ultimately be separated from the microorganisms and other debris and purified to the requisite standard. Complex human proteins may be produced in a similar way by using mammalian host cells instead of bacteria or yeast.

Conventional vaccines, for example, carry the risk of causing the disease in some people because the vaccines are made of killed or attenuated (weakened) viruses or bacteria that cause the disease. Conventional vaccines are designed so that, theoretically, enough activity remains to stimulate the immune system to make antibodies to the disease, but not enough activity remains to cause the disease.³² In fact, however, there is a risk that sufficient virulence remains in the virus or bacteria to cause the disease.³³

The same risk does not exist for vaccines produced via recombinant DNA techniques. Using those techniques, only the portion of the viruses or bacteria that stimulates the immune system is produced, not the portion that would be infectious.³⁴

By way of analogy, imagine the design of a vaccine against being shot. A conventional vaccine would have been produced by inoculating the patient with a small amount of loaded gun in which the firing pins were either removed or bent so as to be inoperative. But sometimes a production worker misses a gun so that an operative gun is included in the vaccine. With recombinant DNA techniques, a loaded gun is not used at all. Instead a metallic shape is made that looks like a gun but is not. Thus, there is no way the recombinant gun can fire, even though the body's immune system identifies it as a gun and accordingly produces the appropriate antibodies.³⁵ The HIV virus is recognized as such by the immune system because of a particular three-dimensional structure on the surface of the virus. A recombinant DNA vaccine would produce only that portion of the virus but no other. The vaccine would not contain either killed or attenuated virus, hence obviating the risk that it could cause AIDS.

The potential advantage of recombinant DNA techniques over conventional processes finds apt illustration in the following actual case. One conventional technique for producing a pharmaceutical involves purifying a substance obtained from human tissue. For many years human growth hormone ("hGH"), used to treat pituitary dwarfs, was obtained by purification of material obtained from the pituitary glands of cadavers.³⁶

32. R.A. Lerner, *Synthetic Vaccines*, SCIENTIFIC AMERICAN, February 1983 at 66.

33. See RECOMBINANT DNA - A SHORT COURSE, *supra* note 24, at 238-39.

34. *Id.*

35. There are parallels and contrasts between the gun example and the hypothetical vaccine against AIDS (i.e. Illustrative Case A in Part I). The example above involves only a harmless unloaded gun. Illustrative Case A involves an unloaded gun that helps prevent AIDS but unexpectedly suppresses the fire of other antibodies.

36. A.S. HARTREE, *Preparation and Properties of Human Growth Hormone*, in HUMAN GROWTH HORMONE 1 (1972).

In the mid-1980's it was discovered that some children so treated had contracted a disease known as Creutzfeldt-Jakob's Disease ("CJD"). CJD is caused by a so-called slow virus that attacks the nervous system but is undetectable for 10 or 15 years after exposure. By the time symptoms appear, the disease has advanced so far that the brain is said to look like Swiss cheese.³⁷

It turned out that the process of purifying hGH failed to eliminate the virus particle that causes CJD, which had evidently infected some of the individuals from whom pituitary glands were obtained.³⁸ Thus, some batches of therapeutic hGH contained the CJD causing virus.

The production of recombinant hGH without using human pituitary glands precludes such a contamination from adventitious viruses or bacteria.

D. Does Biotechnology Present Unusual Risks?

Although the techniques of biotechnology are new, many of its products have a long history. Insulin and human growth hormone have been produced for years using conventional technology. Moreover, the pharmaceutical industry, which markets these products, is closely regulated and must comply with elaborate standards of quality control. Indeed, vaccines produced by biotechnology should prove their superiority to conventional vaccines by minimizing the risk of causing disease.

Although some apprehension persists about the new whiz kid on the block,³⁹ there should be little reason today to fear dangerous "mutations." As for contamination in drug manufacturing processes, it is an old problem.

37. P. Brown, *Potential Epidemic of Creutzfeldt-Jakob Disease from Human Growth Hormone Therapy*, 313 NEW ENG. J. MED. 728 (1985); Gribbs, C.J. Jr., *Clinical and Pathological Features and Laboratory Confirmation of Creutzfeldt-Jakob Disease in a Recipient of Pituitary-Derived Human Growth Hormone*, 313 NEW ENG. J. MED. 734 (1985).

38. *Id.*

39. For example, in Zoon, *The Impact of the New Biotechnology on the Regulation of Drugs and Biologics*, 41 FOOD DRUG COSM. L. J. 429, 431-32 (1986), the author states that given the "meager" experience with continual administration of drugs in humans over many months or years, "the possibility of novel toxicities remains a nagging concern." Moreover, "it is important to ensure that the quality assurance within the manufacturing process is adequate to reduce the possibility of mutations in the coding sequence of the cloned gene during fermentation, which might give rise to an altered drug." Another risk is microbial or viral contamination in the product. "Protein contamination can come from host cells, culture medium constituents, reagents used for purification, and product-related impurities." See also *supra* note 3.

III. ISSUES EXCLUDED FROM THIS ARTICLE BECAUSE OF EXTENSIVE ANALYSIS ELSEWHERE

In the text and footnotes of section A of this part, we will identify the several agencies that regulate various aspects of biotechnology. Because these topics are treated extensively elsewhere we will not discuss them in detail. In Section B, we will discuss briefly the possibility that product liability law for agricultural products may not necessarily develop in the same way as for human pharmaceutical products.

A. Federal Regulation of Drugs

Federal statutes, regulations, and administrative agencies govern various aspects of biotechnology.⁴⁰ These agencies have articulated a Coordinated Framework for the Regulation of Biotechnology.⁴¹ Drugs

40. Industrial chemicals produced by genetically engineered organisms are regulated by the Environmental Protection Administration (EPA) under the Toxic Substances Control Act (TSCA), 15 U.S.C § 2601-2629 (1982), and regulations thereunder. EPA's general policy statement is found in 51 Fed. Reg. 23,313 (1986).

Biological pesticides are regulated by the EPA under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 U.S.C. §§ 136-136y (1982), and regulations thereunder. Regulations cover distribution, sale and use of pesticides, including field testing. The Department of Agriculture has additional authority under the Federal Plant Pest Act, 7 U.S.C. §§ 147a, 149, 150aa-150jj (1982); The Plant Quarantine Act, 7 U.S.C. § 154 (1982); and the Virus-Serum Toxin Act of 1913, 21 U.S.C. § 151-157 (1982). It has issued a general policy statement found in 51 Fed. Reg. 23,336 (1986).

Plants and plant products are regulated by the U.S. Department of Agriculture (USDA) under the Federal Plant Pest Act, and regulations thereunder, and the Plant Quarantine Act, and regulations thereunder. Plants and plant products that are used for food or feed purposes are also regulated by the FDA under the Food Drug and Cosmetic Act. Under the Federal Plant Pest Act, special regulations require a permit to import, move interstate, or release into the environment certain genetically engineered organisms or products. 52 Fed. Reg. 22,892 (1987).

Many veterinary biological products are regulated by the USDA under the Virus-Serum Toxin Act of 1913, and regulations thereunder. Other such products may be regulated by the FDA's Center for Veterinary Medicine.

Recombinant DNA research sponsored or performed by the National Institutes of Health (NIH) must comply with NIH guidelines. 49 Fed. Reg. 46,266 (1984). Many institutions not receiving NIH funding voluntarily comply with the NIH guidelines.

Federally funded agricultural biotechnology research is overseen by USDA, which has published notice of proposed guidelines. See 51 Fed. Reg. 23,367 (1986); 52 Fed. Reg. 29,800 (1987) (modified NIH guidelines pending adoption of USDA guidelines).

41. Office of Science and Technology Policy, Coordinated Framework for the Regulations of Biotechnology, 51 Fed. Reg. 23,302 (1986). See Withers, *Biotechnology: An Industry Perspective*, 34 U. KAN L. REV. 665 (1986); Karny, *Regulation of the Environmental Applications of Biotechnology* (1987) (paper presented to ABA, 17th Annual Conference on the Environment, May 7, 1988). A Biotechnology Science Coordinating Committee is responsible for coordination of scientific policy and reviews. (Its members include representatives of FDA, NIH, EPA, U.S. Dep't. of Agriculture, and the National Science Foundation.) Under this framework, the agencies are expected to operate their programs "in an integrated and coordinated fashion." 51 Fed. Reg. 23,303 (1986).

produced by biotechnology are regulated by the FDA (Food and Drug Administration) under the Food, Drug & Cosmetic Act⁴² and regulations thereunder.⁴³ FDA has issued a general policy statement governing its regulatory practices.⁴⁴ Ordinarily, it takes 5-10 years from the beginning of clinical research to premarketing, to obtain approval of human drugs.⁴⁵

Since the emerging issues relate essentially to prescription drugs and vaccines, we exclude from the scope of this article over-the-counter drugs and products for which package inserts must be given directly to the patient.⁴⁶

The agencies state a goal that "[t]o the extent possible, responsibility for a product use will lie with a single "agency" or "lead agency." *Id.* (This statement sometimes seems more an expression of hope than a reality.)

42. 21 U.S.C. §§ 301-392 (1982).

43. 21 CFR, Parts 1, 71, 171, 314, 500, 571, 807. See Areen, *Regulating Human Gene Therapy*, 88 W. VA. L. REV. 153 (1985); Barkstrom, *Recombinant DNA and the Regulation of Biotechnology: Reflections on the Asilomar Conference, Ten Years After*, 19 AKRON L. REV. 81 (1985); Gore & Owens, *The Challenge of Biotechnology*, 3 YALE L. & POL'Y REV. 336 (1985); Gully & Bird, *Regulation of the Biomedical Applications of Recombinant DNA Research*, 19 U. RICH. L. REV. 1 (1984); Jaffe, *Inadequacies in the Federal Regulation of Biotechnology*, 11 HARV. ENVTL. L. REV. 491 (1987); Mahinka & Sanzo, *Biotechnology Litigation and Federal Regulation: Status and Implications*, 42 FOOD DRUG COSM. L. J. 500 (1987); 2 NOVICK, STEVER & MELLON (ed.), *LAW OF ENVIRONMENTAL PROTECTION*, chapter 18, *BIOTECHNOLOGY* (1987). See also Bonk, *FDA Regulation of Biotechnology*, 43 FOOD DRUG COSM. L.J. 67 (1988); McNamara, *FDA Regulation of Food Substances Produced by New Techniques of Biotechnology*, 42 FOOD DRUG COSM. L.J. 50 (1987).

44. 51 Fed. Reg. 23,309 (1986).

45. The Commissioner of Food and Drugs, Dr. Frank E. Young, has recently stated that "the FDA is taking every action possible to assure that the highest priority is placed on reviewing applications for products intended to treat, cure, or prevent AIDS and AIDS-related diseases". Young, *Promoting Drug Development Against AIDS and the HIV Infection*, 43 FOOD DRUG COSM. L.J. 215, 216 (1988). See also Report of the Presidential Commission on the Human Immunodeficiency Virus Epidemic 47-48 (June 1988).

46. E.g., oral contraceptives. See 21 C.F.R. § 310.50; Pharmaceutical Mfrs. Ass'n. v. Food & Drug Administration, 484 F. Supp. 1179, 1186 (D. Del.), aff'd, 634 F.2d 106 (3d Cir. 1980). See also *infra* note 72.

This article focuses on strict liability in tort or exceptions from strict liability. Except as specifically discussed (for example in connection with comment k to section 402A of the Restatement (Second) of Torts), we exclude from the scope of this article issues of negligence, warranty, misrepresentation, or other possible grounds for manufacturer liability. We assume for discussion that the liability of manufacturers of genetically engineered products for damages caused by negligence, breach of warranty (to whomever the court decides the warranty runs), misrepresentation or other grounds, will be measured according to the same or comparable standards by which the liability of other manufacturers is measured. For a discussion of basic principles, see J. GIBBS, I. COOPER & B. MACKLER, *BIOTECHNOLOGY & THE ENVIRONMENT: INTERNATIONAL REGULATION*, 173-86 (1987); Birnbaum & Lichtman, *Biotechnology: The Lessons to be Learned from Drug Liability Cases*, in *FOURTH ANNUAL (BIOTECHNOLOGY LAW INSTITUTE* 120 (1988); Dunne, *Products Liability for Biotechnology Products*, *id.*, at 165; Wallach, *A Products Liability Primer*, 20 U.C.C. L.J. 40 (1987) (discusses negligence, breach of warranty, strict liability, disclaimers, substituted remedy clauses, damage limitation clauses, loss sharing, and multidefendant problems).

B. Agricultural Products

The development of product liability law for genetically engineered agricultural products is a subject that deserves separate treatment. In some aspects, this area of the law may develop in a way parallel to that governing human pharmaceuticals. In others, there may be significant contrasts. For example, the public health and social utility reasons that led the court in the *Brown* case,⁴⁷ to insulate prescription drug manufacturers from strict liability, provided the drugs are properly prepared and accompanied by adequate warnings, may not extend to agricultural pesticides or genetically engineered plants. Moreover, there are differences in the regulatory structure. For example, with human pharmaceuticals, the manufacturing process occurs in a closely contained system and does not involve releases of organisms into the environment. There are substantial regulations governing manufacture of pharmaceuticals that are not paralleled in the regulation of agricultural products. More agencies govern agricultural products because they are much more diverse and include transplants, pesticides, herbicides, and fertilizers.

To focus discussion on human pharmaceuticals, we exclude agricultural products from the scope of this article.⁴⁸

IV. PRODUCT LIABILITY FOR A BIOTECH DRUG UNDER BROWN V. SUPERIOR COURT

In a crucial new case, the Supreme Court of California concluded that "a drug manufacturer's liability for a defectively designed drug should not be measured by the standards of strict liability" and that "because of the public interest in the development, availability, and reasonable price of drugs, the appropriate test for determining responsibility is the test stated in comment k" to section 402A of the Restatement (Second) of Torts.⁴⁹ In section A of this part, we review the *Brown* decision and its application of comment k. In section B, we analyze the

A plaintiff who is injured or suffers adverse side effects from a drug may choose to sue persons other than or in addition to the manufacturer, for example, physicians and pharmacists. Whether physicians furnish a "service" or a "product" and whether they are subject to strict liability are questions excluded from the scope of this article. See Willig, *Physicians, Pharmacists, Pharmaceutical Manufacturers: Partners in Patient Care, Partners in Litigation*, 37 MERCER L. REV. 755 (1986). Likewise, issues concerning the liability of pharmacists are excluded. See Brushwood & Abood, *Strict Liability in Tort: Appropriateness of the Theory for Retail Pharmacists*, 42 FOOD DRUG COSM. L.J. 269 (1987).

47. *Supra* note 5.

48. For a discussion of issues concerning plant tissue culture, genetic engineering, and microbial pesticides, see Jaworski, *Biotechnology: Prospects and Perspectives*, 34 U. KAN. L. REV. 655 (1986).

49. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1061, 751 P.2d 470, 477, 245 Cal. Rptr. 412, 418 (1988).

policy considerations underlying the *Brown* decision and their applicability to biotech drugs.

A. The *Brown* Decision

The *Brown* case did not deal with a prescription drug produced by recombinant DNA technology. It involved claims by numerous plaintiffs that the defendant manufacturers of DES (diethylstilbestrol) made a drug that "was unsafe for use in preventing miscarriage and resulted in severe injury" to each plaintiff *in utero* when her mother ingested it.⁵⁰ In *Brown*, the California Supreme Court upheld the trial court's pretrial ruling that the manufacturers "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."⁵¹

Comment k, on which the court relied, provides:

k. *Unavoidably unsafe products.* There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. An outstanding example is the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it *unreasonably* dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician. It is also true in particular of many new or experimental drugs as to which, because of lack of time and opportunity for sufficient medical experience, there can be no assurance of safety, or perhaps even of purity of ingredients, but such experience as there is justifies the marketing and use of the drug notwithstanding a medically recognizable risk. The seller of such products, again with 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.⁵²

The court noted that "[w]hile there is some disagreement as to [the] scope and meaning" of comment k, "there is a general consensus that, although it purports to explain the strict liability doctrine, in fact

50. *Id.* at 1055, 751 P.2d at 473, 245 Cal. Rptr. at 414.

51. *Id.* at 1055, 751 P.2d at 473, 245 Cal. Rptr. at 415.

52. *Id.* at 1059, 751 P.2d at 475, 245 Cal. Rptr. at 416-17.

the principle it states is based on negligence."⁵³ "Comment k has been adopted in the overwhelming majority of jurisdictions that have considered the matter."⁵⁴ In applying comment k, the court discussed the underlying policy considerations for and against strict liability and concluded (1) strict liability should not apply to design defects in prescription drugs⁵⁵ (2) strict liability should not apply to a failure to warn of the risk of side effects inherent in a drug if the risk was unknown and could not have been known despite the application of scientific knowledge available at the time of distribution of the drug,⁵⁶ and (3) elimination of strict liability for a drug does not require a preliminary judicial determination that the drug is unavoidably dangerous.⁵⁷

B. Policy Considerations Underlying the *Brown* Decision

Although only the issue of conventional drugs was before the court, the policies articulated in the decision apply equally well to biotech drugs. In this section, we review the court's treatment of the following issues: design defects and the rejection of the "benefit v. risk" test; failure to warn; rejection of case-by-case judicial determinations;

53. *Id.* at 1059, 751 P.2d at 475, 245 Cal. Rptr. at 417 (citations omitted).

54. *Id.* (citations omitted). The court stated that:

Comment k has been analyzed and criticized by numerous commentators (E.g., Schwartz, *Unavoidably Unsafe Products Clarifying the Meaning and Policy Behind Comment k*, 42 Wash. & Lee L. Rev. 1139, 1141 (1985); McClellan, *Drug Induced Injury*, 25 Wayne L. Rev. 1, 2 (1978); Kidwell, *Duty to Warn: A Description of the Model of Decision*, 53 Tex. L. Rev. 1375, 1377-1378 (1975); Merrill, *Compensation for Prescription Drug Injuries*, 59 Va. L. Rev. 1, 50 (1973)). That is, comment k would impose liability on a drug manufacturer only if it failed to warn of a defect of which it either knew or should have known. This concept focuses not on a deficiency in the product -- the hallmark of strict liability -- but on the fault of the producer in failing to warn of dangers inherent in the use of its product that were either known or knowable -- an idea which 'rings of negligence,' in the words of [*Cronin v. J.B.E. Olson Corp.*, 8 Cal. 3d 121, 132, 104 Cal. Rptr. 433 (1972)].

Id. at 1059, 751 P.2d at 475-76, 245 Cal. Rptr. at 417 (footnote omitted). The court also noted that:

[O]ne commentator has pointed out that at the 1961 [ALI] meeting Dean Prosser proposed an exemption even broader than that suggested by the motion to exempt prescription drugs from strict liability. (Page, *Generic Product Risks: The Case Against Comment k and for Strict Tort Liability* (1983) 58 N.Y.U. L.REV. 853, 863, 866.)

Id. at 1057 n.2, 751 P.2d at 475 n.2, 245 Cal. Rptr. at 416 n.2. See also Note, *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 (1984).

55. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1061, 751 P.2d 470, 245 Cal. Rptr. 412, 418 (1988).

56. *Id.* at 1065, 751 P.2d at 477, 245 Cal. Rptr. at 421.

57. *Id.* at 1067-69, 751 P.2d at 480, 245 Cal. Rptr. at 422-24.

and rejection of the "consumer expectation" test.⁵⁸ Then, we discuss the applicability of the court's reasoning to biotech drugs.

1. DESIGN DEFECTS; REJECTION OF BENEFIT V. RISK TEST.

a. Brown Decision.

The court articulated the following six policy issues in deciding that strict liability should not apply to design defects in drugs:

(1) Prescription drugs may be necessary to alleviate pain and suffering or to sustain life. They are distinct from other products, such as construction machinery, which are used to make work easier or to provide pleasure.⁵⁹

(2) "Moreover, unlike other important medical products (wheelchairs, for example), harm to some users from prescription drugs is unavoidable."⁶⁰

(3) The delay involved in withholding a drug from the market "until scientific skill and knowledge advanced to the point at which additional dangerous side effects would be revealed," when added to the delay required for approval from the FDA, "would not serve the public welfare. Public policy favors the development and marketing of beneficial new drugs, even though some risks, perhaps serious ones, might accompany their introduction, because drugs can save lives and reduce pain and suffering."⁶¹

58. In the leading case of *Barker v. Lull Engineering Co.*, 20 Cal. 3d 413, 573 P.2d 443, 143 Cal. Rptr. 225 (1978), which involved a high-lift loader, the Supreme Court of California articulated two alternative tests for determining design defect: The *Benefit v. Risk Test* ("the product's design proximately caused [plaintiff's] injury and the defendant fails to establish . . . that . . . the benefits of the challenged design outweigh the risk of danger inherent in such design") and the *Consumer Expectation Test* (the "plaintiff establishes that the product failed to perform as safely as the ordinary consumer would expect when used as intended in a reasonably foreseeable manner"). See also Edell, *Risk Utility Analysis of Unavoidably Unsafe Products*, 17 SETON HALL L. REV. 623 (1987).

59. *Brown*, 44 Cal. 3d at 1063, 751 P.2d at 478, 245 Cal. Rptr. at 420. The line may not be as bright as the court suggests. Some prescription drugs are used for cosmetic, inconsequential, or imagined ailments. By contrast, an automobile or a lightbulb or a bulldozer could be acutely necessary depending on the circumstances.

Prescription drugs are also distinct from consumer products known by consumers to be "inherently unsafe" such as "sugar, castor oil, alcohol, tobacco, and butter." CAL. CIV. CODE § 1714.45 (1986); RESTATEMENT (SECOND) OF TORTS § 402A, comment i (1965). California's new statutory exemption, § 1714.45, *supra*, was recently applied to sustain a judgment on the pleadings for manufacturers of tobacco products in *American Tobacco Co. v. Superior Court*, ___ Cal. App. 3d ___, 1989 WESTLAW 9049, 1989 Cal. App. LEXIS 102 (1st Dist., February 6, 1989).

60. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1063, 751 P.2d 470, 479, 245 Cal. Rptr. 412, 420 (1988).

61. *Id.*; see e.g., Altman, *Medical Dilemma: Necessary Drugs With Intolerable Dangers*, N.Y. Times, May 3, 1988, at B7. We assume that the court's reference to potentially

(4) "If drug manufacturers were subject to strict liability, they might be reluctant to undertake research programs to develop some pharmaceuticals that would prove beneficial or to distribute others that are available to be marketed, because of the fear of large adverse monetary judgments."⁶²

(5) "Further, the additional expense of insuring against such liability - assuming insurance would be available - and of research programs to reveal possible dangers not detectable by available scientific methods could place the cost of medication beyond the reach of those who need it most."⁶³

(6) The court referred to several examples of products that have greatly increased in price or been withdrawn or withheld from the market "because of the fear that their producers would be held liable for large judgments:" Bendectin; a new vaccine for influenza; diphtheria-tetanus-pertussis vaccine; and a new drug for the treatment of vision problems.⁶⁴

For the foregoing reasons, the court rejected the "Benefit v. Risk" test for determining whether a product's design is defective. In so ruling, the court departed from a major California precedent.⁶⁵

b. Applicability to Biotech Drugs.

The *Brown* decision did not involve a biotech drug. However, the definition of the term "drug" does not depend on what technology is used to produce it.⁶⁶ Biotech drugs must undergo the same FDA

serious risks will be applied with restraint. For example, it seems doubtful that a prescription drug that cured 60% of persons afflicted with a particular disease and killed the remaining 40% would be approved by the FDA or enjoy the protection of the *Brown* case.

62. *Brown*, 44 Cal. 3d at 1063, 751 P.2d at 479, 245 Cal. Rptr. at 420.

63. *Id.*

64. *Id.* at 1064-65, 751 P.2d at 479-80, 245 Cal. Rptr. at 421.

65. *Barker v. Lull Engineering Co.*, 20 Cal. 3d 413, 573 P.2d 443, 143 Cal. Rptr. 225 (1978). In *Barker*, the court noted that "we have no occasion to determine whether a product which entails a substantial risk of harm may be found defective even if no safer alternative design is feasible." 20 Cal. 3d at 431 n.10, 573 P.2d at 455 n.10, 143 Cal. Rptr. at 237 n.10. Given the court's rejection of the "indsight" test for prescription drugs in the *Brown* case and the Legislature's recent declaration of a products liability exemption for certain consumer products known by consumers to be inherently unsafe, CAL. CIV. CODE § 1714.45 (1986), the issue left open in *Barker* may deserve reexamination. One approach would be to limit strict liability. An alternative approach would be to enforce strict liability or even keep such products off the market in the absence of some compelling justification.

66. Section 321 of the Food, Drug and Cosmetic Act defines a drug as (1) an article listed in one of three official lists of drugs which are intended to diagnose, cure, mitigate, treat or prevent disease or (2) an article intended to affect bodily structure or function or (3) a component of one of the foregoing. 21 U.S.C. § 321 (g) (1) (1984).

approval process as conventional drugs. In order to determine how *Brown* might be applied to situations like those described earlier, it is necessary to examine how well the *Brown* court's policy considerations apply to biotech drugs.

The court's first policy consideration, the necessity of alleviating pain and suffering or sustaining life, seems equally applicable to a biotech drug. A biotech drug is just as likely to "alleviate pain and suffering or to sustain life"⁶⁷ as a conventional drug. A biotech drug is certainly not akin to construction machinery; it is not intended to make work easier or to provide pleasure. The AIDS vaccine in the first illustrative case was intended to prevent a disease which leads to death. The cholesterol dissolving drug in the second illustrative case was intended to avoid death due to blocked arteries. Thus, both drugs were intended "to sustain life."

The court's second policy consideration, the unavoidability of harm to some users, also seems applicable to biotech drugs. Common experience tells us that any substance, whether a drug or sugar water, has the potential for harm in some set of users.⁶⁸ Harm in some users of drugs, biotech or conventional, is unavoidable because the drug must have some activity in the human body in order for it to have any efficacy. Because there is such a wide range of human susceptibilities to side effects, it is unavoidable that the very activity which is generally beneficial may be deleterious to certain individuals. Even if the manufacturing process influences what particular harm some specific set of users may experience, the principle remains the same - drugs, however made, carry the inevitable risk of harm for some. Both the hypothetical AIDS vaccine and the cholesterol dissolving drug carried a risk of side effects. Perhaps, if the vaccine had been tested for two or three times as many years, the harmful side effect would have been detected. Even so, the only change might have been in the warnings. Not all users suffered the side effect, and there might not have been any way to change the vaccine to avoid the side effect. If that were the case, the practical consequences of the additional testing would have been

WEBSTERS UNABRIDGED DICTIONARY (3d ed., 1981) defines "drug" as any substance used as, or in the preparation of, a medicine.

67. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1063, 751 P.2d 470, 478, 245 Cal. Rptr. 412, 420.

68. For example, "[g]ood butter is not unreasonably dangerous merely because, if such be the case, it deposits cholesterol in the arteries and leads to heart attacks; but bad butter, contaminated with poisonous fish oil, is unreasonably dangerous." RESTATEMENT (SECOND) OF TORTS, § 402A comment i (1965). Likewise some people could be allergic to the solutions used as the carrier medium for the active ingredient of a biotech drug or vaccine.

delayed approval and additional cost.⁶⁹ Although the vaccine created some risk for a small percentage of the population, it eventually would have been approved because of its great potential benefits. A similar argument can be made with respect to the cholesterol dissolving drug. In that case, the risk of harm was an unusual risk, known to the Army but not to Sponsor. The side effect which caused the injury in that case was associated with only a relatively small subset of the people for whom the drug was potentially beneficial.

The court's third policy consideration was that beneficial new drugs should be made available without undue delay, despite serious risks.⁷⁰ As discussed in the preceding paragraph, this policy consideration applies to all safe and efficacious drugs, regardless of the manufacturing process employed. The public good that would result from the availability of either the AIDS vaccine or the cholesterol dissolving drug could well justify the risk of harm to some. Both drugs were intended to address serious public health problems. In the vaccine case, a panel of medical and scientific experts, at the request of the FDA, specifically found that the incidence of AIDS constituted a critical public health hazard. The decision to approve the marketing of a new drug involves a governmental balancing of risk versus benefit. Benefit is a function both of the seriousness of the disease and the efficacy of the drug in treating it. AIDS and cholesterol are severe problems in that they can lead to suffering and death in a significant proportion of the population. Under these circumstances, a certain amount of risk is surely justified. The test results available to Manufacturer and Sponsor indicated that their products were apparently safe. A balancing of risk and benefit on these facts supports both the conclusion that FDA marketing approval was warranted and that strict liability would be inappropriate.

The court's fourth, fifth and sixth policy considerations dealt with the likelihood that a manufacturer would be reluctant to develop new drugs in the face of strict products liability, that insurance would be expensive and difficult to obtain, and that as a result of these costs, drugs would become very expensive or unavailable.⁷¹ These last three considerations provide no basis for distinguishing between biotech drugs and conventional drugs. In fact, since biotech companies are generally

69. The cost for a clinical trial of a drug or vaccine include, *inter alia*, the cost of production, packaging and shipment of the material to be tested. The cost of arrangements with a clinic to conduct the test, collect the data and transmit it to the sponsor as well as the cost of the sponsor, and assemble the data in the requisite form for FDA submission. This is a very costly process. See H. GRABOWSKI & J. VERNON, THE REGULATION OF PHARMACEUTICALS, *supra* note 8, at 23.

70. *Brown*, 44 Cal. 3d at 1063, 751 P.2d at 479, 245 Cal. Rptr. at 420.

71. *Id.*

smaller than conventional pharmaceutical companies today, they are more likely to be anxious about product liability risks than conventional companies.

In short, the policies articulated in the *Brown* case apply to biotech companies not because they utilize biotechnology but because they are pharmaceutical companies in need of the same incentives and protections as those pharmaceutical companies utilizing conventional technologies.

2. FAILURE TO WARN.

A central issue in product liability cases and under comment k is whether the manufacturer's warning is adequate. This issue is acute in drug cases because of the extensive federal regulation of warnings.⁷² We expect that the warning issue is likely to be as significant in biotech drug cases as in conventional drug cases, hence the pertinence of the *Brown* court's treatment of this issue.

a. Brown Decision

The issue of warning, a crucial one, is also addressed by the *Brown* case. Ordinarily, a product manufacturer is not strictly liable for failure to warn of dangers that the manufacturer neither knew nor could have known given the state of the art at the time the product was manufactured.⁷³ The *Brown* court adopted Professor Wade's suggestion that a manufacturer's knowledge should be measured at the time a drug is distributed.⁷⁴ It ruled that liability for failure to warn "is conditioned on the actual or constructive knowledge of the risk by the manufacturer as of the time the product was sold or distributed."⁷⁵ This rule is consistent

72. For discussion of federal pharmaceutical regulation see Walsh & Klein, *The Conflicting Objectives of Federal and State Tort Law Drug Regulation*, 41 FOOD DRUG COSM. L. J. 171 (1986). The Food, Drug and Cosmetic Act of 1938 gives the FDA full authority to ensure that each drug on the market is both safe and effective. 50 Fed. Reg. 7,452 (1985). Drug labeling serves as the standard under which the FDA determines whether a product is safe and effective. 50 Fed. Reg. 7,470 (1985).

Physician package inserts are federally regulated under 21 U.S.C. § 352 (1984). These inserts are typically reproduced in the Physician's Desk Reference (PDR). As a practical matter, the FDA retains complete control over package inserts with the narrow exception of 21 C.F.R. § 314.70(c). A manufacturer cannot unilaterally alter the FDA approved labeling by adding new information about risks without filing a supplemental new drug application, 21 C.F.R. § 314(b)(3). If its supplemental application is rejected, the manufacturer does not have the authority to alter the package insert without FDA approval.

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

74. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1060 n.8, 751 P.2d 470, 477 n.8, 245 Cal. Rptr. 412, 418 n.8 citing Wade, *On the Effect in Product Liability of Knowledge Unavailable Prior to Marketing*, 58 N.Y.U. L. REV. 734, 753-754 (1983).

75. *Brown*, 44 Cal. 3d at 1066, 751 P.2d at 486, 245 Cal. Rptr. at 422.

with comment j to section 402A of the Restatement (Second) of Torts, which "confines the duty to warn to a situation in which the seller has knowledge or by the application of reasonable, developed human skill and foresight should have knowledge of . . . the danger."⁷⁶

The rationale for the majority rule, as expressed in *Brown* and implicit in the Restatement, is that public interest favors the "development of new and improved drugs to combat disease."⁷⁷ The court was concerned that strict liability would discourage this development. Although the court did not address the potential conflict between extensive and pervasive federal regulations of warnings⁷⁸ and state tort law warning requirements, we note that this issue is percolating in the courts in conventional drug cases⁷⁹ and will very likely arise in biotech drug cases.

76. *Id.*

77. *Id.*

78. See *supra* note 72.

79. In a few cases, courts have held that a manufacturer who fully complied with FDA label requirements nonetheless did not issue a warning sufficient to preclude imposition of strict liability. See e.g., *Brochu v. Ortho Pharmaceutical Corp.*, 642 F.2d 652, 658 (1st Cir. 1981); *Feldman v. Lederle Laboratories*, 97 N.J. 429, 479 A.2d 374, 389-391 (1984). See Cooper, *Drug Labeling and Products Liability: The Role of the Food and Drug Administration*, 41 FOOD DRUG COSM. L.J. 233 (1986); Comment, *The Failure to Warn Defect: Strict Liability of the Prescription Drug Manufacturer in California*, 17 U.S.F. L. REV. 743 (1983). In one commentator's view, these cases give "manufacturers the worst of both worlds: in the drafting of package inserts they are, as a practical matter, subject to the total control of FDA; but, in court, they are assumed to have real freedom to act unilaterally." Cooper, *supra* at 236.

In two cases, at the trial court level, manufacturers successfully argued that the comprehensive FDA regulations preempt state tort law remedies. However, in both cases the trial court decisions were reversed. The Eastern District of Texas held, for example, that federal regulation of diphtheria-pertussis-tetanus vaccines preempted state law and that uniform drug design and labeling, as goals of the FDA, should not be hampered by state imposed design and labeling requirements, enforced by verdicts in tort cases. *Hurley v. Lederle Laboratories*, 651 F. Supp. 993 (E.D. Tex. 1986), *opinion superceded by* 851 F.2d 1536 (5th Cir. 1988); *Abbot v. American Cyanamid Co.*, No. 86-0857-A (E.D. Va. 1987), *rev'd*, 844 F.2d 1108 (4th Cir. 1987), *cert. denied*, ___ U.S. ___, 109 S. Ct. 260 (1988).

It bears emphasis, however, that the Court of Appeals in *Hurley, supra*, left open the possibility of a preemption argument on the warning issue. Noting that "manufacturers cannot change the language in the product insert," the court stated that "[i]t 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." 851 F.2d at 1542. Most courts, however, have held that the National Vaccine Act of 1986 evinces Congressional intent not to preempt state remedies. See, e.g., *Abbot v. American Cyanamid Co.*, *supra*, 844 F.2d at 1111-14; *Foyle v. Lederle Laboratories*, 674 F. Supp. 530, 532-34 (E.D.N.C. 1987). See also *Osburn v. Anchor Laboratories, Inc.*, 825 F.2d 908, 911-914 (5th Cir. 1987), *cert. denied sub nom, Rachelle Laboratories Inc. v. Osburn*, ___ U.S. ___, 108 S. Ct. 1476 (1988); *Hurley v. Lederle Laboratories*, 851 F.2d at 1539 n.2 (collecting cases).

b. Applicability to Biotech Drugs.

In our opinion, biotech drug manufacturers are as adverse to being "virtual insurers" as conventional drug manufacturers. There is no reason to suppose that the *Brown* court would apply its policy considerations any differently to biotech drugs than to conventional drugs.

However, the AIDS vaccine illustration suggests a related problem. The manufacturer must warn of side effects known at the time of distribution.⁸⁰ In that illustration, Manufacturer may not have distributed all the vaccine at one time. It probably manufactured and distributed periodically. Did the court intend to test a pharmaceutical company's knowledge at each distribution time or only at the time it commenced distribution? If the former, the manufacturer presumably must change the warnings when it discovers relevant information. However, the FDA must approve any label change, something it may or may not do.⁸¹ A further related question arises as to the vaccine still in the hands of the hospitals and others who were to actually administer the vaccine. Had that material been "distributed"? One reading, perhaps the most likely, is that the court was referring to distribution by the manufacturer. Another reading, however, might be that the drug is not distributed until actually administered to the patient.

Compare Landen, *Federal Preemption and the Drug Industry: Can Courts Co-Regulate?*, 43 FOOD DRUG COSM. L.J. 85 (1988) (urging that federal preemption is fully warranted) with Wilson & McKown, *Federal Preemption in DPT cases*, 24 (TRIAL 59 (Jan. 1988)) (urging that courts should reject the preemption defense).

There is a crucial tension here since the FDA sometimes does not wish to include disclosures that the manufacturer (and its products liability counsel) may deem necessary. The FDA requires that only "[t]he known hazards [of a drug] and not theoretical possibilities shall be listed . . .", 21 CFR § 520.157(d) (1988). The adverse consequences of overdisclosure were recognized by the California Supreme Court in *Finn v. G.D. Searle & Co.*, 35 Cal. 3d 691, 701, 677 P.2d 1147, 1153, 200 Cal. Rptr. 870, 876, (1984):

[B]oth common sense and experience suggests that if every report of a possible risk . . . imposed an affirmative duty to give some warning, a manufacturer would be required to inundate physicians indiscriminately with notice of any and every hint of danger, thereby inevitably diluting the force of any specific warning given.

The tension in this area is exacerbated in a situation of unreported third party reactions, as described in illustrative Case B, *supra* Part I.

Other commentators have suggested that courts should defer to the specific scientific and policy judgments made by the FDA or that in any case FDA should act to clarify its authority over the warning process. *Walsh & Klein, supra* note 72; *Cooper, supra*.

Another warning issue concerns the duty to warn consumers subsequent to manufacture and distribution. See e.g., *Reyes v. Wyeth Laboratories*, 498 F.2d 1264, 1276 (5th Cir.), cert. denied, 419 U.S. 1096 (1974). "Biotech safety research also moves so rapidly that manufacturers may have post-manufacture warning duties greater than those of conventional manufacturers." *O'Reilly, supra* note 2 at 466.

80. See *Brown v. Superior Court*, 44 Cal. 3d 1049, 1059-60 n.8, 751 P.2d 470, 477 n.8, 245 Cal. Rptr. 412, 418 n.8.

81. See *Cooper, supra* note 79.

Biotech companies may have a greater risk in this area than conventional companies. If young biotech companies have a greater research focus than conventional companies, then they may be more likely to learn new information about their drugs faster than conventional companies. From the flood of newspaper announcements in recent years, it appears that the pace of development and understanding of biotechnology and biology is accelerating. Today's scientific beliefs may turn out to be incorrect when reexamined in light of tomorrow's knowledge and with the benefit of future scientific tools. In such circumstances, the application of the *Brown* opinion's duty to warn of everything known or reasonably knowable at the time of distribution may result in biotech drugs becoming a rapidly moving target for product liability suits.

3. REJECTION OF CASE BY CASE JUDICIAL DETERMINATIONS.

a. Brown Decision

Prior to the *Brown* decision, the leading California case on drug product liability was *Kearl v. Lederle Laboratories*.⁸² The *Kearl* test attempts to separate products that meet the description of "unavoidably dangerous" from those that do not.⁸³ If the product is "unavoidably

82. 172 Cal. App. 3d 812, 218 Cal. Rptr. 453 (1985). In *Kearl*, an oral polio vaccine case, the court of appeal reversed a judgment for plaintiff. It ruled, first, that before admitting strict liability design defect evidence, the trial court should first take evidence, out of the jury's presence, to ascertain whether the "unavoidably dangerous" exception from strict liability applies, 172 Cal. App. 3d at 829-31, 218 Cal. Rptr. at 463-65, and, second, that the manufacturer's warning was adequate as a matter of law. 172 Cal. App. 3d at 834-36, 218 Cal. Rptr. at 467-69.

83. A recent, important, but now repealed California statute provided that the manufacturer of an FDA-approved AIDS vaccine would not be strictly liable for damages caused by design or warning defects of the vaccine if the trial judge determined that the vaccine was "unavoidably dangerous." CAL. HEALTH & SAFETY CODE § 199.49(a)(2) (West 1986), enacted by 1986 Cal. Stat. ch. 1463, § 1; repealed, 1988 Cal. Stat. ch. 1555. The term "unavoidably dangerous" was defined to mean "unavoidably unsafe," the words used in comment k. CAL. HEALTH & SAFETY CODE § 199.49(c) (West 1986), repealed 1988 Cal. Stat. ch 1555. See discussion of the California statute, now repealed, in McKenna, *The Impact of Product Liability Law on the Development of a Vaccine Against the AIDS Virus*, 55 U. CHI. L. REV. 943, 962-63 (1988). Under the statute, the manufacturer had the burden of proving that all three of the following criteria were met:

(A) At the time of distribution, the vaccine was intended to confer an exceptionally important benefit on society that made its availability highly desirable.

(B) At the time of distribution, the then existing risk posed by the vaccine was both substantial and unavoidable

dangerous" under the *Kearl* test, "the liability of the manufacturer is tested by comment k; otherwise, strict liability is the applicable test."⁸⁴

The *Brown* court rejected the *Kearl* test for the following reasons:

(1) It is not feasible at the front end to distinguish clearly between drugs that will prove useful to mankind (e.g., penicillin) and those that will prove *clearly* harmful (e.g., thalidomide).

(2) The process of attempting to make this distinction impairs the public interest in the development and marketing of new drugs.

(3) "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 side effects because a trial judge could decide, perhaps many years later, that in fact another product which was available on the market would have accomplished the same result."⁸⁵

(4) The superiority of one drug over another would have to be decided not in the abstract but in reference to the plaintiff; however, "in one case the drug that injured the plaintiff might be the better choice, while this would not be true as to another user."⁸⁶

(5) Different trial judges might reach different conclusions about the same drug.

(6) The findings of the judge and the jury may be inconsistent.

(7) Establishing the *Kearl* test is costly and requires the drug to "survive two risk/benefit challenges, first by the judge and then by the jury. In order to vindicate the public's interest in the availability and affordability of prescription drugs, a manufacturer must have a greater

(C) At the time of distribution, the interest in availability of the subject AIDS vaccine outweighed the interest in promoting enhanced accountability through either strict products liability design and warning defect, or implied warranty, review.

The Legislature stated expressly that its intent was "to codify, in part, certain portions of the court ruling in *Kearl v. Lederle Laboratories*." CAL. HEALTH & SAFETY CODE § 199.49(c) (1986).

The California statute has recently been repealed in light of the *Brown* case. 1988 Cal. Stat., ch. 1555, § 3; Letters from Assemblyman John Vasconcellos (author of the original statute and of the repealing statute) to Michael Traynor (June 24, 1988 and June 30, 1988).

84. *Brown*, 44 Cal. 3d at 1067, 751 P.2d at 481, 245 Cal. Rptr. at 423. The emphasis in *Kearl* on a particular product is akin to the case-by-case approach of *Feldman v. Lederle Laboratories*, 97 N.J. 429, 479 A.2d 374 (1984). The *Feldman* court held "that generally the principle of strict liability is applicable to manufacturers of prescription drugs," 97 N.J. at 442, 479 A.2d at 380, and whether a comment k exception is available, i.e., "whether a drug is unavoidably unsafe should be decided on a case-by-case basis," 479 A.2d at 383.

85. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1067-68, 751 P.2d 470, 482, 245 Cal. Rptr. 412, 423.

86. *Id.*

assurance that his products will not be measured by the strict liability standard that is provided by the test stated in *Kearl*.⁸⁷

b. Applicability to Biotech Drugs

Each of the policy considerations articulated in *Brown* applies equally whether the manufacturer uses biotechnology or conventional methods. Biotech pharmaceutical companies compete in the same markets as do conventional pharmaceutical companies. They both conduct clinical trials in the same hospitals and respond to many of the same incentives and concerns.

The public policy consideration which favors development of new drugs is especially relevant to biotechnologically produced pharmaceuticals because biotechnology is a powerful new science which promises new therapies for major diseases. Public policy should encourage biotech companies to develop and produce new therapies in responsible ways. Because many are relatively young and small, they are particularly vulnerable to the costs, both financial and human, of product liability litigation.

4. REJECTION OF CONSUMER EXPECTATION TEST

a. Brown Decision

The court rejected the "Consumer Expectation Test" on the following ground: while the 'ordinary consumer' may have a reasonable expectation that a product he purchases, such as a machine, will operate safely when used as intended, a patient's expectations regarding the effects of such a drug are those related to him by his physician, to whom the manufacturer directs the warnings regarding the drug's properties.⁸⁸

b. Applicability to Biotech Drugs

Although the *Brown* court's reasoning seems plainly applicable to prescription drugs produced by biotechnology, some cautionary notes are in order.

87. *Id.* at 1068, 751 P.2d at 482, 245 Cal. Rptr. at 424. For additional criticism of the *Kearl* test, see *Collins v. Ortho Pharmaceutical Corp.*, 195 Cal. App. 3d 1539, 231 Cal. Rptr. 396 (1986), review granted *sub nom. Collins v. Karoll*, 732 P.2d 542, 234 Cal. Rptr. 596 (1987), dismissed and remanded to Court of Appeal, 761 P.2d 102, 251 Cal. Rptr. 642 (1988).

88. *Brown*, 44 Cal. 3d at 1061-62, 751 P.2d at 477-78, 245 Cal. Rptr. at 419. The "learned intermediary" issue is discussed in more detail in paragraph V-A-1, *infra*.

"[W]hen technology produces a substitute for a conventional drug and the substitute exhibits a risk different from that of the original version, can the substitute assert that its danger is unavoidable?"⁸⁹ Although that argument may prove persuasive to some, we think it more likely that the technology encouraged by the comment k principles and the *Brown* case will be favored and that the courts will not impede innovative biotechnology or create a preferred status for conventional drugs. A contrary result would require an improved version of an existing drug to be completely free of defects in order to have the benefit of comment k and avoid strict liability. A "zero defects" standard would, in our judgment, be a significant disincentive to pharmaceutical companies to invest in improving drugs already on the market. It would be difficult to be certain that the improved version would not have a risk different from the original.

In fact, there is some indication in the court's opinion, and in comment k, that the policy justifications for insulating prescription drug manufacturers from strict liability are most compelling in the case of new or experimental drugs.⁹⁰ The new biotech drugs are likely to meet even this narrower standard, at least during the early stages of marketing and distribution. Whether the insulation afforded by the *Brown* case will extend to prescription drugs that are no longer new or experimental or whether the requirement of adequate warning will be augmented in such cases (perhaps after the initial "honeymoon" period) are questions that remain open after *Brown*.

Brown is a path-breaking case that departs from the judiciary's usual case-by-case approach. We expect that it will gradually gain acceptance in other jurisdictions and may be resisted in some.⁹¹

89. O'Reilly, *supra* note 2, at 460-61, 477-78.

It can be argued that by having a conventional alternative drug readily available for substitution, albeit at a higher cost, the biotechnology product should not receive coverage of an exemption for 'the unavoidably high degree of risk' which a comment k product includes. The higher risk experienced by that plaintiff from that particular substitution is the operative fact before the court in that case.

Id. at 466 n.53.

We do not agree that the risk is necessarily higher; it may be lower. Moreover, the foregoing argument may prove too much since it could apply to any differentiated product, whether or not a biotechnology product. The Army beans example at the beginning of this paper could involve a lesser or different risk.

90. "Public policy favors the development and marketing of beneficial new drugs, even though some risks, perhaps serious ones, might accompany their introduction, because drugs can save lives and reduce pain and suffering." *Brown*, 44 Cal. 3d at 1063, 751 P.2d at 479, 245 Cal. Rptr. at 420.

91. See *Shirkey v. Eli Lilly & Co.*, 852 F.2d 227, 231-35 (7th Cir. 1988) (in DES case, certifying strict liability questions to Wisconsin Supreme Court); *Needham v. White Laboratories, Inc.*, 847 F.2d 355 (7th Cir. 1988) (affirming judgment for the plaintiff in a DES case against the manufacturer based on a failure-to-warn theory); *Hill v. Searle Laboratories*, 686 F. Supp. 720, 724-25 (E.D. Ark. 1988) (following comment k and grant-

V. EMERGING ISSUES FOR BIOTECH DRUGS

A. Will the Liability of a Manufacturer of a Genetically Engineered Vaccine Be Measured by the Standards of Strict Liability?

The policies underlying comment k and the *Brown* case would seem to apply with equal or greater force to vaccines. The principal exception, discussed below, would appear to be the court's reliance on physicians relating the effects of a prescription drug to their patients. There is widespread concern that if manufacturers are held strictly liable for vaccines, they will be deterred from manufacturing products necessary for public health. Indeed, the *Brown* court stated that "[d]rug manufacturers refused to supply a newly discovered vaccine for influenza on the ground that mass inoculation would subject them to enormous liability."⁹² Such concerns led, for example, to the National Childhood Vaccine Injury Act of 1986.⁹³

ing summary judgment to manufacturer in intrauterine device case); *Kociemba v. G. D. Searle & Co.*, 680 F. Supp. 1293 (D. Minn. 1988) (court declines to follow *Brown* and concludes that California law is distinguishable from applicable Minnesota law); *Castrignano v. E. R. Squibb & Sons, Inc.*, ___ R.I. ___, 546 A.2d 775 (1988) (citing *Brown* but electing to extend comment k protection to prescription drugs on a case-by-case basis).

92. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1064, 751 P.2d 470, 479, 245 Cal. Rptr. 412, 421.

In a review of the polio vaccine, the author states that if liability continues to be placed on manufacturers, "availability of much-needed vaccines in the United States will drop to levels which could result in the lack of national immunity against communicable diseases in this country, and thus may also result in an ensuing revisit of such diseases in the United States on an epidemic scale." Hardin, *Poliomyelitis Vaccine -- History, Regulations and Recommendations*, 40 FOOD DRUG COSM. L.J. 145, 146 (1985). See also Franklin & Mais, *Tort Law and Mass Immunization Programs: Lessons from the Polio and Flu Episodes*, 65 CALIF. L. REV. 754 (1977); Note, *Mass Immunization Cases: Drug Manufacturers' Liability for Failure to Warn*, 29 VAND. L. REV. 235 (1976); Comment, *Strict Liability for Prescription Drugs: Which Shall Govern -- Comment k or Strict Liability Applicable to Ordinary Products?*, 16 GOLDEN GATE U. L. REV. 309, 325-27 (1986). For a contrary view, that drug companies are highly profitable, engage in "aggressive marketing techniques," and survived the polio vaccine crisis with "buoyancy . . . in the face of extensive verdicts and settlements," see Note, *An Escape From Strict Liability*, *supra* note 54, at 217-18.

93. See Schwartz & Mahshigian, *National Childhood Vaccine Injury Act of 1986: An Ad Hoc Remedy or a Window for the Future?*, 48 OHIO ST. L.J. 387 (1987). The Act "establishes a mandatory no-fault compensation system for persons injured through childhood vaccines. After the no-fault proceedings, the claimant has the option of accepting the compensation awarded, if the injury were found to be vaccine-related, or bringing a civil action against the vaccine manufacturer in which several limitations on the manufacturer's tort liability would apply." Neraas, *The National Childhood Vaccine Injury Act of 1986: A Solution to the Vaccine Liability Crisis?*, 63 WASH. L. REV. 149 (1988). See also Hardin, *Poliomyelitis Vaccine -- History, Regulations and Recommendations*, 40 FOOD DRUG COSM. L.J. 145 (1985); Spence, *Alternatives to Manufacturer Liability for Injuries Caused by the Sabin-Type Oral Polio Vaccines*, 28 WM. & MARY L. REV. 711 (1987).

To encourage manufacturers to produce vaccines, such as an AIDS vaccine, it seems likely that the courts would invoke the *Brown* case and measure the liability of a manufacturer of a genetically engineered vaccine by the same basic standards applicable to the manufacturer of prescription drugs. The court's rejection of the "hindsight" and case-by-case approaches to strict liability would lead to comment k protection of the manufacturer in the hypothetical vaccine case discussed at the beginning of this article. Both the *Brown* case and the hypothetical case involve products where more is known about the risks now than when they were first approved. Thus, the products would be made differently, contain new warnings, or not be marketed depending on the circumstances. Nonetheless, the policy of encouraging much needed innovation precludes adoption of a "hindsight" test.

The vaccine case may more strongly warrant relaxed standards of strict liability of manufacturers than the prescription drug case. "Vaccines offer the classic case of an externality, in that my vaccination reduces your risk of contracting the disease . . ."⁹⁴ Some individuals might consider it wise to avoid vaccination while supporting a program for vaccinating everyone else.⁹⁵ (In AIDS cases, an individual's reluctance to be vaccinated may be greater than in flu or childhood disease cases because the AIDS virus is not perceived to be transmitted as easily.) Therefore, "it is not surprising that vaccinations have traditionally been provided either directly or indirectly [subsidized] by the government."⁹⁶ If the government is unwilling to provide compensation, subsidize, or enter the insurance market (or some combination of these approaches), and private insurance is unavailable or insufficient to cover the potential compensatory costs of victims, it may be especially onerous and counter-productive to impose the compensation burden solely on manufacturers.⁹⁷

A comparable problem involves "orphan drugs," i.e., "a useful pharmaceutical agent for an illness whose small patient population leaves the developer without a reasonable expectation of an economic return on investment." O'Reilly, *Orphan Drugs: The Strange Case of "Baby M,"* 42 FOOD DRUG COSM. L.J. 516 (1987).

94. Letter from Peter Reuter, Economist, The RAND Corporation, to Michael Traynor (July 25, 1988) (copy on file with Authors). See also *infra* notes 117-18.

95. Letter from Professor Marjorie M. Schultz, Boalt Hall School of Law, to Michael Traynor (July 14, 1988) (copy on file with Authors).

96. See *supra* note 94.

97. We recognize that there are important countervailing arguments. Protecting manufacturers from strict liability recognizes the social utility of manufacturing vaccines for our collective benefit. There is also a social utility in testing and using them. The occasional victim of adverse side effects suffers individual harm which helps achieve a public good. Such victims' claims for compensation are appealing. Whether the tort system should be used to resolve the competing claims is an important policy question.

Although we expect the *Brown* case to be applied to vaccines, it is important to examine whether the distribution of vaccines via mass inoculation rather than via individual prescriptions from physicians requires a different result.

1. THE "LEARNED INTERMEDIARY" DOCTRINE

Manufacturers of prescription drugs frequently defend against failure-to-warn claims on the ground that they provide adequate information and warnings to "learned intermediaries," i.e. physicians, who can be relied on to explain the pros and cons of the drugs to their patients.⁹⁸ "As a learned intermediary, the physician has a duty to know the product he prescribes, to evaluate the needs of the patient, and to assess the benefits and risks of alternative courses of treatment. He is also under a duty to judiciously administer or prescribe pharmaceutical products which he is in the best position to supervise, but only after obtaining the patient's informed consent."⁹⁹

There are significant exceptions to the learned intermediary defense. It has been held unavailable for vaccines administered in mass immunization programs.¹⁰⁰ It may not even be available when the vaccination, though in a doctor's office, is administered more in the manner of a county health clinic than of a private physician.¹⁰¹ It may not be

So long as it is the operative system, however, choices within it must be made. On balance, we think the innovation-encouraging approach of the *Brown* case is preferable and more beneficial to the public.

98. Ordinarily, a manufacturer must warn users directly of dangers inherent in the use of the product. RESTATEMENT (SECOND) OF TORT, § 402A comment j (1965). But see *Walsh & Klein, supra* note 72, at 188:

In the context of prescription drugs, courts have long recognized an exception to the general rule. The 'learned intermediary' doctrine, first adopted in *Sterling Drug, Inc. v. Cornish*, [370 F.2d 82, 85 (8th Cir. 1966)], holds that a manufacturer's duty to warn is satisfied 'if the doctor is properly warned of the possibility of a side effect.' Consequently, under the learned intermediary doctrine, the manufacturer has no duty to warn the user directly.

99. *Hardin, supra* note 91, at 157.

100. E.g., *Davis v. Wyeth Laboratories*, 399 F.2d 121 (9th Cir. 1968) (polio vaccine); see also *Reyes v. Wyeth Laboratories*, 498 F.2d 1264 (5th Cir. 1974), cert. denied, 419 U.S. 1096 (1974) (polio vaccine); *Grinnell v. Charles Pfizer & Co.*, 274 Cal. App. 2d 424, 79 Cal. Rptr. 369 (1969); 2 M. DIXON, DRUG PRODUCT LIABILITY § 15.05[2] (Woodside rev. 1988); *Rheingold, The Expanding Liability of the Drug Manufacturer to the Consumer*, 40 FOOD DRUG COSM. L.J. 135-36 (1985). See also *Unthank v. United States*, 732 F.2d 1517 (10th Cir. 1984) (swine flu vaccine); *Petty v. United States*, 740 F.2d 1428 (8th Cir. 1984); *Ezagui v. Dow Chemical Corp.*, 598 F.2d 727 (2d Cir. 1979); *Brazzell v. United States*, 633 F.Supp. 62 (N.D. Iowa 1985); *Fraley v. American Cyanamid Co.*, 570 F.Supp. 497 (D. Colo. 1983) (polio vaccine).

101. See *Givens v. Lederle*, 556 F.2d 1341 (5th Cir. 1977); 2 M. DIXON, *supra* note 99 at § 15.02[2]; *Rheingold, supra* note 99 at 137. But cf. *Schindler v. Lederle Laboratories*, 725 F.2d 1036 (6th Cir. 1983) (private physician dispensed polio vaccine as prescription drug); *Sheffield v. Eli Lilly & Co.*, 144 Cal. App. 3d 583, 192 Cal. Rptr. 870 (1983); *Johnson v. American Cyanamid Co.*, 239 Kan. 279, 718 P.2d 1318 (1986); *Dunn v.*

available under certain other circumstances: for example, such drugs as birth control pills or tranquilizers may be prescribed at a single patient visit, though intended to be used for a long period of time, without frequent or even any return visits to see the physician.¹⁰²

The "learned intermediary" defense may depend on assumptions about the education and knowledge, the "learnedness," of physicians that are not necessarily reliable.¹⁰³ Moreover, it may divert attention from the fundamental public policy concerns developed in comment k and the *Brown* case.

Finally, at least until physicians become better educated and informed about biotechnology, the defense may need refinement. One commentator, Lewis Thomas, has admonished that "medicine will always tend to lag behind the rest of biology, because any comprehension of the underlying mechanisms of disease must always await a deep understanding of the normal processes of life."¹⁰⁴

Although physicians may experience difficulty keeping current with technical developments, they are still likely, by reason of training and exposure, to be much more knowledgeable than their typical patients. For the same reason, they are more likely to understand the information, including warnings, provided by pharmaceutical manufacturers with their new drugs. Moreover, it is reasonable to expect physicians

Lederle Laboratories, 121 Mich. App. 73, 328 N.W.2d 576 (1983). See also Schwartz, *Products Liability Law and Pharmaceuticals; New Developments and Divergent Trends*, 43 FOOD DRUG COSM. L.J. 33 (1988).

102. Rheingold, *supra* note 100, at 137-38 (listing ten potential exceptions). See, e.g., MacDonald v. Ortho Pharmaceutical Corp., 394 Mass. 131, 475 N.E.2d 65, cert. denied, 474 U.S. 920 (1985); Stephens v. G. D. Searle & Co., 602 F. Supp. 379 (E. D. Mich. 1985); Odgers v. Ortho Pharmaceutical Corp., 609 F. Supp. 867 (E. D. Mich. 1985); Walsh & Klein, *supra* note 72, at 188-92. See also Thompson, *The Drug Manufacturer's Duty to Warn: To Whom Does It Extend?*, 13 FLA. ST. U.L. REV. 135, 137 (1985); McKenna, *supra* note 83, at 957-61; Comment, *Products Liability: The Continuing Viability of the Learned Intermediary Rule As It Applies to Product Warnings for Prescription Drugs*, 20 MICH. L. REV. 405, 417-19 (1986). Cf. Note, *Failures to Warn and the Sophisticated User Defense*, 74 VA. L. REV. 579, 592 (1988).

103. The volume of information concerning new drugs and medical knowledge seems likely to be greater than a physician can assimilate. Given this information gap, the average individual physician may be less "learned" about the new therapies than may be tacitly assumed by the courts applying the learned intermediary defense doctrine.

104. Thomas, *Overview: Regulating Biotechnology*, 3 YALE L. & POL'Y REV. 309, 311 (1985). See O'Reilly, *supra* note 2, at 467:

In the biotech case, the seller knows much more about the product and its benefits and risks compared to conventional therapeutics or diagnostics than the average physician or laboratory director who selects the drug or diagnostic product 'Learned intermediary' physicians without an understanding of the unconventional methodologies cannot select a biotechnologically engineered product with the same set of pharmacology knowledge they gained in past years at medical school.

See also Gilhooley, *Learned Intermediaries, Prescription Drugs, and Patient Information*, 30 ST. LOUIS U.L.J. 633 (1986); O'Reilly, *supra* note 2, at 478-80.

to know their patients' particular conditions and to assess the warnings accordingly.

2. THE "LEARNED INTERMEDIARY" DOCTRINE IN LIGHT OF THE BROWN CASE

In *Brown*, the California Supreme Court stated that the consumer of prescription drugs is not the patient "but the physician who prescribes the drug."¹⁰⁵

A physician appreciates the fact that all prescription drugs involve inherent risks, known and unknown, and he does not expect that the drug is without such risks [A] patient's expectations regarding the effects of such a drug are those related to him by his physician, to whom the manufacturer directs the warnings regarding the drug's properties.¹⁰⁶

The court referred to the "well-established" rule that "a manufacturer fulfills its duty to warn if it provides adequate warning to the physician."¹⁰⁷

The foregoing reasoning does not apply directly to vaccines except perhaps to the limited extent that they are administered individually by physicians rather than on a mass-inoculation basis. However, from the patient's perspective, there may still be an element of strong reliance on professionals other than the manufacturer, e.g., the public health officials responsible for an inoculation program. In the case of mass inoculations, the medical community at large or the government or both have decided that a vaccine is necessary.

An emerging issue, however, is whether the distinction between vaccines and prescription drugs will persuade the court to distinguish the *Brown* case and impose strict liability or whether the courts will learn from the hard lessons of the polio vaccine litigation¹⁰⁸ and apply the basic policy of encouraging manufacturers by limiting strict liability. It is likely that the courts, at least in jurisdictions sympathetic to the comment k approach, will apply these basic policies and not rely on a rationale that makes limited liability under comment k depend on a physician's prescription. It bears emphasis, moreover, that one of the key examples referred to in comment k involves a vaccine. The decision should turn, not on the presence or absence of a "learned intermediary"

105. *Brown*, 44 Cal. 3d at 1061, 751 P.2d at 477, 245 Cal. Rptr. at 419.

106. *Id.*

107. *Id.* at n.9 (citations omitted).

108. "The polio vaccine litigation has resulted in all but one of the U.S. manufacturers pulling out of the polio vaccine-production market. The one manufacturer that continues to produce polio vaccine cannot acquire adequate insurance to cover its inevitable liability." Hardin, *supra* note 92, at 164.

or the availability of a malpractice action against a doctor, but on the fundamental policies of *Brown* and comment k. In the hypothetical AIDS vaccine case set forth, it is likely that a court would afford comment k protection to the manufacturer notwithstanding the absence of a learned intermediary in many instances. Issues of negligence, adequacy of warning, and regulatory compliance remain in the case. The *Brown* case does not excuse manufacturers from other grounds of liability or preclude compensation to victims on such grounds.¹⁰⁹

B. What will be the Effect of a Manufacturer's Compliance with Applicable Regulations?

We anticipate that in biotech drug cases, as in conventional drug cases, plaintiffs may urge that failure to comply with applicable FDA regulations may be negligence *per se*.¹¹⁰ Such failure may also preclude a manufacturer from urging that its product was "properly prepared" and hence eligible for protection under comment k and *Brown*.

In general, courts have rejected the argument that compliance with FDA regulations constitutes a defense to strict liability.¹¹¹ Given expanded product development but limited regulatory resources, there is a question whether courts will hold generally that regulatory compliance is a defense to liability. In particular cases, however, a defense of regulatory compliance may be upheld. For example, in a recent California case, *Collins v. Ortho Pharmaceutical Corp.*,¹¹² summary judgment for the manufacturer of an IUD device was upheld on appeal. The court held that:

[w]hen the product which allegedly caused a plaintiff's injury is a prescription product, which is distributed with the approval of the FDA provided the manufacturer accompany the product with warnings of foreseeable risks, we conclude the product must be considered unavoidably unsafe as a matter of law and thus outside the parameters of strict liability for defective design.¹¹³

109. See *Brown*, 44 Cal. 3d at 1069 n.12, 751 P.2d at 482 n.12, 245 Cal. Rptr. at 424 n.12.

110. *Stanton v. Astra Pharmaceuticals, Inc.*, 718 F.2d 553, 563-64 n.22 (3d Cir. 1983); RESTATEMENT (SECOND) OF TORTS § 288B(i) (1965).

111. See *Walsh & Klein*, *supra* note 72. Cf. *Foundation on Economic Trends v. Heckler*, 756 F.2d 143, 151 n.5 (D.C. Cir. 1985) (dictum that NIH guidelines are likely "yardstick" for common law liability).

112. 195 Cal. App. 3d 1539, 231 Cal. Rptr. 396 (1986), *review granted sub nom.*, *Collins v. Karoll*, ___ Cal. 3d ___, 732 P.2d 542, 234 Cal. Rptr. 596 (1987), *dismissed and remanded to Court of Appeal*, ___ Cal. 3d ___, 761 P.2d 102, 251 Cal. Rptr. 642 (1988).

113. *Collins*, 195 Cal. App. 3d at 1551, 231 Cal. Rptr. at 404 (emphasis in original). However, the court rejected a defense of federal preemption.

Moreover, as courts reexamine the law of punitive damages,¹¹⁴ it seems quite possible that regulatory compliance will become a defense against claims for punitive damages. In appropriate cases, establishing such a defense as a matter of law might be possible, perhaps on a motion for summary judgment. State statutes are beginning to provide that a drug manufacturer is not liable for punitive damages if the drug is manufactured and labeled in accordance with federal law.¹¹⁵

C. To What Extent Will The "State Of The Art" Defense Be Available?

There may be "special liability exposure problems for the products being made by means of biotechnology as a substitute for the conventional methods."¹¹⁶ One such problem concerns the "state of the art"

114. E.g., *Browning-Ferris Industries v. Kelco Disposal Inc.*, cert. granted, ___ U.S. ___, 109 S. Ct. 527 (1988). The opinion of the U.S. Court of Appeals for the Second Circuit, from which certiorari was granted, is reported at *Kelco Disposal, Inc. v. Browning Ferris Industries*, 845 F.2d 404 (2d Cir. 1988). The Supreme Court is considering the following question: "Is award of \$6 million in punitive damages, amounting to more than 100 times plaintiff's actual damages from purely economic tort, is [sic] excessive under Eighth Amendment or otherwise." ___ U.S. ___, 109 S. Ct. 527 (1988). See also *infra* note 147.

115. E.g. 1987 OR. LAWS ch. 774, § 5; TEX. CIV. PRAC. & REM. CODE ANN. §§ 81.001-81.003 (Vernon 1987); OHIO REV. CODE ANN. §§ 2307.71-2307.80 (1987); 1987 N.J. LAWS ch. 197, §§ 4, 5.

California recently amended its punitive damages statute, CAL. CIV. CODE § 3294, to require proof of oppression, fraud, or malice "by clear and convincing evidence" and to define "malice" and "oppression" in terms of "despicable conduct." 1987 Cal. Stat. ch. 1498.

116. O'Reilly, *supra* note 2. This section of our paper draws extensively upon the O'Reilly article.

"State of the art" is a much used term, which "is a chameleon-like term, referring to everything from ordinary customs of the trade to the objective existence of technological information to economic feasibility. Its meanings are so diverse and so easily confused that the wise course of action, I think, is to eschew its use completely." Wade, *On the Effect in Product Liability of Knowledge Unavailable Prior to Marketing*, 58 N.Y.U. L. REV. 734, 750-51 (1983) (footnote omitted).

defense.¹¹⁷ The defense is

inapplicable until the plaintiff has met the burden of establishing either a 'defective product,' for strict liability law, or a failure in the duty of care, for negligence cases. In the strict liability case, the plaintiff asserts that the product was unreasonably dangerous, while in the negligence case the assertion focuses on breach of duty which proximately resulted in harm to the consumer who used that product.¹¹⁸

Given comment k and *Brown*, one emerging issue is whether a "state of the art" defense will become relevant and, if so, when. Under comment k and *Brown*, strict liability may be avoided if the product is "properly prepared" and "accompanied by proper directions and warning."¹¹⁹

In referring to new and experimental drugs, the *Brown* court relied on comment k which states that "there can be no assurance of safety, or perhaps even of *purity of ingredients . . .*"¹²⁰ Thus, the court may have implicitly distinguished "manufacturing defects" from "design defects." Whether a manufacturer of prescription drugs can invoke *Brown* to avoid strict liability even for manufacturing defects, e.g., impurities, as well as for design defects remains to be seen.

In jurisdictions that do not follow comment k and *Brown*, we envisage manufacturers will invoke the "state of the art" defense after the plaintiff produces evidence that the product is "defective."

The major additional issues regarding the "state of the art" defense for biotechnology products are:

(1) Is "state of the art" to be "defined by industry practice or by technological feasibility?"¹²¹

117. See O'Reilly, *supra* note 2 at 464. A recent design defect case, *McLaughlin v. Sikorsky Aircraft*, 148 Cal. App. 3d 203, 210, 195 Cal. Rptr. 764, 767 (1983), distinguishes industry capability from industry custom in applying the "state of the art" defense:

Among the relevant factors, and peculiarly within the manufacturer's knowledge, are the feasibility and cost of alternative designs . . . [E]vidence the design comported with the state of the art is relevant to a proper determination of such cost and feasibility factors . . . In reaching this conclusion, we recognize the rule, . . . that evidence of industry custom and usage is relevant in a products liability case . . . The distinction between what are the capabilities of an industry and what practice is customary in an industry must be kept in mind. There was no error here in admitting the state of the art evidence showing industry capability.

See also *Aguayo v. Crompton & Knowles Corp.*, 183 Cal. App. 3d 1032, 1038-40, 228 Cal. Rptr. 768, 772-74 (1986) (upholding trial court's exclusion of evidence of improvements in machinery manufactured fifteen years after machine in controversy).

118. O'Reilly, *supra* note 2, at 455 (citations omitted).

119. *Brown v. Superior Court*, 44 Cal. 3d 1049, 1058, 751 P.2d 470, 475, 245 Cal. Rptr. 412, 417.

120. *Id* (emphasis added).

121. O'Reilly, *supra* note 2. See also *supra* note 110.

(2) Will courts view the technology realistically or respond to fears that "biotechnologically derived products can be less safe or efficacious than the conventional products which they may replace?"¹²²

(3) Will jury skepticism or "technology-phobia" about new technology create greater exposure for manufacturers of genetically engineered products?¹²³

(4) Will "state of the art" be tested at the time of design, preparation, treatment of the patient, or trial? The "time of trial" standard "makes a defense based on knowledge of the product design virtually impossible."¹²⁴

(5) Can the defense can be established as a practical matter given that "[b]iotechnology research and publications are booming in volume, diversity, and novelty of inquiry"?¹²⁵ "It will be very difficult for defense lawyers in a four-year-old injury case to determine what was the state of the art for monoclonal antibody products on September 18, 1986, because the 1990 state of the art will have advanced so very much."¹²⁶

D. Other New Issues: A Brief Review

There is always the possibility that alternatives to the present tort approach to problems of product liability may be adopted. Such proposals, which we identify but do not attempt to analyze in this article, might include:

(1) A combination of no-fault and negligence, with emphasis on the changing role of health care delivery systems.

In a recent, innovative article,¹²⁷ the author surveyed the health care industry and suggested that "the existence of health maintenance organizations ('HMOs') and similar prepaid providers with superior

122. O'Reilly, *supra* note 2, at 460. Cf. *Toner v. Lederle Laboratories*, 112 Idaho 328, 732 P.2d 297 (1987) (manufacturer negligent for marketing only vaccine licensed by FDA instead of obtaining FDA approval for another vaccine), cert. denied, ___ U.S. ___, 108 S. Ct. 1122 (1988); Burke, *DPT Vaccine Controversy: An Assessment of the Liabilities of Manufacturers and Administering Physicians Under Several Legal Theories*, 17 SETON HALL L. REV. 541, 575 (1987) ("The strongest argument against classification of the whole-cell pertussis vaccine as an unavoidably unsafe product, however, is the existence of an alternative product, the non-cellular or extracted vaccine, which is supposedly as effective but less dangerous than its counterpart.").

123. O'Reilly, *supra* note 2 at 467, 477-78.

124. *Id.* at 464. Cf. Wade, *supra* note 81, at 754-56.

125. O'Reilly, *supra* note 2, at 466. We doubt, however, that this phenomenon is unique to biotechnology.

126. *Id.* at 476.

127. Sage, *Drug Product Liability and Health Care Delivery Systems*, 40 STAN. L. REV. 989 (1988).

information capacity and total patient care responsibility may create a context in which current standards of drug liability should be revised.¹²⁸ He concluded that:

Should large HMOs with near-universal enrollment control future health care delivery, a market mechanism without liability rules could lead to efficient care and consumption decisions with respect to drugs, since the HMO which purchases the drug must pay for the treatment required for any adverse effect it produces. If nonmonetary damages, such as pain and suffering, are to be compensated, a uniform negligence [sic] rule should be applied to the entire health care industry, including drug manufacturers, since organizations will manage both the production of medical goods and the delivery of medical services.¹²⁹

(2) An "alternative nonfault framework for compensation for certain medical injuries."¹³⁰

An alternative framework for compensation would entail the creation of a "special compensation fund which would utilize separate processes to achieve the compensatory objectives of the program."¹³¹ Compensation awards would be provided to victims according to "non-fault principles."¹³² The fund could be financed by subrogating the fund to the tort claims of accident victims. This suggestion is "in the service of a moral vision that offers greater inspiration than the competing vision of law and economics scholars."¹³³

(3) A federal product liability act. Federal legislation to establish a uniform body of product liability law is now before Congress.¹³⁴

(4) Strict joint and several liability with presumptions favoring plaintiffs.¹³⁵

128. *Id.* at 991.

129. *Id.* at 1026. In light of consumers' wishes for choice and physicians' desire for autonomy, there may be a question whether HMOs will reach near universal enrollment or control health care delivery systems.

130. Weisbard, *On Not Compensating for Bad Outcomes to Biomedical Innovations: A Response and Modest Proposal*, 8 CARDozo L. REV. 1161, 1162 (1987).

131. *Id.* at 1181.

132. *Id.*

133. *Id.* at 1188.

134. See e.g., H.R. 1115, 100th Cong., 2d Sess. (1988) (proposing the Uniform Product Safety Act of 1988); Eginton, *An Overview of Federal and State Legislation Developments in Torts and Products Liability*, in 2 ALI-ABA COURSE OF STUDY MATERIALS: TOXIC TORTS AND PRODUCT LIABILITY, COMPENSATORY AND PUNITIVE DAMAGES, INSURANCE COVERAGE DISPUTES, LEGAL MALPRACTICE, CHAPTER 11 BANKRUPTCY PROCEEDINGS, AND CIVIL LITIGATION 847 (1988); Cortese, *Products Liability Reform Proposal Would Eliminate Unpredictability*, Nat'l L.J., Jul. 25, 1988, at 18.

135. See Note, *Designer Genes That Don't Fit: A Tort Regime for Commercial Release of Genetic Engineering Products*, 100 HARV. L. REV. 1086 (1987). See also Comment, *Strict Product Liability for Injuries Caused by Recombinant DNA Bacteria*, 22 SANTA CLARA L. REV. 117 (1982).

(5) In vaccine cases, statutory schemes modeled on federal statutes for childhood vaccines or the swine flu vaccine or on the California statute for an AIDS vaccine.¹³⁶

(6) A compromise that would involve strict liability to assure adequate compensation to hapless victims, limits to prevent excessive damages for pain and suffering,¹³⁷ preclusion of punitive damages, insistence on rational bases for compensation and sufficient proof of causation, and ceilings on lawyers' and experts' fees in the event of dispute. Perhaps such a compromise would allay manufacturers' concern and promote their reconciliation to strict liability won by such a compromise, particularly in jurisdictions that elect not to follow the *Brown* case.

Some advocates may urge a continuation of the status quo. For example, one commentator has recently concluded that "it is incorrect to assume that the liability associated with existing vaccines will carry over to the HIV [AIDS] vaccine; therefore, it is unnecessary to enact legislation or to modify the common law in order to guarantee that pharmaceutical companies will develop and produce the vaccine."¹³⁸

Additional issues are likely to involve causation and joint and several liability.¹³⁹ The prospect of government liability for nondiscretionary acts in licensing new drugs and vaccines seems likely to be explored.¹⁴⁰ Moreover, if the government contracts with a private entity to manufacture or distribute a vaccine, issues will arise whether a "government contractor defense" is available to the private entity, particularly if the ultimate financial liability would fall on the government via indemnity or otherwise.¹⁴¹ Depending on the circumstances, the hypothetical

136. See Cooper, *The Product Liability of an AIDS Cure*, *The Recorder*, June 13, 1988, at 8-9 (article distributed through the Am-Law News Service). See also *supra* notes 92-93.

137. See R. Traynor, *The Ways and Meanings of Defective Products and Strict Liability*, 32 TENN. L. REV. 363, 376 (1965) ("[O]nce adequate compensation for economic loss is assured, consideration might well be given to establishing curbs on such potentially inflationary damages as those for pain and suffering. Otherwise the cost of assured compensation could become prohibitive.")

138. McKenna, *supra* note 76, at 944.

139. See Symposium, *Causation in the Law of Torts*, 63 CHI-KENT L. REV. 397 (1987); Jacob, *Of Causation in Science and Law: Consequences of the Erosion of Safeguards*, 40 BUS. L. 1229 (1985); Novick, *Use of Epidemiological Studies to Prove Legal Causation: Aspirin and Reyes Syndrome, A Case in Point*, 22 TORT & INS. L.J. 536 (1987).

In *Brown v. Superior Court*, the court decided that each defendant in a DES market share action is liable only for the portion of a plaintiff's damages that corresponds to its percentage share of the relevant market for DES, 44 Cal. 3d 1049, 1069-72, 751 P.2d 470, 475, 245 Cal. Rptr. 412, 424-25. It rejected joint and several liability, thereby resolving an issue left open after *Sindell v. Abbott Laboratories*, 26 Cal. 3d 588, 607 P.2d 924, 163 Cal. Rptr. 132 (1980).

140. See *Berkovitz v. United States*, ___ U.S. ___, 108 S. Ct. 1954 (1988).

141. See *Boyle v. United Technologies Corp.*, ___ U.S. ___, 108 S. Ct. 2510 (1988).

cases at the beginning of this article could raise such issues. A large question also looms as to whether liability in the case of exported products will be tested by U.S. or foreign standards.¹⁴²

E. What will be the Role of Courts in Addressing the Emerging Product Liability Issues in Biotechnology?

In resolving specific cases, by following the *Brown* case or adopting one of the foregoing or other approaches, courts are bound to recognize the extensive federal regulation. Two central issues then emerge: (1) is compliance with federal regulations a defense against liability or at least against punitive damages,¹⁴³ and (2) should federal regulations, for example on warnings, preempt state tort liability rules if they conflict?¹⁴⁴

Emerging state statutes afford a defense against punitive damages to manufacturers who have complied with federal law.¹⁴⁵ These statutes may serve as possible sources for common law development.¹⁴⁶ The law of punitive damages is undergoing serious challenge and review.¹⁴⁷ A

142. See Bonk, *FDA Regulation of Biotechnology*, 43 FOOD DRUG COSM. L.J. 67, 77-79 (1988) (reviewing the Drug Export Amendments Act of 1986, 21 U.S.C. § 382, 43 U.S.C. § 262); Pirt, *Regulation of the Export of Pharmaceuticals to Developing Countries*, 25 DUQ. L. REV. 255 (1987); Stewart, *International Aspects of Biotechnology: Implications for Environmental Law and Policy* (1988) (paper presented to ABA, 17th Annual Conference on the Environment, May 7, 1988) 9 Environmental law, No. 2, p. 1-3, ABA Standing Committee on Environmental Law, Quarterly Newsletter (Winter 1989); cf. La Prade, *Biotechnology in the Manufacture of Pharmaceuticals: The Need for International Regulation*, 19 TEX. INT'L L. J. 675 (1984).

The societal dilemma presented by the moral cost of creating impediments to continuing development of biotechnology procedures and the corresponding cost of failing to adequately regulate a potentially dangerous procedure is crucial in the context of United States foreign export laws as applied to pharmaceuticals. Prohibiting the export of unapproved drugs is one way to alleviate the problem of widespread drug dumping, particularly in the Third World. However, foreign nations have a right to make autonomous decisions regarding the potential risks and benefits of new pharmaceuticals. The regulation of the actions of foreign subsidiaries of domestic parent corporations must also be evaluated in the context of the ethical choices presented by new technology. La Prade, *supra* at 696. One author suggests that the "United States must seek to obtain extraterritorial jurisdiction wherever warranted." *Id.* at 697. Another commentator suggests that the Orphan Drug Act could help encourage research and development of new drugs and biotechnologies if applied in developing countries. Pirt, *supra* at 278.

143. See *supra* text accompanying notes 111-19.

144. See *supra* note 79.

145. See *supra* note 115.

146. See Landis, *Statutes and the Sources of the Law*, HARVARD LEGAL ESSAYS 213 (1934); R. Traynor, *Statutes Revolving in Common-Law Orbit*, 17 CATH. U.L. REV. 401 (1968); *In re Waltreus*, 62 Cal. 2d 218, 397 P.2d 1001, 42 Cal. Rptr. 9 (federal rule as model for state common law), cert. denied, 382 U.S. 853 (1965). See also *Decorative Carpets, Inc. v. State Board of Equalization*, 58 Cal. 2d 252, 23 Cal. Rptr. 589 (1962) (statute served as appropriate model for court to adopt in ordering return of funds to customers).

147. *Colonial Pipeline Co. v. Wright Contracting Co.*, 258 Ga. 115, 365 S.E.2d 827 (1988), *appeal dismissed*, ___ U.S. ___, 109 S. Ct. 36 (1988); *Browning-Ferris Industries v.*

reexamination of punitive damages in product liability cases involving a compliance defense seems likely.

A lesson from the polio vaccine cases may be that too strict a concept of liability is counterproductive. Although it may foster compensation in a few individual cases, it may deter manufacturers from manufacturing vaccines urgently needed for public health. A paucity of empirical evidence is available to a court, however, for resolving the questions presented by new technology where contributions to the health of many may entail adverse reactions to a few. "The creation of a risk utility balancing test has, in the view of some, forced the courts into an area that they are not equipped to handle."¹⁴⁸ Depending on the situation, product liability may or may not be a deterrent to manufacturers.¹⁴⁹ In the pharmaceutical area, expanded product liability may result in a declining rate of product innovation "since new products represent unknown hazards; more investment must now be made in pinpointing those hazards and in presenting the results to management and insurers."¹⁵⁰ The "inhibiting effect of expanded product liability is difficult to quantify because it permeates a firm's decisionmaking process."¹⁵¹

In a context of extensive federal regulation, emerging state statutes, and limited empirical data, courts should also be aware that there are two principal perspectives on the tort system and proposals for changing it. The "tort-centered perspective" views tort "as the general and predominant remedy for personal injuries." The "mixed system perspective" views tort as "only one among many remedial systems for dealing with personal injury."¹⁵² Significant proposals for changes in the allocation of responsibility between tort and other remedies¹⁵³ include "proposals to make compliance with regulatory requirements a defense to

Kelco Disposal Inc., 845 F.2d 404 (2d Cir. 1988), cert granted, ___ U.S. ___, 109 S. Ct. 527 (1988); see, e.g., Bittle, *Punitive Damages and the Eighth Amendment: An Analytical Framework for Determining Excessiveness*, 75 CALIF. L. REV. 1433 (1987); Jeffries, *A Comment on the Constitutionality of Punitive Damages*, 72 VA. L. REV. 139 (1986).

148. G. Eads & P. Reuter, *Designing Safer Products: Corporate Responses to Product Liability Law and Regulation* 17 (Institute for Civil Justice, The RAND Corporation, R-3022ICJ (1983)).

149. "All the firms [interviewed] viewed product liability litigation as essentially a random influence, generating no clear signals as to how to adjust design behavior." *Id.* at 107.

150. P. Reuter, *The Economic Consequences of Expanded Corporate Liability: An Exploratory Study* 26 (Institute of Civil Justice, The RAND Corporation, N-2807-ICJ (1988)).

151. *Id.* "The pharmaceutical group . . . offered the example of the bench chemist who simply chooses not to pursue his curiosity about pregnancy-related drugs because he knows that the firm's senior management is unlikely to fund later and more costly stages of the development process for such a high-hazard product." *Id.*

152. American Law Institute, *Compensation and Liability for Product and Process Injuries*, Spring 1988 Progress Report 6, 8 (1988).

153. *Id.* at 26-28.

punitive or compensatory damages in tort, provided certain conditions are met."¹⁵⁴

CONCLUSION

In our opinion, the California Supreme Court decision in the *Brown* case makes sense and should apply to drugs produced by biotechnology just as it applies to conventionally produced drugs. The policies invoked by the court do not depend on the technology used to produce the drug. By limiting strict liability while preserving liability for negligence under the principles of comment k, we believe the court has articulated a balanced approach that will encourage research and development of drugs that hold the promise of benefiting our lives while also allowing compensation for victims of negligent manufacturing or inadequate warning. We recognize that competing views will be presented to courts and legislatures and that the emerging product liability issues in biotechnology are not simple one-cell structures. One can only hope that judges and legislators will be equal to the task of resolving these complex and significant issues. The most wondrous man-made organisms, the most perplexing problems arising from their creation, may yet be more than matched by the everlasting capacity of reasoning minds to respond to the challenge of new problems by resolving them as justly as is humanly possible.

¹⁵⁴. *Id.* at 25. See Stewart, *The Roles of Liability and Regulation in Controlling Enterprise Risks*, forthcoming paper in connection with the American Law Institute Project on Compensation and Liability for Product and Process Injuries.