1983

Drugs during Pregnancy: Dangerous Business—The Continued Movement to Provide Adequate Warnings for the Consumer

David DeTar Newbert

University of Nebraska College of Law

Follow this and additional works at: https://digitalcommons.unl.edu/nlr

Recommended Citation


Available at: https://digitalcommons.unl.edu/nlr/vol62/iss3/4

This Article is brought to you for free and open access by the Law, College of at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in Nebraska Law Review by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.
Drugs During Pregnancy: Dangerous Business—The Continued Movement to Provide Adequate Warnings for the Consumer

[The child] was born on June 9, 1979 with birth defects in both arms and both legs. [Her] right arm is totally missing. Her left arm consists of a single short segment of bone which tapers to a point. [Her] right leg consists of an appendage less than one centimeter long which she can move voluntarily.¹

1. Description of Anne Elisabeth Koller, a plaintiff in the controversial Bendectin suit against Richardson-Merrell, Inc. Plaintiff’s Memorandum of Law in Opposition to Motion for Summary Judgment on the Issue of Causation at 8, Koller v. Richardson-Merrell, Inc., No. 80-1258 (D.D.C. Dec., 1982). Bendectin is a prescription drug manufactured by Richardson-Merrell, Inc. and sold in the United States for the alleviation of nausea and vomiting during pregnancy. Id. at 10. The same product is sold under other names (not by prescription but over-the-counter) in certain other countries such as the United Kingdom. The ingredients found in Bendectin are sold over-the-counter in the United States in other products such as Unisom, Vicks Formula 44, and Nyquil. Doxylamine succinate, a major ingredient of Bendectin, was shown in a 1982 FDA computer print-out to be present in nine over-the-counter products and 13 prescription products. Id. The plaintiffs in the Koller case claim that Bendectin is a teratogen. Id. at 16. See infra notes 58-60 and accompanying text. Bendectin was first marketed in 1956. Originally it contained three ingredients: dicyclomine, an anti-spasmodic; dextylamine, an anti-histamine; and pyridoxine (vitamin B₆), which has antinauseant properties. The drug was reformulated in 1976 to eliminate dicyclomine, which was found not to add to the drug’s effectiveness. 11 FDA Drug Bulletin (March 1981). An estimated 10-25% of the pregnant women in the United States receive prescriptions for Bendectin, usually in the first trimester. Id.

By its own admission, Merrell Dow Pharmaceuticals, Inc. has observed that since Bendectin’s introduction to the American market, over 33 million patients have successfully used the product. Mailgram from Merrell Dow Pharmaceuticals, Inc. to pharmacists, (June 9, 1983). Yet, researchers and clinicians in and out of government as well as Dr. William McBride, the world renowned teratologist responsible for pointing the finger at thalidomide, claim that Bendectin may be, for a variety of complex reasons, even more
The above description represents but a single life. It is, of course, a tragedy for even one child to be born with a serious malformation or abnormality. But the tragedy extends beyond the individual child and the child's family, affecting the community as well. More than 250,000 infants with birth defects were born last year in the United States. The thalidomide and DES disasters focused America's attention on the damaging effects drugs have on the unborn.

Certainly no one would quarrel with the assertion that the man-

insidious than thalidomide. "Bendectin, a possible low-grade teratogen, may be more dangerous than thalidomide, a high-grade teratogen [because]:

Most teratogens remain unknown. They are mysterious but often devastating assailants of our unborn children. They carefully guard their secrets, almost mockingly beckoning us to find them out. T.H. Bleakley & J.D. Peters, Bendectin, 16 TRIAL 56 (May 1980). Because of the lower incidence of teratogenesis with Bendectin, a "false sense of security and safety in physicians, resulting in even greater usage" is more probable. Id.

In its correspondence to pharmacists announcing the company's decision to cease production of Bendectin worldwide, Merrell Dow Pharmaceuticals, Inc. cited Bendectin as "a victim of these litigious times." Mailgram from Merrell Dow Pharmaceuticals, Inc. to pharmacists (June 9, 1983). But, perhaps the real reason behind the withdrawal of Bendectin can best be summed up as relating to a realization on the part of Bendectin's manufacturers that, "The best that can be said . . . is that there is no scientifically valid proof which shows Bendectin to be safe. . . ." T.H. Bleakley & J.D. Peters, Bendectin, 16 TRIAL 56, 61 (May 1980). For an interesting discussion of the controversy surrounding the Koller case, see Lauter, Bendectin Trial Disintegrates, NAT. L.J., Feb. 21, 1983, at 1. See infra notes 195-200 and accompanying text.

2. The Nebraska Legislature recognized this fact when it enacted "The Birth Defects Prevention Program" in 1972. The "occurrence of malformation or inherited disease at the time of birth is a tragedy for the child, the family, and the community, and a matter of vital concern to public health." Neb. LB 1203, 82d Leg., 2d Sess., 1972.

3. By the age of one year, 5-6% of the children born in the United States are recognized as having some sort of birth defect. Hutchings, Neurobehavioral Effects of Prenatal Origin: Drugs of Use and Abuse, in DRUG AND CHEMICAL RISKS TO THE FETUS AND NEWBORN 111 (1980). This percentage means that 250,000 defective children are born each year in the U.S. Id. See NATIONAL FOUNDATION MARCH OF DAMES, FACTS/1983 at 2 (1983).

4. See infra notes 55, 73, 87, & 198-99 and accompanying text.

5. From 1947 to 1971, physicians prescribed diethylstilbestrol (DES) to millions of pregnant women after the FDA had approved the use of DES to prevent miscarriages in 1947. Bichler v. Eli Lilly & Co., 79 A.D.2d 317, 321-22, 436 N.Y.S.2d 625, 628-29 (N.Y. App. Div. 1981), aff'd, 450 N.Y.S.2d 776, 780-81 (1982). Many daughters of these women have developed vaginal and cervical cancer which has been linked to their exposure to DES (a synthetic form of the natural female hormone estrogen) in utero. See infra notes 221-22 and accompanying text.
manufacture of "over-the-counter" and prescription drugs is big business in the United States. Literally billions of prescription and nonprescription drugs are sold each year in this country. Thousands of drugs espousing cures for every malady from the common cold to constipation are offered to the public. But what should consumers expect when they purchase and use these products? Should the manufacturer warn the consumer that certain side effects may sometimes accompany the cure? How should warnings be communicated?

The last two decades have seen a concerted effort on the part of the courts and government to deal with these complex questions. Recently, the Food and Drug Administration (FDA) amended the general drug labeling provisions so as to include warnings on numerous over-the-counter drugs. These changes are directed at protecting consumers who are either pregnant or nursing their infants. As a result, manufacturers of thousands of over-the-counter drug products will have until December 5, 1983 to comply with the new labeling requirements.

This Comment will briefly review the scientific information which led to the new labeling requirements and give a historical perspective of the government's role in protecting the American consumer from dangerous drugs. This article will also explore the drug manufacturer's role in the entire process and examine the

---

6. The term "over-the-counter" (OTC) derives from the basic marketing predicate that nonprescription drugs are purchased over-the-counter by consumers for the purposes of self-medication, typically without any intended or actual intervention by a physician. See, e.g., Torsiello v. Whitehall Laboratories, etc., 165 N.J. Super. 311, 398 A.2d 132 (1979).


8. In 1973 alone, 2.3 billion prescriptions and drug orders were dispensed in this country. Rucker, Drug Use, 229 J. A.M.A. 888-90 (1974).

9. For a discussion of the FDA's role, see infra notes 165, 182 & 185-87 and accompanying text.


11. Id. For the warning language and a discussion of the new provisions, see infra notes 297-323 and accompanying text.

12. FDA spokesman Ed Nida stated that as many as 300,000 products may be affected by the new warning. Omaha World Herald, Dec. 3, 1982, at 4, col. 3. The FDA already requires certain types of nonprescription drugs to carry specific label warnings about their use by pregnant or nursing women. Id. These special warnings, based on scientific information which suggests that the drug(s) may pose a potential danger to developing or newborn children, will not be affected by the new requirement. Id.

various tort liability theories involved. Finally, this Comment will analyze the new federal regulations, including their potentially unwelcome side effects.

II. BACKGROUND: THE PROBLEM

"We are living in a sea of chemicals that have not been tested for their ability to cause cancer or birth defects." From a medical standpoint, we truly are living in the era of the drug. In no other society are therapeutic drug products so plentiful, so faithfully used by the consumer, and so widely prescribed and recommended. New drugs appear on the market at an unprecedented rate, far faster than the medical profession can possibly digest all of the information about them. Almost every day brings news of still another drug, once thought to have been useful as well as safe, that has instead proved to be either worthless or lethal. It is not known how many deaths occur each year in the United States as the result of adverse drug reactions. Likewise, precise statistical data revealing the number of malformations caused by drugs are not available. Studies do suggest staggering figures—in the tens of thousands for the former, and in the hundreds of thousands for the latter.

17. An adverse drug reaction is defined as a “noxious and unintended” response “which occurs at doses used in man for prophylaxis, diagnosis or therapy.” Bennett & Lipman, Comparative Study of Prospective Surveillance and Voluntary Reporting in Determining the Incidence of Adverse Drug Reactions, in TEXTBOOK OF ADVERSE DRUG REACTIONS 1 (D. Davies ed. 1977). The Code of Hammurabi declared over 4,000 years ago that a physician who caused the death of a patient should suffer the loss of his hand. Id. For an insightful discussion of drug manufacturers' liability for unforeseen adverse drug reactions, see Note, The Liability of Pharmaceutical Manufacturers for Unforeseen Adverse Drug Reactions, 48 FORDHAM L. REV. 735 (1980) [hereinafter cited as Adverse Drug Reactions].
18. Some suggest as many as 140,000 deaths from adverse drug reactions (among hospital patients alone) occur each year. See Talley & Laventurier letter, 229 J. A.M.A. 1043 (1974). HEW's National Health Services Research Center estimates that 1.5 million hospital admissions a year are due to adverse drug reactions. 14 P.M.A. NEWSLETTER, Dec. 21, 1972, at 3. In addition to the physical effects measured in terms of human life and suffering, estimates of the monetary cost of adverse drug reactions range from one to four-and-one-half billion dollars per year (one-seventh of all hospital days). Adverse Drug Reactions, supra note 17, at 737.
19. These figures are the combination of the oft-accepted figure of 250,000 chil-
Biologists generally agree that the human embryo is susceptible to many outside factors. The naive belief that the fetus was somehow protected from environmental influences and thus safe within the mother’s womb is obsolete. It is remarkable, though, that prior to 1941, little credibility was given to the notion that environmental factors might cause malformations to develop in the human embryo. Unfortunately, although the dangers of so-called “ethical drugs” are well-documented throughout society, a complacent belief continues to exist that over-the-counter drugs are harmless. This belief, especially if held by pregnant or nursing women, is both naive and potentially tragic.

A. “Drugs”

One relatively common over-the-counter drug is acetylsalicylic acid, an analgesic (pain killer) classified as one of the safest of drugs. Approximately 15,000 tons of acetylsalicylic acid are produced and consumed in this country each year. A former Commissioner of Food and Drugs asserted, “There is no such thing as

dræn born with birth defects each year and one authority’s estimate that about 10% of all birth defects can be attributed to known environmental factors (including drugs). J. WILSON, ENVIRONMENT AND BIRTH DEFECTS 49 (1973). Of course, this is not a maximum. Wilson estimates that the cause of fully 65% of malformations is still unknown. Id. See infra notes 61-72 and accompanying text.


21. Id. In 1941, N.M. Gregg’s classic demonstration showed that rubella infection of women during pregnancy could cause severe malformations in their offspring. Id. But it was widely assumed by biologists and medical practitioners through the 1950’s that the developing mammalian fetus was protected from harmful environmental factors by the placenta. J. WILSON, ENVIRONMENT AND BIRTH DEFECTS (1973). The placenta was then believed to provide an impervious shelter. Prior to 1960, the “placental barrier” was commonly believed to effectively protect the human fetus from drugs given to the mother. Id..

22. The term “ethical drug” may be used interchangeably with “prescription drug” in contrast to over-the-counter medications. See supra note 6, see also infra notes 266, 287-88 and accompanying text.

23. “It has been recognized that every drug is inherently dangerous and every prescription drug has a potential for causing harm.” M. DIXON, DRUG PRODUCT LIABILITY (1981 Revision). The Dixon text clearly and comprehensively provides an excellent overview of the complex drug product liability area.

24. Better known as aspirin, it has been linked to adverse reactions, sometimes serious and occasionally fatal. MALPRACTICE AND PRODUCT LIABILITY ACTIONS INVOLVING DRUGS 6-7 (R. Patterson ed. 1976). Suggestions that drugs containing aspirin should be available only by prescription and contain warning labels have appeared recently. Weiss, Aspirin—A Dangerous Drug?, 229 J. A.M.A. 1221-22 (1974).

25. Weiss, supra note 24, at 1222. Taken during pregnancy, aspirin has been associated with unwelcome side effects for both the mother and her unborn child. See infra note 34.
absolute safety in drugs. There are some drugs that are less liable to cause harmful reaction than others, but people die every year from drugs generally regarded as innocuous.26 This not too reassuring statement was made nearly twenty years ago and continues to ring true today.

Drugs can be used for the prevention or cure of sickness and disease, the diagnosis of conditions, the alleviation of symptoms, and of course, the promotion of health. It is the chemical structure of each drug that determines the way it will interact with and alter the cells and chemicals of the body.27 Factors influencing the effect of a drug on the body include the body’s ability to absorb, distribute, metabolize, detoxify, and excrete it as well as the selectivity or “targeting” of the drug to a specific organ or site of action.28 Direct action drugs may have one or more target organs. Other drugs produce their effects on the target organ indirectly, either by preventing another drug or chemical normally present in the body from acting or by stimulating an organ which will in turn affect target organs.29 The vast majority of drugs exert their effects by modifying the metabolic activities of the body’s cells.30 Since drugs are chemicals, even if their specific therapeutic action is limited, they may produce nontherapeutic secondary reactions throughout the body.31 In addition, many drugs on the market are actually combinations of several different drugs or therapeutic chemical elements. When taken together, one drug may enhance the potency of the other or prevent the other’s operation. Likewise, one element may bring the desired cure while the other element causes an unwanted side effect.32 In the case of acetylsalicylic acid, the drug acts on the nervous system to relieve

28. Rheingold, supra note 16, at 950. Many drugs act directly to produce their effects by stimulating “target” organs. Direct action drugs may have one target organ or many. For instance, aspirin acts on the nervous system to relieve pain and reduce fever and on connective tissue in the joints to reduce swelling. L. Goodman & A. Gilman, The Pharmacological Basis of Therapeutics 327, 332 (5th ed. 1975).
29. See supra note 28.
31. Id.
32. Drugs that act by competing with other drugs or chemicals are called antimetabolites, antagonists, or blockers. Id. at 4-4. For a good discussion about the side effects of drugs, see Rheingold, supra note 16, at 950-53. If, when taken together, one drug enhances the potency of the other drug, the action is synergistic; if the drug tends to prevent the operation of the other drug, it is antagonistic in effect. Id. at 951.
pain and on connective tissue in the joints to reduce swelling, yet when the drug is taken during pregnancy, it has been associated with unwelcome side effects for both the mother and her unborn child.

B. The Embryo and Fetus

The complexity of human development involves a staggering 100 billion bits of information. The development process is much like a genetically preprogrammed series of instructions carried within the structure of the DNA of the human egg. In the human developmental program, the nine months prior to birth are the most critical in the entire process. Most of the handicapping disorders of infants and children are consequences of problems in prenatal development. Each year in the United States, some 1.2 million infants, children, and adults are hospitalized for treatment and more than 62,000 persons of all ages die as a consequence of birth defects.

Every human being begins life as a single cell. This cell (fertilized egg) will grow and develop into a normal human being if conditions in the womb (environment) are favorable. The development of an unfertilized egg, however, begins much earlier

34. Reports have associated the following defects with aspirin consumption: congenital heart disease, mongolism, congenital dislocation of the hip, hydrocele, talipes, and papilloma of the forehead. Hays, Teratogenesis: A Review of the Basic Principles With a Discussion of Selected Agents: Part II, 15 Drug Intelligence and Clinical Pharmacy 542, 548 (1981). Another study found that aspirin was associated with an increased length of gestation, post-maturity syndrome, and increased duration of labor. Id. at 548. There have been reports of neonatal bleeding problems in infants whose mothers consumed aspirin shortly before delivery; one case required a transfusion for the infant. Id. at 548. There have been reports of increased incidence of blood loss. Id. Aspirin has also been shown to be a teratogen in animal studies. Id. at 550. What makes these reports and statistics about the “common” (over-the-counter) aspirin alarming is the fact that approximately 80% of mothers ingest aspirin some time during pregnancy! Id. at 548. See infra text accompanying notes 76-90.
36. Id.
38. National Foundation March of Dimes, Birth Defects: Tragedy and Hope (1977). In addition, another half-million potential lives are destroyed each year as the result of miscarriage and stillbirth—largely the consequence of faulty fetal development. Id. A birth defect is an abnormality of structure, function or metabolism. It may be genetically determined or the result of environmental influence on the unborn child. Id.
in the mother's ovaries while she herself is a fetus. The nine-month span between fertilization of the egg and birth is an incredibly complicated and fast-paced period of human development. With the exception of identical twins, the genetic potential and environment of every individual during this period is different from that of all others. The environment will continue to interact with the preprogrammed set of genetic instructions throughout the entire development of the egg.

The embryonic stage of development commences during the second week after conception and continues until the end of the eighth week. It is during this time that the critical period for congenital malformations occurs. The development of the embryo is most easily disturbed during organogenesis. As the organs grow, their susceptibility to structural damage from outside influences decreases. But each organ has a critical period during which formation may be deranged. The three major variables causing nongenetic malformation include the type and amount of outside influence in conjunction with the timing of the interference.

The distinction between an "embryo" and the "fetus" occurs at about sixty days following conception. By this time, the beginnings of all major structures are present. The fetal period extends from approximately eight or nine weeks until birth and is primarily a time of fetal growth. The growth rate greatly accelerates, with tremendous weight gain during the final months prior to birth. During this period many organ systems develop further, although developmental changes are not as dramatic as throughout the embryonic stage.

---

40. See supra notes 35-36 and accompanying text.
42. Goldman, supra note 39, at 207; Dixon, supra note 23, at 4A-11.
43. There exists a critical period of greatest teratogenic susceptibility for the embryo which corresponds to the first trimester, which is when organogenesis occurs. It is, therefore, "during the first three months that the major anatomical malformations may be induced." Hays, supra note 34, at 543. See Dixon, supra note 23, at 4A-15.
44. Dixon, supra note 23, at 4A-15. For instance, the number of weeks from conception of greatest susceptibility for certain organs are as follows: heart—2½-5½; external genitalia—7-9; arms and legs—3½-7½; ear—3-8½; central nervous system—3-5; and eyes—3½-7½. *Id.*
45. See infra notes 54-58 and accompanying text. See also Hays, supra note 34, at 543. Of these external variables, timing is the most important. *Id.* See Goldman, supra note 39, at 203.
46. Shepard & Fantel, *Embryonic and Early Fetal Loss*, in 6 CLINICS IN PERINATOLOGY 219 (1979). The term "embryo" is reserved for the conceptus undergoing organogenesis. *Id.* See supra notes 42 & 43 and accompanying text.
Prior to 1960, it was widely assumed by medical practitioners and biologists that the placenta protected the developing fetus from harmful environmental factors. The placenta, the membrane which surrounds the fetus, was believed to provide an impervious shelter, a "placental barrier." As a result, it was commonly believed that the placental barrier would effectively protect the human fetus from drugs taken by the mother. This belief was consistent with the widespread view that birth defects were the result of maternal and paternal genetic traits. Today, the placenta is known to act instead as a sieve and not as a barrier.

One noted commentator has observed, "Mothering before birth is direct mothering." This is not difficult to understand when one realizes that most chemical agents taken by the mother are also "taken" by the fetus. The placenta operates as a bridge between the fetal and maternal circulatory systems. All nutrients, oxygen, and waste products cross this bridge. Thus, part of everything that a mother ingests during her pregnancy reaches the developing life within her. Once a drug has crossed the placenta, it enters the fetal circulation system. Children have been born with the smell of alcohol on their breath as well as with blood alcohol levels high enough to be considered legally intoxicated. The major mechanism by which drugs cross the placenta is passive diffusion. The placental membrane becomes progressively thinner during pregnancy, thereby decreasing diffusion distance.

Embryotoxicity is defined as a disturbance of the embryonic and/or fetal development by chemical dose levels which do not adversely affect the mother. The presence or absence of toxicity in the mother is not a reliable indicator for embryotoxicity. Toxic agents which are completely harmless to the mother may prove devastating to the embryo. This is primarily because the embryo has a higher susceptibility to drugs than has the adult, due in part

48. Id. at 4A-6.
49. Id. See supra note 21.
50. Smith, supra note 37, at 73.
51. Id.
52. Hays, supra note 34, at 546.
53. Id. at 542.
55. The "classic" human teratogen is thalidomide. Thalidomide was a safe and nontoxic sedative when administered to nonpregnant recipients. Dixon, supra note 23, at 4A-39. In fact, several suicide attempts with thalidomide were unsuccessful with no apparent ill effects. Id. But thalidomide produced severe phocomelic-type (affecting the arms, legs) defects in offspring of women when the drug was administered during the susceptible period of limb organogenesis. Id. at 4A-38. See Goldman, supra note 45, at 203. It has been reported that virtually every drug can be shown to be embryotoxic when administered in the right dose at the susceptible stage of embryonic develop-
to the particular vulnerability of certain embryonic cells that are not found in corresponding adult cells. Another factor relates to the sheer differences in dosage effect. A drug targeted at the 1,200 gram brain of the adult mother could have a much different effect on the developing embryo, whose brain weighs less than a gram during its most vulnerable stage of development. A drug or other agent which, when administered during pregnancy, is capable of producing a structural malformation present at birth or a functional defect in the offspring (including psychological or behavioral alterations) either at birth or in the immediate postnatal period, is known as a teratogen.

C. Teratogens and Birth Defects

"Birth defects due to teratogens have a special poignancy—they cause suffering to the most innocent of the innocent." Unfortunately, the search for drugs which are teratogens is both a complex and most difficult one. There exists neither compelling evidence for nor against classifying the vast majority of drugs as teratogens. Numerous variables account for this lack of knowledge.

Birth defects represent an intricate interplay of genetics and
environment. One frequently quoted scientific study found that the cause of fully 65 percent of all malformations is unknown, while 25 percent may be due to genetic and chromosomal factors. Only about 10 percent of the malformations could actually be attributed to known environmental factors. These figures obviously do not mean that only 10 percent or less of all birth defects are caused by drugs, nor should they be interpreted to imply that 75 percent of all birth defects are caused by unknown teratogens. These statistics are merely indicative of the serious lack of recognizable data on the problem of identifying the causes of malformations, spontaneous abortions, and stillbirths. It is generally assumed that as many as 25 percent of all human pregnancies end in spontaneous abortion, with the majority occurring during the first trimester. Yet, one should bear in mind the fact that studies arriving at the 25 percent figure have considered only those recognizable pregnancies which survived through the implantation of the egg and caused a missed menstrual period. There can be a considerable time lapse before a woman realizes she is pregnant. During this time, the delicate process discussed earlier is already well underway. When perinatal death occurs, it is often unexplained. Because the frequency of abnormalities and malformations is perhaps ten times higher among abortuses than newborn infants, spontaneous abortion is believed to be nature's selective elimination process. If a teratogen strikes early in the process

---

Down syndrome (formerly called mongolism); and (5) perinatal high-risk conditions, including markedly low birth weight, often accompanied by hypoglycemia (low blood sugar level). Underweight newborns have a higher death rate because of problems with breathing, heart action, digestion and resistance to infection. NATIONAL FOUNDATION MARCH OF DIMES BIRTH DEFECTS: TRAGEDY AND HOPE at 3, (1977).

63. Id. "Every observed association between drug exposure and a birth defect represents only one of two possibilities: a cause and effect relationship or a coincidental association occurring by chance alone without any causal relationship to drug exposure." Dixon, supra note 23, at 4A-69. "Distinguishing between these two possibilities is often exceedingly difficult . . . ." Id.
64. Shepard & Fantel, supra note 46, at 219.
65. Id.
66. Id. at 220.
67. See supra notes 42-44 and accompanying text.
68. "Perinatal" medicine focuses on the care and protection of the unborn and the newborn from soon after conception through the first month of life. "Death" in this context means the destruction of the life before birth as well. Driscoll, Placental Lesions, in 6 CLINICS IN PERINATOLOGY 397, 398 (1979).
69. Shepard & Fantel, supra note 46, at 222. Preterm and stillborn infants have significantly higher rates of congenital malformations. But approximately 75 percent of structurally abnormal embryos and fetuses never reach the viable stage. Id. at 225.
causing the death of an embryo,\textsuperscript{70} the resulting spontaneous abortion may very likely be attributed to nature's plan as well. The fact is in most instances, structural defects, whether genetic or environmental, are morphologically identical.\textsuperscript{71} A particular teratogen can produce a variety of birth defects that may arise singly or as a syndrome. Due to this lack of specificity it becomes difficult to establish an unambiguous causal relationship in humans.\textsuperscript{72} The teratogenicity of thalidomide was discovered only because it produced such a rare syndrome of defects.\textsuperscript{73} More recently, alcohol has been identified as a teratogen for the same reason.\textsuperscript{74} This led one commentator to suggest that if thalidomide—or even aspirin—produced a more common type of defect, like cleft palate in perhaps 5 percent of the cases in which it was consumed in the first

\textsuperscript{70} See supra note 68.

\textsuperscript{71} Hutchings, \textit{Neurobehavioral Effects of Prenatal Origin: Drugs of Use and Abuse}, in \textit{Drug and Chemical Risks to the Fetus and Newborn} 108, 111 (1980). See supra notes 64-73 and accompanying text. In addition, a teratogen tends to give rise to a spectrum of defects, a spectrum that may vary greatly both in extent and severity. Smith, supra note 37, at 74. Another problem is that a teratogen seldom causes defects in 100% of exposed fetuses. Id.

\textsuperscript{72} Hutchings, supra note 71, at 111.

\textsuperscript{73} Id. The evidence implicating thalidomide as a teratogen is now overwhelming, but no evidence of teratogenic effect was seen when thalidomide was tested on certain animals prior to release for clinical use. O. Heinonen, D. Slone & S. Shapiro, \textit{Birth Defects and Drugs in Pregnancy} 2 (1977). In pregnant women, exposure to even a single dose, from the twentieth to the thirty-fifth day after conception produced a unique syndrome characterized principally by deformities of the arms, legs and face, often together with more widespread deformities. Id.

\textsuperscript{74} Hutchings, supra note 71, at 111. Actually the serious impact of alcohol in fetal development was independently implied in 1834, in the 1880's and the early 1900's. Smith, supra note 37, at 75. "Behold, thou shalt conceive, and bear a son; and now drink no wine or strong drink . . . ." Judges 13:7. Thus, over two thousand years ago a link between birth defects and alcohol was recognized. The "fetal alcohol syndrome" (FAS) was first associated with heavy alcohol consumption, but later studies have shown an increased risk with moderate alcohol consumption as well. Hays, supra note 34, at 546. The defects in FAS can be divided into four major groups: (1) central nervous system dysfunction; (2) growth deficiency; (3) characteristic facies; and (4) associated anomalies. Id. FAS children often have defects which are manifested in one or more of the following areas: (1) cardiac—murmurs, especially in early childhood; muscular—hernias of diaphragm and groin; (2) nose—short-upturned; (3) central nervous system—mild to moderate mental retardation in over 80 percent of the cases; (4) mouth—small teeth with faulty enamels, cleft lip or cleft palate; and (5) eyes—short palpebral fissures; and marked growth deficiency. Id. at 548. Besides long-term problems, FAS infants face the possibility of acute alcohol withdrawal at birth manifested by seizures, irritability, hypoglycemia, and tremors. Id. at 546.
trimester, it would probably not have been suspected. Attempts have been made to establish a relationship between prenatal drug exposure and later neurobehavioral impairments. There is strong evidence which indicates that some impairments such as gross structural defects are of genetic origin but can also be produced by early exposure to environmental agents. Whether genetic or environmental, the symptomatology is virtually identical. One good example is hyperactivity. Genetic factors have been implicated as playing a significant role in the hyperkinetic syndrome, but this same behavioral impairment has also been reported in children following prenatal exposure to alcohol and cigarette smoke. The products of cigarette smoking—nicotine, carbon monoxide, and cyanide have also been linked to an increased spontaneous abortion rate, decreased birth weight, and mental retardation in the surviving offspring. In addition, the infants of mothers who smoke were shown to experience a direct dose-response relationship between the amount smoked and the level of nicotine in the mothers’ breast milk. Mental retardation is common with fetal alcohol syndrome offspring.

Frequently, multiple drugs are administered during pregnancy. One study found that a woman may take from three to twenty-nine drugs while pregnant, including labor and delivery medication, with ten being the average number. As a result, it becomes very difficult to isolate the teratogen that may have induced an abnormality. A woman who has had a baby born with a birth defect has probably pondered in great detail the events and stages of her pregnancy, looking for an explanation. Women who bear normal, healthy children seldom do such reflecting.

Research on the effects of drugs on animals is often used to

75. See A. Barnes, Intra-Uterine Development 362-77 (1968).
76. Hutchings, supra note 71, at 111.
77. Id.
78. Id. See Dixon, supra note 23.
80. Witter & King, Cigarettes and Pregnancy, in Drug and Chemical Risks to the Fetus and Newborn 83, 89-90 (1980). Smoking exposure in utero may have a long-term effect on both the physical health and mental function of the offspring. Id. Observed defects include: increased fetal heart rate; decreased fetal breathing movements; decreased IQ; increased incidence of sudden infant death syndrome; increased neonatal mortality; decreased head circumference; decreased post-natal growth; increased behavioral disturbances; and decreased length at birth. Hays, supra note 34, at 565. Such dangers have prompted Congress to consider new, stiffer label warnings on cigarettes. See infra note 334 and accompanying text.
81. Witter & King, supra note 80, at 89.
82. Hays, supra note 34, at 546. See supra note 74.
83. Id. at 545.
elicit data which can be applied to predict which substances will likely be harmful to the developing human fetus. However, such findings are not always conclusive. As one leading experimental teratologist observed, "A drug that is not demonstrably teratogenic in experimental animals may be so in man. A drug that is demonstrably teratogenic in animals may not be so in man. Therefore, the final proof of whether a drug is likely to be teratogenic in man must be sought in man." But even this less-than-encouraging observation may be somewhat misleading, for the impact of a given teratogen can seldom be predicted from its effects on the mature individual. Although considered a "classic" human teratogen, thalidomide was a safe and nontoxic sedative when administered to nonpregnant recipients. In addition, surveillance of drugs for their damaging effects on the human fetus is not readily accomplished through voluntary reporting by physicians. As noted earlier, unless a striking and rare abnormality is observed in association with an administered drug, physicians will most probably be unaware of the resulting defects. Finally, the delayed effects of drugs on humans following intrauterine exposure must also be considered. DES was found to lead to a high incidence of vaginal carcinoma in humans, but fifteen to twenty years were required for the effect of the intrauterine exposure to be evident.

The socio-medical aspects of the problem can thus be capsulized as follows: Drugs have become an almost subliminal part of everyday life for millions of American women, with many simply assuming that nonprescription, over-the-counter drugs are, by their very nature, safe; yet, the unborn life carried within each

84. Dixon, supra note 24, at 4A-21, 4A-22.
85. Id. at 4A-20 (quoting F.C. Fraser) (emphasis added).
86. See supra notes 71-73, 76, 77 & 85 and accompanying text; see infra notes 87-88 and accompanying text.
87. See supra note 55; infra notes 196-99 and accompanying text.
89. See supra notes 73-75 and accompanying text.
90. Yaffe, Summary: Pediatrician's View, in Drug and Chemical Risks to the Fetus and Newborn 157, 158 (1980). It has also become apparent that some male offspring were also affected, having abnormalities of the reproductive system including epididymal cysts, hypotropic testes, and pathologic semen. Id. Furthermore, cancer researchers in Boston have recently reported that sons of DES mothers may be likely to develop testicle cancer. Study: Synthetic Hormone May Produce 'DES Sons', L.A. Times Report published in Omaha World-Herald, March 11, 1983 at 16, col. 3. A great deal has been written about the DES tragedy. Several comprehensive discussions include: Abrahams & Musgrave, The DES Labyrinth, 33 S.C. L. Rev. 663 (1982); Comment, DES and a Proposed Theory of Enterprise Liability, 46 Fordham L. Rev. 983 (1978); Note, Market Share Liability: An Answer to the DES Causation Problem, 94 Harv. L. Rev. 668 (1981).
pregnant woman is exceedingly fragile and vulnerable to damaging influences throughout every stage of development; much, much more is unknown about the effects during pregnancy (both short- and long-term) of thousands of drugs than is known. This brief discussion of the effects of drugs on fetal development may be helpful in gaining a better understanding of the motivating factors which led to the promulgation of the new FDA warning regulations. However, a historical look at the consumer’s niche in the food and drug marketplace may provide further insight.

III. HISTORICAL PERSPECTIVE: GOVERNMENT’S ROLE AS CONSUMER PROTECTOR

Men with the muck-rake are often indispensable to the well-being of society, but only if they know when to stop raking the muck.\textsuperscript{91}

In 1810, the life expectancy of the average consumer living in Boston was twenty-seven years.\textsuperscript{92} In 1845, the average life expectancy had fallen to only twenty-one years.\textsuperscript{93} The first federal drug law came three years later. The Import Drugs Act of 1848 was enacted to prevent the importation of adulterated drugs.\textsuperscript{94} But it would take Congress another fifty-four years to pass a national piece of drug legislation that would provide any protection for the consumer.\textsuperscript{95} Unfortunately, the history of the government’s role as protector of the American consumer is “highlighted” by an on-going need for tragedy and scandal to serve as catalysts for congressional action, with the courts themselves only occasionally rising to the consumers’ defense.

A. The Early Years: Government Apathy

In 1902, twelve children died as the result of ingesting a diphtheria antitoxin.\textsuperscript{96} This tragedy spurred Congress to pass the strongest drug control legislation it had ever enacted: the Bio-


\textsuperscript{93} \textit{Id.}


\textsuperscript{95} In 1902, Congress enacted the Biologics Act, ch. 1378, 32 Stat. 728 (1902).

\textsuperscript{96} Janssen, supra note 94, at 425. The St. Louis Health Department was concocting its own diphtheria antitoxin when a tetanus contamination occurred. Twelve children died and ten recovered. \textit{Id.}
logics Act. But during the 19th century, the only federal law that could have been used against drug misbranding and quackery was the first mail fraud statute, enacted in 1872. Yet, for nearly three decades there was no record of its enforcement in the drug area. The federal government instead relied on a potpourri of state laws, many dating from colonial times. Furthermore, most of these laws were not consumer laws at all, but were enacted to serve the needs of trade and business. After the Civil War, change from an agricultural to an industrial economy made it necessary to provide the rapidly increasing urban population centers with food from distant areas. A boom in commercial food processing resulted and the use of chemical preservatives such as formaldehyde, borax, and salicylates became commonplace. In addition, artificial colors, some toxic, were indiscriminately used. Labeling gave no hint as to the dangerous ingredients employed.

During this period the United States, lacking the laws and regulations of European countries, found its export market suffering from the discredit cast upon American food and drug products. National inspection procedures abroad were so stringent and thorough that the complete absence of any such standards in this country was viewed as evidence of a disinclination on the part of the federal government to protect consumers against commercial avarice and fraud. The apparent philosophy of government was the old policy of caveat emptor—let the buyer beware. As a result, advertising campaigns in industrial America encouraged consumers to take patent-medicines without knowing what chemicals or ingredients they were consuming. Most of the drugs were over-the-counter preparations guaranteed to cure all manner of diseases and ailments. Many were plainly worthless, but others were often poisonous or addictive. Poisonous “women’s remedies” were sold in amazing quantities, and the sum total of their harmful effects will never be known. “Poor mothers doped their babies into insensibility at night with soothing syrups containing opium, morphine, cocaine, laudanum and alcohol.”

The organized patent-medicines industry wielded tremendous

97. Id. See supra note 95.
98. Janssen, supra note 95, at 424.
99. Id.
100. Id. at 425.
101. Id. at 421.
102. Id.
103. Litman, supra note 91, at 661.
104. Id.
105. Id.
106. Id. at 652.
107. Id.
power over the press through its vast expenditures for advertising. It was estimated that over $100,000,000 a year was paid to newspapers and magazines to advertise patent-medicines.\textsuperscript{108} And no wonder, the profits were unbelievable. Many patent-medicines cost about eight cents to produce and sold for a dollar.\textsuperscript{109} Furthermore, many of these concoctions, containing water and sulphuric acid, also contained a variety of habit-forming drugs. Thus, the "cure" often continued to be in demand long after the patient's sickness had subsided. In order to prevent adverse legislation, one drug manufacturer inserted in its advertising contracts with over 15,000 newspapers this clause: "It is hereby agreed that should your State, or the United States Government, pass any law that would interfere with or restrict the sale of proprietary medicines, this contract shall become void."\textsuperscript{110}

How effective was the industry's attempt to block national legislation that would protect the American public from dangerous and worthless drugs? Between January 20, 1879 and June 30, 1906, when the Pure Food and Drug Act\textsuperscript{111} was finally passed, 190 measures were presented in Congress which were designed in some fashion to protect the consumer from adulterated and misbranded food and drugs.\textsuperscript{112} Of the 190 bills introduced during this twenty-seven year span, only eight became law.\textsuperscript{113}

\section*{B. The Battle of the Muckrakers}

Four years before the passage of the 1906 Pure Food and Drug Act, Dr. Harvey Wiley, a leading proponent for consumer drug legislation, organized a "Poison Squad."\textsuperscript{114} Referred to by a commentator as the "ultimate in human experimentation,"\textsuperscript{115} the Poison Squad was comprised of twelve "young robust men" from the Department of Agriculture who were placed on a regimented diet containing many different food preservatives.\textsuperscript{116} The experiments were carried on for five years and conclusively proved that such preservatives were indeed harmful.\textsuperscript{117}

\textsuperscript{108} Id. at 663.
\textsuperscript{109} Id. After 50 years, the drug industry's profits have apparently changed little. See R. Harris, The Real Voice 59-63 (1964) (discussing 1,118 percent mark-ups, and the selling of drug products for $8 that were purchased for 28c).
\textsuperscript{110} M. Mintz, By Prescription Only 43 n.4 (1967). See infra note 121.
\textsuperscript{111} Ch. 3915, 34 Stat. 768 (1906).
\textsuperscript{112} Litman, supra note 91, at 661.
\textsuperscript{113} Id.
\textsuperscript{114} Id. at 662.
\textsuperscript{115} Id.
\textsuperscript{116} Id.
\textsuperscript{117} Lew Dockstader, a minstrel star of the times, introduced a song dedicated to the poison squad with the refrain:
As early as 1892, one magazine, the *Ladies’ Home Journal*, had denied its advertising pages to manufacturers of patent-medicines.\(^{118}\) But it was not until over a decade later that the efforts of Wiley, a group of journalists, and a novelist named Upton Sinclair aroused the American consumer. While Wiley’s Poison Squad was making headlines and music,\(^{119}\) a group of crusading writers joined the campaign for consumer legislation. The journalists became known as the “muckrakers”\(^{120}\) and shocked public opinion with their editorials, articles, and cartoons which graphically described the fraud, high profits, and squalid conditions in the industry.\(^{121}\) This publicity together with Sinclair’s novel, *The Jungle*,\(^{122}\) which horrified the American public with its sickening depiction of the meat packing industry, finally provided Congress with the necessary political prodding.

A Pure Food and Drug bill had sat in limbo on committee tables for over twenty-five years without passage. It was the belated support of President Theodore Roosevelt that proved to be the chief

---

O, they may get over it but they'll never look the same.
That kind of bill of fare would drive most men insane.
Next week he'll give them mothballs, a la Newburgh or else plain;
O, they may get over it but they'll never look the same.

118. Litman, *supra* note 91, at 663.
119. *See supra* note 97.
120. Numerous books and magazine articles decried the greed and lawlessness of big business and the “venality of politicians.” Litman, *supra* note 91. Upton Sinclair most vividly “raked up the muck” in his novel *The Jungle*. *See infra* note 122. “The muckrakers advocated the pure food and drug legislation because it increased the protection of the public health, decreased the amount of sickness, and lengthened the average American’s life span.” Litman, *supra* note 91, at 655.

121. One of the worst abuses of the era was the addiction of babies to “soothing syrups”, often given to make them stop crying. There were at least a hundred such products on the market, containing varying amounts of morphine, opium, or heroin. Janssen, *supra* note 94, at 428. The *Chicago Tribune* led the fight against these “soothers”, calling them “baby killers” instead. *Id.*


122. *The Jungle* told of the life of a Lithuanian peasant working in the Chicago meatpacking establishments. Litman, *supra* note 91, at 665. Meant to serve as propaganda for socialism, it was the information it revealed about the unhealthy conditions prevalent in the packing houses as well as about the unclean meat which was regularly sold to the consumer that caught the public’s attention. *Id.* “Sinclair described how diseased cattle were butchered, marked by the government inspectors, thrown into dumps, loaded on carts and wheeled back again and mingled with other carcasses and treated and sold as clean meat.” *Id.* The author later observed that he had aimed at the public’s heart but by accident had hit the stomach. Such sensational passages about the squalid conditions comprised only about eight pages out of the 308 pages in *The Jungle*, but those eight pages horrified and outraged the American consumer. *Id.*
stimulus for final enactment of the bill.\textsuperscript{123} Roosevelt had not been involved in the long struggle for the bill's passage until the surge of public support and outrage caused by the muckrakers and \textit{The Jungle}.\textsuperscript{124} As a result of the scandal exposed by Sinclair's novel, a national meat inspection bill would have to be signed or the politicians would have had to answer to their voting constituents. The Federal Meat Inspection Act\textsuperscript{125} proved to be the catalyst needed to get the Pure Food and Drug Act of 1906 passed.\textsuperscript{126} On June 30, 1906, Roosevelt signed the original Pure Food and Drug Act, which also became known as the Wiley Act.\textsuperscript{127}

C. The Elixir Tragedy and the Act of 1938

It has been asserted that no single event has had greater significance in the history of consumer protection laws or the industries they regulate than the 1906 Act.\textsuperscript{128} The primary purposes of the 1906 Act were to prohibit misbranded, false, or misleading labels on drugs,\textsuperscript{129} and to keep such drugs from being sold in interstate commerce.\textsuperscript{130} These goals quickly proved to be ineffective. The drug industry, having lost the twenty-seven year battle over the enactment of the Act, wasn't about to concede the war and was determined not to be bound by the new law. Various political maneuvers were quickly designed to prevent strict enforcement of the new law.\textsuperscript{131} As Wiley later observed, the drug industry "caused long and agonized trouble. Having lost the fight in Congress, a number of adulterators and misbranders sought to destroy the law and prevent its enforcement."\textsuperscript{132} The 1906 Act also proved to contain many serious loopholes\textsuperscript{133} and the industry was quick to capi-

\begin{itemize}
  \item \textsuperscript{123} Id. at 668.
  \item \textsuperscript{124} Id.
  \item \textsuperscript{125} Ch. 3919, 34 Stat. 669 at 674 (1906).
  \item \textsuperscript{126} Ch. 3915, 34 Stat. 768 (1906).
  \item \textsuperscript{127} Janssen, supra note 94, at 420. See Litman & Litman, Protection of the American Consumer: The Congressional Battle for the Enactment of the First Federal Food and Drug Law in the United States, 37 Food Drug Cosm. U.J. 310 (1982). The 1906 Act was commonly referred to as the Wiley Act because its enactment was largely the result of Dr. Harvey Wiley's (chief chemist of the U.S. Dept. of Agriculture) efforts.
  \item \textsuperscript{128} Janssen, supra note 94, at 420.
  \item \textsuperscript{129} McClellan, Tate & Eaton, Strict Liability for Prescription Drug Injuries: The Improper Marketing Theory, 26 St. Louis U.L.J. 1, 14 (1981) [hereinafter cited as Eaton].
  \item \textsuperscript{130} Id.
  \item \textsuperscript{131} Id. The politically appointed solicitor of the Federal Department of Agriculture moved rapidly to prevent strict enforcement of the 1906 Act by diluting Dr. Wiley's authority. \textit{Id}.
  \item \textsuperscript{132} Id.
  \item \textsuperscript{133} The 1906 Act did not provide any control over advertising, as distinguished from labeling of drugs. Møniz, supra note 110, at 44. Neither did the 1906
talize on them. In addition, the United States Supreme Court dealt a severe blow to the Act in 1911 in the first drug case to come before the Court. In United States v. Johnson, the Court interpreted the Act as prohibiting false and misleading claims as to the ingredients of the drug but not as prohibiting false therapeutic claims as to the curative properties of the drugs themselves. Congress passed the Sherley Amendments in 1912 to overrule the Court's decision. The 1912 amendments specifically forbade false and fraudulent therapeutic claims on the labeling of medicine intended to defraud the purchaser. This simple change in phraseology was observed to practically legalize false therapeutic statements because, "to be illegal, they had to be both false and fraudulent, a fact very difficult to prove [because fraud involves intent to deceive]." The same commentator wrote that "the phraseology was advocated at the hearings on the amendment by Charles M. Woodruff at Parke-Davis and Company," one of the nation's largest drug manufacturers.

Dr. Wiley, in his autobiography, stated, "The trouble now is that no one takes much interest in the Food and Drugs Act—that is to

---

134 See supra note 133. As a result, "Nostrum advertising boomed. The damage to health, the waste of life, the squandering of money for worthless medications—all of these kept pace." Mintz, supra note 110, at 44.

135 221 U.S. 488 (1911).

136 Id. at 497. Thus, in the case of "Dr. Johnson's Mild Combination Treatment for Cancer," the promoter could not be prosecuted for "mistaken praise," even though the indictment charged that he knew his claims were false. Id. at 488 (notice of judgment no. 1058). Janssen, supra note 94, at 427. President Taft immediately called on Congress to close this dangerous loophole in the 1906 law, saying:

There are none so credulous as sufferers from disease. The need is urgent for legislation that will prevent the raising of false hopes of speedy cures of serious ailments by misstatements of facts as to worthless mixtures on which the sick will rely while their disease progresses unchecked.

(Message from President Taft). 62 CONG. REC. 1st Sess. 2380 (June 21, 1911). Congress passed the Sherley Amendments in 1912 to overrule the Johnson Court's decision. See infra notes 137-38 and accompanying text.


138 Eaton, supra note 129, at 15.

139 Mintz, supra note 110, at 44 (quoting Stephen Wilson from the Food and Drug Regulation). The Sherley Amendments were thus ineffective.

140 Id.
say, no one in Congress. It is regarded as established and in perfect operation. This is a great mistake.” 141 Unfortunately, among the public at large, the 1906 Act was also mistakenly thought to be providing adequate protection. The economic hardships of the depression years magnified the Act’s many shortcomings. 142 The book, Your Money’s Worth, 143 signaled the start of a new worldwide consumer movement. 144 But it would take another tragedy with the loss of over one-hundred lives to make Congress take action.

In 1937, the Massengill Company marketed an “Elixir of Sulfamilamide.” 145 The solvent was diethylene glycol, a chemical relative of permanent radiator antifreeze. 146 The 1906 Act did not require testing of the chemical before making it available to the consumer. Massengill did not test the “Elixir” beyond checking it for fragrance, appearance, and flavor. 147 Of 240 gallons manufactured, 11¾ were distributed across drug counters with and without prescriptions. With the first reports of deaths in October 1937, seizure of the chemical immediately began and all but the 11¾ gallons that had been distributed were confiscated. 148 Ironically, these seizures were possible only because the drug had been misbranded as an “Elixir,” which wrongly implied that it contained alcohol. 149 Had the deadly mixture instead been called a “solution”, the federal authorities could not have legally seized the product. When it was all over, 108 persons were dead, including the pharmaceutical chemist who had developed the drug; but unlike the other victims, his death was a suicide. 150 Later testimony revealed that by simply testing the drug on animals, the poisonous danger of the Elixir would have been exposed to the manufacturer. 151 Again the public reacted with outrage. When Congress finally addressed the need to overhaul the 1906 Act, thirty-two years had elapsed.

Among the many important advances contained in the Federal Food, Drug, and Cosmetic Act of 1938 152 was a section which required manufacturers to test each new drug for safety and to re-

141. Mintz, supra note 110, at 44.
143. S. Chase, Your Money’s Worth (1934).
146. Mintz, supra note 110, at 48.
147. Id.
148. Id.
149. Id. at 49.
150. Id.
151. Id. at 48.
port the results to the Food and Drug Administration.153 Unfortunately, as had been the case with its predecessor, the 1938 Act contained some large loopholes. For instance, unless the FDA acted within 180 days to prevent marketing, a new drug could automatically be sold to the consumer.154 The FDA was empowered to delay the release of a drug even longer if it found that the manufacturer's test did not show the drug to be safe under recommended conditions, and the agency was given authority to remove from the market a drug it could prove to be unsafe.155 But the 1938 Act also contained a grandfather clause which exempted drugs on the market prior to 1938 from the premarketing clearance procedures.156 As a result, the stricter new provisions were applied solely to new drugs to be sold in interstate commerce. The 1938 Act also failed to require manufacturers to establish that their products were effective as well as safe for intended use.157 An efficacy requirement had been proposed in the original 1933 bill,158 but Congress, in killing the consumer-oriented aspect "was, some contend, recognizing the economic, lobbying and political—not the medical—facts of life."159 In any respect, almost thirty years would pass before the FDA would be given specific authority to examine "new" drugs to


154. Federal Food, Drug, and Cosmetic Act, ch. 675, 52 Stat. 1040, 1052 (1938), amended by 21 U.S.C. § 355(c) (1976). In addition, there still was no requirement that the manufacturer establish the efficacy of the product prior to marketing. Federal Food, Drug, and Cosmetic Act, ch. 675, 52 Stat. 1040, 1052 (1938). This was capitalized on by many manufacturers and led to the sale of ineffective drugs, "allow[ing] the manufacturers to make exaggerated and unsubstantiated claims about the efficacy" of their products. Eaton, supra note 129, at 16.

155. Mintz, supra note 110, at 49. See supra notes 152-54. Although many compromises had been made to secure passage of the 1938 Act, the new law did provide some major improvements: proof of fraud was no longer required to stop false claims for drugs; cosmetics and therapeutic devices were regulated for the first time; specific authority was given for factory inspections; addition of poisonous substances to foods was prohibited except where unavoidable or required in production; federal court injunctions against violations were added to the previous legal remedies of product seizures and criminal prosecutions; and, drug manufacturers were mandated to provide scientific proof that new products were safe before putting them in the marketplace. Janssen, supra note 94, at 429.

156. Eaton, supra note 129, at 17.

157. See infra notes 158-59 and accompanying text.

158. The "Tugwell Bill" introduced in Congress in 1933 "was a legislative disaster" with "[t]he opposition of industry and advertising interests to this New Deal legislation . . . total and overwhelming." Janssen, supra note 94, at 429.

159. Mintz, supra note 110, at 49 (emphasis added).
determine whether or not these drugs produced the results promised by their manufacturers.160

D. Enter the FDA

Important pharmaceutical history resulted from section 502(f) of the 1938 Act which required drug packages to be labeled with adequate warnings and directions for proper use.161 However, the Act exempted manufacturers from having to provide directions when they were "not necessary for the protection of the public health."162 The new statute fell far short of providing a clear, complete, and workable system of drug labeling and regulation.163 Yet, because the new Act was in such contrast to its 1906 predecessor, many of the shortcomings of the 1938 statute were not apparent.

From 1906 until 1927, the Bureau of Chemistry enforced the original 1906 Act.164 In 1927 the Food, Drug, and Insecticide Administration was formed and in 1931 renamed the Food and Drug Administration.165 On December 28, 1938, the FDA published in the Federal Register its general regulations for the enforcement of the Federal Food, Drug and Cosmetic Act of 1938.166 Drugs whose common uses were known to the ordinary individual were exempted from labeling with "adequate directions."167 In addition, drugs identified with what was soon to be called the RX Legend—"Caution: to be used only by or on the prescription of a..." (physician, dentist, or veterinarian)—were also exempt.168 Furthermore, "all representations or suggestions" with respect to the uses of these drugs were required to appear only in such medical terms as are not likely to be understood by the ordinary individual."169 Shipments were to be made only "for use exclusively by or on the prescription of physicians, dentists or veterinarians licensed by law to administer or apply such drugs..."170 Distributions via other channels would not be exempted, thus making the shipments illegal.171 As a result, the FDA attempted, for the first time,

160. See infra notes 192-93 and accompanying text.
162. Id.
163. Id. Another problem was that "drugs too dangerous for lay use were increasingly being sold over-the-counter." Id. See infra notes 173, 294 & 295 and accompanying text.
165. Id.
167. Id.
168. Id.
169. Id.
170. Id.
171. Id.
to restrict to professional channels those drugs deemed to be unsafe for use by the lay consumer. In 1939 a letter was sent to drug manufacturers stating that label warnings such as “[t]o be used under the direction of a physician only” were not effective in preventing over-the-counter sales. A stronger, more conspicuous warning was urged.

On April 15, 1941, revised regulations on directions for the use of drugs were published in the Federal Register. These regulations repeated the original wording of the RX Legend. Shortly thereafter, the FDA finally supplied a list of drugs which the agency considered too dangerous for self-treatment and therefore required a prescription. The FDA had previously refused trade requests to supply such a list for two reasons: (1) it was the manufacturer’s responsibility for deciding how to label its drugs, and (2) the FDA was not authorized under the 1938 statute to provide such a list. As one commentator noted, “[T]he Agency hedged its list by saying that it was impossible to provide a complete list of drugs which could be dangerous in self-medication.”

Nine months later, the United States entered World War II. The war effort would divert the FDA’s resources to the important new assignment of testing drugs for the military. The end of World War II brought the “drug revolution.” New prescription drugs, some being of unimagined chemical formations with completely unknown effects, entered the marketplace at the rate of 300 to 400 a year.

Although the role of the FDA had originally been to protect the American public from the “nostrums, folk remedies, and other medications which were widely advertised and sold without serious attention to their presentation,” the problem of efficacy in drugs had now, for the first time, shifted heavily to prescription products. Between 1938 and 1960 an average of 375 new drug

172. Id.
173. Id.
174. Id.
175. Id. at 432.
176. Id.
177. Id.
178. Id. at 432-33.
179. Id. at 433.
180. Mintz, supra note 110, at 50.
181. Id.
182. Dixon, supra note 23, at 5-3. Today the FDA controls manufacturing procedures, drug advertising, drug labeling and practically all communications between the drug manufacturer and the practitioner who prescribed the drug. Id. at 5-10. The FDA is also charged with evaluating the effectiveness of approved drugs. Id. See infra notes 202-09 and accompanying text.
183. Mintz, supra note 110, at 50.
products a year were cleared by the FDA. Although many of these drugs did not contain unique ingredients or chemical entities, the task of reviewing them was far beyond the capacity of the agency. Consequently, the FDA delegated the review of drugs entering the marketplace between 1938 and 1962 (including those drugs for which new approval was sought) to the panels of the National Academy of Science and the National Research Council. During this twenty-four year period, pharmaceutical manufacturers filed 13,023 new-drug applications, of which 9,097 were cleared by the FDA.

According to one expert, this rapid increase in the introduction of new drugs (especially as seen in the 1950s) made the FDA increasingly conscious of a very serious problem:

The drug manufacturers were replacing the medical schools as the principal source of information for physicians in their use of new drugs. The informative labeling worked out by FDA with applicants in the course of processing New Drug Applications, was not reaching physicians. This labeling, in accord with the regulations, was referred to on the drug label as “available to physicians on request.” The pharmaceutical industry, however, was [instead] promoting the use of these potent new drugs to physicians by detail men, mailing pieces, medical journal advertising, and reference publications that frequently failed to disclose their hazards. As a result, the more informative labeling was rarely “requested” by the physician and there was no assurance that the information would indeed be provided in response to requests. As this danger was recognized, the FDA required new drugs to include the informative labeling as part of the prescription drug package. But such actions proved to be an inadequate solution to a dangerous problem. The flood of new products had created an “information lag” and with it the need for new legislation.

E. The 1962 Drug Act Amendments and “Kevadon”

On April 12, 1961, Estes Kefauver, a United States Senator from Tennessee, introduced legislation which required the manufacturers of prescription drugs to prove that their drugs were both safe

184. Id. at 51.
185. Eaton, supra note 129, at 21; see infra note 215.
186. Eaton, supra note 129, at 21. This action did not occur until after the 1962 amendments were passed. See 21 C.F.R. § 130.38 (1967). See also infra notes 202-06 and accompanying text.
188. Dr. Ralph G. Smith, former director of the FDA’s division of new drugs, in a 1968 paper to the American Society of Hospital Pharmacists, reprinted in Janssen, supra note 94, at 436 (emphasis added).
190. Id.
191. Id. at 437.
and efficacious before they would be allowed to market them.\textsuperscript{192} This shift in the burden of proof regarding a drug's attributes from the FDA to the drug manufacturers\textsuperscript{193} resulted in a battle in Congress of the intensity like none other since the 1906 Act. Kefauver's steadfast fight in the Senate against his colleagues (particularly Senators Hruska and Dirksen, from Nebraska and Illinois, respectively) to gain passage of the drug reform amendments is interestingly and enlighteningly portrayed in the book \textit{The Real Voice}.\textsuperscript{194} When the smoke had cleared, the impetus that pushed the legislation past its many opponents came from a most unlikely source.

The Wm. S. Merrell Company filed a new drug application on September 12, 1960.\textsuperscript{195} The new drug, to be sold in the United States as "Kevadon," would have carried labeling which stressed its value in combatting nausea during pregnancy.\textsuperscript{196} Merrell distributed 2,528,412 tablets in a variety of colors and sizes to 1,267 doctors nationally on an investigational basis. The doctors, in turn, gave the tablets to some 20,000 patients in containers that bore nothing more than directions for use.\textsuperscript{197} This new drug soon made worldwide headlines as the results of its terrifying side effects on the newborn babies of thousands of women throughout Europe became apparent.\textsuperscript{198} The drug, whose American trade name was

\textsuperscript{192} Eaton, \textit{supra} note 129, at 19-20.
\textsuperscript{193} \textit{Id.}
\textsuperscript{194} R. \textsc{Harris}, \textit{The Real Voice} (1964). "Ultimately, the job of serving as [drug] industry spokesman fell to Senator Roman B. Hruska, an archconservative from Nebraska . . . . According to one industry representative, Hruska was, if anything, too devoted to his task." \textit{Id.} at 69. As the representative explained, "Instead of concentrating on the drug industry's considerable achievements and letting the ugly facts pass by as quickly and unobtrusively as possible, Hruska defended everything the industry had ever done and attacked the least significant criticisms of it at endless length." \textit{Id.} Kefauver was especially annoyed by Hruska's behavior, stating, "In all my years in Congress, I've never encountered such harassment, obstructionism, and vitri-\textsuperscript{195}lation." \textit{Id.}
\textsuperscript{195} Eaton, \textit{supra} note 129, at 18 n.72.
\textsuperscript{196} \textit{Id.}
\textsuperscript{197} \textsc{Harris}, \textit{supra} note 194, at 209.
\textsuperscript{198} The drug, developed by the German firm, Chemie Grunenthal, was extensively sold in Western Europe, England, Canada, Brazil, Japan, and other countries as a sedative. Since it produced a deep sleep without the "hangover" effects of other sedatives, it achieved great popularity and was "manufactured literally by the ton." S. \textsc{Rep.} No. 1744, 87th Cong., 2nd Sess. \textit{reprinted} in 1962 U.S. \textsc{Code} Cong. & Ad. \textsc{News} 2884, 2905-06. When given to expectant mothers in early pregnancy, their babies in some cases were born with assorted malformations, particularly a condition called phocomelia, or "seal limbs" because the hands and feet are attached close to the body like flippers, with little or no arms or legs. \textit{Id.} As many as 5,000 malformed babies were born in Europe, reaching "epidemic proportions" in the fall of 1961. \textit{Id.}
Kevadon, was the sedative thalidomide.\textsuperscript{199} The only reason that the drug had not been marketed commercially in the United States was because a FDA medical officer, Dr. Frances O. Kelsey, had refused to release the drug based on what she believed was inadequate evidence.\textsuperscript{200} One commentator described what followed next: "The headlines screamed, the public was aroused, the drug manufacturers ran scared, and the opponents of [Kefauver's] tough bill jumped for cover."\textsuperscript{201}

One of the most important elements of the 1962 Amendments was the additional authority given to the FDA. The Act required drug manufacturers to not only keep records, but to report on experiences with each drug on the market as new data became available.\textsuperscript{202} One of the primary purposes of the new amendments was to ensure that the FDA had access to current information, so that the agency could make informed judgments about the marketing of the drug.\textsuperscript{203} The Act empowered the FDA to require drug manufacturers to make reports on human experiences with experimental drugs prior to the submission of a new drug application, as well as to keep records of all adverse drug reactions.\textsuperscript{204} Other new provisions with respect to investigational drugs required informed patient consent before trials on human subjects. Drug companies were required to register their establishments with the FDA and be subject to an inspection at least once every two years.\textsuperscript{205} Very importantly, companies were required to show, by substantial evi-

\textsuperscript{199} See supra notes 195-98 and accompanying text.

\textsuperscript{200} Janssen, supra note 94, at 437.

\textsuperscript{201} Id. (quoting from Dr. Harry Dowling's book, \textit{MEDICINES FOR MEN}).

\textsuperscript{202} See infra note 203.

\textsuperscript{203} Eaton, supra note 129, at 21. See infra notes 204-06, 209 and accompanying text. The new regulations require drug manufacturers to make periodic safety reports. Furthermore, manufacturers must report within 15 days any information they receive regarding adverse effects if such effects had not been reported in the new drug application or encountered during subsequent clinical trials. Eaton, supra note 129, at 23.

\textsuperscript{204} At the heart of the 1962 law was the requirement that no new prescription drug could be admitted into interstate commerce until the manufacturer had filed application with the FDA providing proof that the drug was both safe and effective. Rheingold, supra note 16, at 960. For a lengthy discussion and definition of what the term "new drug" means, see Dixon, supra note 23, at 5-12 & 5-20-23. After the clinical trials are complete, the manufacturer will submit a new drug application (NDA). The NDA is the required proof that the drug is safe and effective as represented by the manufacturer. For a discussion of the NDA process, see Dixon, supra note 23, at 5-22 to 25; see infra note 206. The 1962 amendments placed the burden on the proponent of the NDA to show "by substantial evidence" that the drug would have the effect it promises. Drug Amendments of 1962, Pub. L. No. 87-781, § 102(b), 76 Stat. 780, 781 (1962) (amending ch. 675, 52 Stat. 1052 (1938)).

\textsuperscript{205} See Dixon, supra note 23, at 5-5—5-6 for a discussion of the thrust of the 1962 amendments.
dence from controlled studies, the *effectiveness* as well as the *safety* of new drugs, in order to obtain requisite FDA approval for marketing. The new regulations implementing the 1962 Amendments closed many of the loopholes which had previously existed.206 Obviously, preventing violations through premarketing clearance procedures affords consumers far better protection than does the alternative of merely prosecuting violations after the injuries have been reported. The trend towards preventive law has slowly evolved with each successive step in the legislative process.

As had been the case with the 1906 Act, most drug manufacturers did not react kindly to the new restrictions and regulations.207 One commentator observed that after passage of the 1962 Amendments, “the drug industry, acting primarily through the Pharmaceutical Manufacturers Association (PMA), continued to fight a legal, political, and regulatory battle against enforcement of the Act’s reporting provisions.”208 Claims by certain drug companies that the H.E.W. Secretary could *not* require them to file reports because their drugs were “old drugs”209 reached the United States

---

206. The reporting provisions took immediate effect for NDA’s received after October 10, 1962, the effective date of the Act. The regulations require drug manufacturers to establish and maintain records as well as prepare reports necessary to allow the FDA to determine whether the drug should be suspended or approval withdrawn under section 505(e) of the Act. 21 C.F.R. § 310.300 (1980). See *supra* notes 203-05; *infra* note 209.

207. See *supra* notes 131-32 and accompanying text.

208. Eaton, *supra* note 129, at 24. The PMA, as one commentator observes, is a “heavily financed organization [which] has waged battle against every enemy of the industry.” *Dixon*, *supra* note 23, at 6-2. The PMA has been “particularly effective” with legislative groups, physicians’ organizations and the FDA. “The PMA has . . . maintained a very close relationship with the FDA,” with informal meetings between the FDA and the PMA “held on a frequent, regular basis.” Id.

209. Eaton, *supra* note 129, at 24-25. The requirements for “new drug” applications (NDA’s) underwent major revisions under the 1962 Amendments. Before the 1962 Amendments, previous legislation had made an NDA automatically effective if the FDA did not take affirmative steps within 60 days by acting either to accept, deny, postpone, or suspend the application where untrue statements were made or where new methods were developed which revealed the drug to be unsafe after the date of the application. Federal Food, Drug, and Cosmetic Act, ch. 675, § 505(c), 52 Stat. 1040, 1052 (1938). The 1962 Amendments no longer allowed automatic clearance of new drugs merely due to the FDA’s failure to act. Furthermore, a drug cannot be marketed until it has received affirmative FDA approval as having met the requirements for safety and efficacy. The FDA was also given a 180-day period for initial consideration of the NDA, subject to further extension. The final decision, based on a formal hearing, could be postponed for another 180 days or more. Drug Amendments of 1962, Pub. L. No. 87-781, § 104(b), 76 Stat. 780, 784 (1962) (amending Federal Food, Drug, and Cosmetic Act, ch. 675, § 505(c), 52 Stat. 1040, 1052 (1938)). The usual NDA today is a massive document comprised of data collected over a period of years which includes clinical trial information,
Supreme Court. Unlike the Court's action in *United States v. Johnson*,\(^{210}\) where consumer drug legislation had been weakened, the Court affirmed that the power indeed existed to enforce the new provisions.\(^{211}\) But although in theory the power is there, the FDA has repeatedly been criticized not only for failing to fully enforce the provisions of the 1962 Amendments, but for maintaining a "close working relationship" with the PMA as well as with individual members of the drug industry.\(^{212}\) Critics of the FDA have noted that the FDA's position has been that it can work more closely with individual manufacturers "as a partner rather than a policeman."\(^{213}\) But since 1962, literally thousands of prescription drug products have been taken out of the U.S. marketplace because they lacked evidence of effectiveness and/or safety, or because their labeling required changes to reflect known medical facts. Product recalls have become a major means of consumer protection under the law. Although the FDA prefers to promote compliance by means other than going to court, when a manufacturer refuses either on its own initiative to recall its product or upon the request of the FDA to do so, the court route is taken. Generally, the recall of products by a manufacturer on its own initiative is the fastest and most effective way to protect the public.\(^{214}\) Unfortunately, many manufacturers have not made the requisite submissions,\(^{215}\) "claiming that serious reactions such as limb

animal testing results, and of utmost importance, the manufacturer's claims for the drug's safety and efficacy. Rheingold, *supra* note 16, at 961. The FDA usually has very little significant active involvement with the drug while it is in the preliminary evaluation stage and investigational new drug stage. Dixon, *supra* note 23, at 5-26. No independent tests are performed by the FDA or its agents; reporting requirements on adverse and toxic reactions provide the FDA with notice of drug dangers. *Id.* See *supra* note 204.

210. See *supra* notes 135-36 and accompanying text.


213. *Id.* at 6-3.


215. See *supra* notes 203-09. It is just not possible for the FDA to annually inspect all of the firms falling within its jurisdiction. For example, in the food industry alone, there are over 85,000 establishments under the FDA's "regulatory veil." Weeda, *FDA Seizure and Injunction Actions: Judicial Means of Protecting the Public Health*, 35 FOOD DRUG COSM. L.J. 112, 114 (1980). In fiscal 1978, the FDA conducted 19,016 inspections of food establishments, leading to 187 seizure actions, 21 injunctions, and 27 criminal prosecutions. Overall, in 1978 the FDA conducted 34,493 establishment inspections of food, drug, medical device, cosmetic and biological firms resulting in 829 recalls, 385 seizures,
deformities or deaths were not ‘unexpected’,” \textsuperscript{216} even though the companies had neither previously reported this type of reaction to the FDA in their new drug application nor encountered the reaction during clinical tests.\textsuperscript{217} As a result of so many questionable actions in the past, the “motivations” of the drug manufacturer often continue to be suspect when the issues of consumer protection and profits conflict.\textsuperscript{218}

IV. THE MANUFACTURERS’ ROLE

Where life and health are at stake no specious argument should prevent the speedy punishment of those unscrupulous men who are willing, for the sake of gain to endanger the health of unsuspecting purchasers.\textsuperscript{219}

Any discussion about the pharmaceutical manufacturer's role in the entire complicated process of supplying safe and effective drugs to the consumer must be prefaced with a few acknowledgements.

The powerful chemical agents produced by the new technology of the last few decades often have “personalities” that may not be fully unveiled until they have been used for years by great numbers of people.\textsuperscript{220} This mandates that testing of these products should “be extraordinarily cautious, thorough, and imaginative before marketing begins.”\textsuperscript{221} The lesson from the DES tragedy is clear on this point. Yet, on the other hand, how much testing is enough? How long should investigatory tests using humans last

\textsuperscript{50} injunctions, and 35 criminal prosecutions. \textit{Id.} “It is obvious, therefore, that consumer protection for those firms which escaped FDA inspection during 1978 depended upon voluntary compliance.” \textit{Id.} (emphasis added).

\textsuperscript{216} Eaton, \textit{supra} note 129, at 25.

\textsuperscript{217} \textit{Id.} See \textit{Dixon}, \textit{supra} note 23, at 9-59.

\textsuperscript{218} See \textit{supra} notes 108-10 and accompanying text; \textit{infra} notes 219, 221 & 246-49 and accompanying text.

\textsuperscript{219} Peter Collier, U.S. Dept. of Agriculture, 1879 \textit{noted in} Litman, \textit{supra} note 91, at 660.

\textsuperscript{220} \textit{Mnrrz}, \textit{supra} note 110, at 161. \textit{See supra} notes 5 & 90. \textit{See also infra} notes 221 & 222.

\textsuperscript{221} \textit{Mnrrz}, \textit{supra} note 110, at 161 (emphasis added). Testing procedures may be affected by the profit motivation. A drug with numerous potential advantages and a large potential market may create pressure for rapid completion of mandated tests and prompt market approval in order to “corner the market.” \textit{Dixon}, \textit{supra} note 23, at 6-9. “This conflict between scientific prudence and profit motivation may lead the manufacturer to take calculated risks with the life of the ultimate consumer in order to gain a competitive advantage.” \textit{Id.} As one court observed: “[T]here are two risks involved in the development of new drugs: (1) the risk that unforeseen, perhaps catastrophic, injuries will result because a new drug is used in man too soon; and (2) the risk that needless human suffering and death will occur because a beneficial drug is withheld from mankind too long.” Gaston v. Hunter, 121 Ariz. 33, 48-49, 586 P.2d 326, 341-42 (Ct. App. 1978). \textit{See infra} note 222.
before a drug is marketed? As one commentator observed, “Just as it is intolerable to have a drug released too quickly, so would it be intolerable—although this has not been shown to be a problem—to hold back a valuable new drug out of fear, or out of unwillingness to take a knowledgeable and intelligently calculated risk.”

Likewise, drugs are perhaps different from any other product available, because every drug is a potential poison. Unlike other products, which are designed to be safe when properly used, a drug can cause a disaster even when the most painstaking precautions known to science have been taken. In spite of these dangers, the drug may prove to be beneficial and even life-saving. Another element which makes drugs unique from other products is the fact that knowledge about a drug is an inherent part of the drug as a product. “Without knowledge of a drug, it is valueless. With knowledge, society accepts the place of drugs as a meaningful part of our world.” Thus, the drug manufacturer is actually selling knowledge as well as a product.

From the manufacturers' perspective, new drugs require very large investments of capital, energy and time. Investments for development and testing as well as adherence to FDA requirements and procedures are all essential ingredients in the process that will put a new drug in the consumer's hand. Of course, as with any product, extensive planning, advertising, and promotion of the new drug and its desirability and benefits must take place.

222. MINTZ, supra note 110, at 161-62. “The drug industry is one of both high profits and high returns.” Comment, DES and a Proposed Theory of Enterprise Liability, 46 FORDHAM L. REV. 963, 975 (1978). The number of women who took DES will never be known, but one source estimates that as many as three million women ingested the drug during their pregnancies. Id. at 965 n.6. Fortunately, the risk of cancer developing in their exposed offspring is relatively small given the large numbers involved. But this is no consolation to the perhaps thousands of women who were affected. Estimates range from a high of one in 250 (12,000) to a low of one in 10,000 (300). Id. at 965 n.7. It is true that a “drug lag” results when drugs are withheld from the public when the manufacturer attempts, through testing, to uncover potentially serious side effects. It is also true that a drug manufacturer will never be sued by those who suffer because a drug was not released. The painfully slow progress in consumer drug law protection requires that the time be taken.

223. DIXON, supra note 23, at 9-2. “In a sense, drugs are different from other products because every drug can be a poison.” Id. (emphasis added). See infra note 224.

224. Id. at 9-3. Likewise, drug labeling is different from the labeling of other products in the marketplace. The information in drug labeling can be just as important to the physician and the patient (consumer) as the drug itself. Janssen, supra note 94, at 440. See supra note 223 and accompanying text.
A. Marketing and Overpromotion

A recent Harvard study reveals both interesting and perhaps surprising data about factors which influence physicians’ choices of drugs for their patients. Dr. Jerry Avorn and his colleagues asked eighty-five randomly chosen Boston-area physicians how they choose the drugs they prescribe. Most of the doctors stated that scientific papers were “very important” in their decision-making, while drug advertisements, “detail men,” and patient preference were only “minimally important.” The Harvard team then asked the same physicians questions regarding the proper use of two kinds of widely misused drugs—cerebral vasodilators (drugs that open up blood vessels and theoretically improve circulation) and propoxyphene (a pain killer best known under the trade name Darvon). Dr. Avorn noted that had these doctors been reading the medical literature they would have known that vasodilators were no longer considered useful in the treatment of senile mental failure, and that Darvon was considered to be less effective than common aspirin in treating moderately severe pain. Instead, the responses of most of the physicians indicated that they had accepted the claims of the manufacturers.

1. Publicity and Promotion

As in any industry, control of demand for a product is compelled by the need to assure a corporation’s growth, stability, or even its survival. Be it General Motors or Eli Lilly and Company, advertising and promotion are the basic tools used in controlling demand. But in the case of the drug marketplace, different variables must be taken into consideration. Although a consumer may be quite capable of deciding whether an automobile is good or bad, he cannot reliably ascertain whether a medicine is really good or bad. This is especially true about prescription drugs, but it is also true on a lesser scale about nonprescription over-the-counter drugs. Thus, with prescription drugs, the physician acts as a “learned intermediary” between the manufacturer and the ultimate user (consumer). Because of this special status, the prescribing doctor usually decides which prescription drug to buy and in this context, the ultimate user’s importance as a consumer is secondary. The physician then becomes the target of a wide vari-

226. Id. at 4-5.
227. Id. at 5-6.
228. Id. at 6-8.
229. See infra notes 230-32 and accompanying text.
230. See infra notes 265 & 288 and accompanying text.
ety of publicity regarding a new drug. The manufacturer’s challenge is consequently to develop its new product, to “patent it, promote it, advertise it, make a big profit, and then repeat the cycle.” Hopefully, the patented drug will become the product that physicians believe should be prescribed. Widely used methods to meet this end include labeling and package inserts, free samples and gifts distributed by manufacturers’ detail men, the Physicians’ Desk Reference, and numerous advertisements via the mass media. The pharmaceutical industry, in public relations


232. Mintz, supra note 110, at 163.

233. The drug package insert is a brochure which contains information about the drug. It has also been called a “stuffer”, “labeling information”, and the “warning sheet.” Dixon, supra note 23, at 6-32. The package insert carries a summary of adverse reaction information, dosage data, and is included with the drug package or container when shipped to the pharmacist. The purpose of the insert is to provide current information regarding the product to the physician. The information on the insert must be revised whenever necessary to warn of new drug dangers. Id. at 6-32-33. The package insert grew out of a need to give physicians accurate information regarding a drug’s effects, usage, and dosage, apart from that imparted in the advertising and promotional literature of the drug manufacturer. Barnett, Drug Reactions: The Role of the Package Insert, 1 J. Legal Med. 19 (March/April 1973). In 1961 the FDA promulgated regulations providing for a package insert to be on or within all prescription drug packages. 21 C.F.R. § 106(3)(i) (1961). Known as the “full disclosure” regulation, it required that labeling on or within the package containing the drug bear adequate information for use of the drug, including: indications, effects, dosages, methods, and frequency. The theory behind the package insert is that the availability of such information should help to protect the patient in the use of the drug. Dixon, supra note 23, at 6-33. Unfortunately, this reasoning is flawed. See infra notes 292-96 and accompanying text. One problem is that the package insert may well be outdated, as many drugs can be safely stored for years without significant change. Dixon, supra note 23, at 6-34.

234. A detail man is a salesman for the drug manufacturer. Generally commissioned based on earnings from an assigned territory, the detail man “is the most important liason between the pharmaceutical company and the medical profession.” Dixon, supra note 23, at 6-28. Trained as a salesman, he uses sales techniques and managerial skills to promote the product. The detail man personally contacts physicians, attempting to educate them and to induce them to use the company’s wares. The average visit lasts for eight to ten minutes, and may involve the use of gimmicks and gifts as part of the approach in building rapport with the physician. Id. at 6-29. See infra notes 242-49 and accompanying text.

235. The Physician’s Desk Reference (PDR) is a reference book containing information given by drug manufacturers on about 90% of the drugs on the market. The PDR is commonly referred to by the physician when prescribing drugs. See infra note 270.

236. As one commentator asserted: “The cleverest techniques of modern Madison Avenue merchandising are being focused on the physician as a prime target
role, has widely publicized to both physicians and lay consumers alike the vast amounts of money it spends annually on research. As one source asserted:

One would assume from the tone of the publicity that vast sums of money are being spent to discover new drugs, to cure heretofore incurable diseases, and that, as a result of this research, we will rapidly approach a disease-free world. If this is the intended implication, then some criticism is in order, for the bulk of pharmaceutical research is definitely directed toward increasing company profits by developing marketable drugs which will sell in the largest volumes and make the largest profits.\(^{237}\)

Although such self-praise may warrant passing criticism, the problems and dangers presented by the zealous and sometimes unethical over-promotion of drug products have led to serious harm to the consumer.

2. Publicity and Overpromotion

Drug companies have learned that doctors are influenced by the same advertising techniques that are used for mass consumer advertising. They accept new drugs with amazing rapidity . . . in part because it would appear that a physician's own market position is strongly influenced by his reputation for using the latest drug.\(^{238}\)

As Dr. Avorn and the aforementioned Harvard study concluded, "Drug advertisements are simply more visually arresting and conceptually accessible than are papers in . . . medical literature, and physicians appear to respond to this difference."\(^{239}\)

The 1960's saw the FDA espouse regulations which required a fair balance in all forms of drug advertising, with the practitioner to be properly warned about any dangers or side-effects of a drug in equal balance to the manufacturer's claims about the drug's benefits.\(^{240}\) Before this crackdown, manufacturers had been free to make outrageous claims about the value of their drugs. Unproven claims of effectiveness and superiority over competitors' brands were the rule rather than the exception.\(^{241}\) Limited only by their imaginations and ethics, manufacturers had been able to "puff up" their wares in the hope of inducing physicians into selecting Brand X over Brand Y. If the new regulations of the 1960's have toned down promotion abuses, they have not lessened their costs. The drug industry reportedly spent one billion dollars per who has the potential to markedly increase the drug company's profit."\(^{237}\) Dixon, supra note 23, at 6-5. And these techniques are very effective. \(^{238}\) See supra notes 225-28 and accompanying text. \(^{239}\) See also infra notes 238-39 and accompanying text. \(^{240}\) Dixon, supra note 23, at 6-23. \(^{241}\) Id.
year in the early 1970's on advertising promotion (amounting to about $5,000 per physician), with a major part of this cost going to pay the industry's 20,000 drug detail men.\textsuperscript{242} Often regarded as the physician's principle source of drug information, detail men frequently find themselves living with "an inherent conflict of interest" created by the pharmaceutical manufacturer.\textsuperscript{243} On the one hand, the detail man is a salesman with a product to sell with a variety of reasons to do so. But the detail man also may be in the best position to warn physicians of any of his product's dangerous propensities.\textsuperscript{244} Unfortunately, negative news about his products could frighten away customers, turning them to his competition. Of course, most detail men answer that they are above such temptations and company pressure, but many of the cases on over-promotion have emphasized the role of the drug detail man.\textsuperscript{245} In Toole v. Richardson-Merrell,\textsuperscript{246} the manufacturer had knowledge of the dangerous effects of its drug, yet concealed this information from both the FDA and the medical profession.\textsuperscript{247} In Toole, a California court held that the drug company's continued promotion of the drug with knowledge of its dangerous side-effects constituted "malice" within the California statute allowing punitive damages.\textsuperscript{248} In many such instances, company pressure and sales sus-

\textsuperscript{242} Id. at 6-27 & 28. See supra note 234.
\textsuperscript{243} Id. at 6-30.
\textsuperscript{244} Id. See infra notes 247-49, 272-73 and accompanying text. See Note, Torts: Drug Manufacturer Held Negligent for Failure to Use Detail Men to Warn Physicians of Dangerous Side Effect, 55 Minn. L. Rev. 148 (1970).
\textsuperscript{245} See infra notes 247-49, 272-73 and accompanying text. See Note, Products Liability: Drug Manufacturer Found Liable for "Over-promotion" by Detail Men—A Diminution in the Standard of Proof, 45 Temp. L.Q. 134 (1971).
\textsuperscript{246} 251 Cal. App. 2d 689, 60 Cal. Rptr. 398 (Cal. Ct. App. 1967). In Toole, detail men were instructed to blame drug side effects on other drugs. \textit{Id.} For a good discussion of Toole, see Dixon, supra note 23, at 9-73-75.
\textsuperscript{248} Richardson-Merrell, it should be remembered, is the same manufacturer that tried to market thalidomide in the United States. See supra notes 195-200 and accompanying text. Richardson-Merrell is presently marketing Bendectin in this country. See supra note 1 and accompanying text. The following excerpt appeared in The \textit{New Republic} and was read into the Congressional Record. It describes instructions given to Merrell Company detail men regarding the promotion of one drug:

The William S. Merrell Co. (a division of Richardson-Merrell) whose anti-cholestral drug MER/29 was ultimately taken off the market because of side-effects that included liver damage, hair loss, hepatitis and cataracts, promoted MER/29 with elaborate . . . manuals asking detail men to assure doctors that the drug worked, was safe, and should be prescribed. Salesmen were told, in sentences punctuated [sic] with multiple exclamation marks, to memorize a pitch and know it well enough that it could not be seen through as "canned." They were instructed to affect excitement ("You owe it to yourself— to your company—to the millions of people who need MER/29, to be
ceptibility and not the desire to warn the physician (consumer) of uncertain dangers have proved to be the true motivating factor behind detail men's actions.249

B. Warnings, Warranties, and Products Liability

Thou shalt warn your fellow man, do not let sin befall him.250

Section 402A of the Restatement of Torts exempts dangerous products from strict liability if they are properly prepared and marketed and a "proper warning is given."251 Thus, under the reasoning of comment k to section 402A, the special treatment estab-

enthusiastic!!") and told how to deliver the line ("Lean forward—toward the doctor. Automatically tighten your stomach muscles as you make your presentation. This forces a change in the inflection of your voice and paves the way for deeper penetration of the benefits you are describing.") Finally, the detail men were told how to shift any doctor's suspicions about a Merrell drug to medicine made by other firms ("Even if you know your drug can cause the side-effect mentioned, chances are equally good the same effect is being caused by the second drug. You let your drug take the blame when you counter with a defensive answer. Know how to answer side-effects honestly, yes, but get the facts first. Doctor, what other drugs is the patient taking? Been doing it for years? Why didn't you tell us then?"). This line supposedly got the clottish physician to attribute undesirable side-effects to Upjohn or Lilly. The tactic was rationalized because, rhetoric aside, the cause was good: "There is no longer any valid question as to its (MER/29) safety or lack of significant side effects."


249. See supra notes 244-48 and accompanying text. See also infra notes 272-73 and accompanying text. It should be observed that the physician, approached by detail men giving large volumes of drug samples, gimmicks, and assorted gifts, is also placed in a position of vulnerability. DIXON, supra note 23, at 6-51. Sales presentations are carefully framed to describe the finest attributes of the drug, and gifts are calculated to reinforce the physician's memory of the product's virtues. Id. at 6-51, 32. Salesmen's discussions are not regulated by the FDA and those gifts to doctors have been known to include such trifles as color television sets, freezers, and expense-paid trips. Id. at 6-52. See Kennedy Committee Hearings, Washington Post, March 9, 1974. See also The Ubiquitous Detail Man, 1 HOFSTRA L Rsv. 183 (1973).


251. RESTATEMENT (SECOND) OF TORTS § 402A (1965). Although a prescription drug manufacturer is able to avoid strict liability by giving a warning that describes a drug's dangerous side effects, the manufacturer's burden in issuing a proper warning is "more onerous" than that of most other manufacturers. Note, Torts—Product Liability—Duty to Warn—A Drug Manufacturer's Detail Men Must Warn Physicians on Whom They Regularly Call of the Dangers Involved in the Use of the Manufacturer's Drugs, 45 NOTRE DAME LAW. 135, 137 (1969). While the manufacturer of other products generally is not required to warn of dangers that would affect a small group of "idiosyncratic or allergic" users, this rule has a stricter application for drug manufacturers. Id. See infra note 256 and accompanying text.
lished for drug manufacturers recognizes that balancing the desirability of marketing useful drugs to combat disease with the risk of severe side effects to a handful of susceptible users will offer drug companies some limited protection and induce them to provide society with valuable drugs. But the important question remains as to what constitutes a "proper warning." The courts have addressed this question on numerous occasions. The result has been a good deal of disagreement and a dearth of clear-cut answers. The large majority of drug-related litigation in the 1960's was based upon the manufacturer's obligation to warn of known drug dangers. As a result, manufacturers soon developed the defense that early reports of drug reactions were just too rare to require a full warning of danger. Consequently, "the duty to discover" resulted from the manufacturers' successful use of this defense. As one source asserts, "In the world of drug testing and marketing, the question is not whether a drug does cause a particular injury, but whether it may." This lower threshold is perhaps one advantage for the consumer seeking compensation for drug-related harm. In a 1968 decision, the United States Court of Appeals for the Ninth Circuit held that the lower court had erred

---

252. Comment k of the Restatement of Torts defines unavoidably unsafe products as those "which, in the present state of human knowledge, are quite incapable of being safe for their intended and ordinary use . . . . Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it unreasonably dangerous." RESTATEMENT (SECOND) OF TORTS § 402A comment k (1965). In the case of drug manufacturers:

The seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, . . . 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.

Id. Thus, strict liability does not attach to the drug manufacturer unless the drug is "defective" or "unreasonably dangerous." The drug is "unreasonably dangerous" only if manufactured improperly or if the manufacturer failed to properly warn the physician of any dangers inherent in the use of the drug. Note, Products Liability—Drug Manufacturer's Liability for Overpromotion of the Use of a Prescription Drug, 10 GA. ST. B.J. 450, 455 (1974).


254. Id. The duty to test requires a manufacturer to take reasonable steps to discover the dangerous properties of its products. Id. at 9-44. A large number of cases have discussed the manufacturers' obligation to test or discover as part of basic principles of liability. Id. "Usually the cases have discussed both the obligation to discover and the obligation to test because they have both been part of the same factual situation which placed the manufacturer on notice of facts which require further action." Id. The MER/29 (triparanol) cases involved some of the "most aggravated breaches of this duty," as typified by Toole v. Richardson-Merrell, Inc. Id. See supra notes 246-48 and accompanying text.

in failing to instruct the jury that strict liability attached to the sale of a drug to the plaintiff (and consequently there was a duty to warn the plaintiff) even though there had been only a one-in-a-million chance that the drug would cause the plaintiff’s poliomyelitis.\footnote{Davis v. Wyeth Laboratories, Inc., 399 F.2d 121 (9th Cir. 1968).}

Today, when a manufacturer has notice of a drug injury, its advertising literature must warn of the danger,\footnote{DIXON, supra note 23, at 9-25. See DIXON, supra note 23, at 9-25 to 34. In a 1966 case, the Eighth Circuit Court of Appeals held that the manufacturer had a duty to reasonably warn plaintiff’s doctor, notwithstanding plaintiff’s hypersensitivity. Sterling Drug, Inc. v. Cornish, 370 F.2d 82, 85 (8th Cir. 1966).} and the warning must be “proper.” As a matter of practice, drug package inserts\footnote{See supra notes 233-36; infra note 266 and accompanying text.} warn of potential drug injuries which are very rare. For instance, one expert states that a serious reaction with a suspected incidence rate of less than one in ten thousand is now regularly included in the warning information about the drug on the package insert.\footnote{See supra note 233.}

In the drug litigation arena, the classic “failure to warn” fact situation lies at the heart of the manufacturer’s liability, perhaps overshadowing many of the more traditional product liability theories such as negligence,\footnote{A negligence theory requires the plaintiff to establish the existence of a duty and a corresponding breach of that duty which in turn is the proximate cause of the harm done. Originally, a negligence action was the primary method for recovering damages from manufacturers for physical injuries caused by their products. The success or failure of the negligence action turned on the plaintiff’s ability to isolate the defendant’s specific negligent act and prove by a preponderance of the evidence that negligence was the proximate cause of the plaintiff’s injury. The theory of defective manufacture in a negligence action is rarely used in drug liability cases for a number of reasons. The product is “inherently consumed during its use” and “is rarely available for analysis to determine whether it was safely manufactured, made in the right quantities, or was even the right drug.” DIXON, supra note 23, at 9-34. Another problem relates to the recognition of an injury. “If a steering column in a car fails, the effects are immediate and apparent. This does not occur with drugs. A wide range of complicating problems may develop in a patient, and

256. Davis v. Wyeth Laboratories, Inc., 399 F.2d 121 (9th Cir. 1968). For a discussion of the Davis case, see Note, Products Liability—Drug Manufacturers—An Absolute Duty to Warn Exists Notwithstanding Miniscule Statistical Probability of Harm, 18 De Paul L. Rev. 829 (1969). Many idiosyncratic reactions are known to frequently occur. Because of this, the test for liability should not be whether the drug user is an unusually sensitive person, but rather whether the drug reaction can be anticipated or predicted. “[T]his is particularly important where the adverse drug reaction, even though possibly rare, may have catastrophic results.” DIXON, supra note 23, at 9-25. See DIXON, supra note 23, at 9-25 to 34. In a 1966 case, the Eighth Circuit Court of Appeals held that the manufacturer had a duty to reasonably warn plaintiff’s doctor, notwithstanding plaintiff’s hypersensitivity. Sterling Drug, Inc. v. Cornish, 370 F.2d 82, 85 (8th Cir. 1966).

257. DIXON at 6-19. The quality of the warning and the balance of warning versus promotion now receive “tremendous scrutiny.” Id. at 9-7. See supra notes 233-36; infra note 266 and accompanying text.

258. See supra note 233.

259. DIXON, supra note 23, at 6-19.

260. DIXON, supra note 23, at 6-19.
It is the very nature of the drug product itself that has influenced the trend away from some of these areas of products liability law, although in reality, they are all interrelated. Public policy demands that certain drugs be used notwithstanding the a drug-related problem may be one of a multitude of possible causes. Id. at 9-34 to 35. Recently, the Oregon Supreme Court ruled that a physician who prescribes a drug based on the manufacturer's representations, which negligently failed to warn of the drug's attendant risks, may recover from the drug company for the damage to his reputation. Oksenholt v. Lederle Labs., 294 Or. 213, 656 P.2d 253 (1982). The court noted that FDA regulations impose a duty to inform doctors of possible effects of prescription medicines. Breach of that duty constitutes negligence per se. Id. A warranty theory requires the plaintiff to prove the existence of an express or implied warranty and its subsequent breach. Courts, frequently faced with a severely injured plaintiff "strained to ease this burden" and recognized a cause of action for personal injury under a contract-like theory of breach of implied warranty. Adverse Drug Reactions, supra note 17 at 738, 39. One commentator has asserted that drug litigation has been less dependent upon warranty and strict liability theories of recovery than on other areas of products liability law. Dixon, supra note 23 at 9-82.1. For an in depth look at the warranty theories (implied and express) of recovery, see Dixon, supra note 23 at 9-82.1 to 106. Nuisance theory holds that the manufacturer's or supplier's responsibility runs not only to the ultimate consumer, but also to anyone who could reasonably have been expected to be exposed to the products use. See Note, Products Liability—Drug Manufacturers—An Absolute Duty to Warn Exists Notwithstanding Miniscule Statistical Probability of Harm, 18 De Paul L. Rev. 829, 831 (1969). Fraud or misrepresentation theories require the plaintiff to prove the false statements were made as to a specific product, that the defendant had knowledge of the product's dangerous properties, that the plaintiff relied on the defendant's representations, and, that a reasonable use of the product as represented resulted in the harm done to the plaintiff. Dixon, supra note 23, at 9-59-69. As the Michigan Supreme Court stated:

Determination of whether a product defect exists because of an inadequate warning requires the use of an identical standard. Consequently, when liability turns on the adequacy of a warning, the issue is one of reasonable care, regardless of whether the theory pleaded is negligence, implied warranty, or strict liability in tort. Smith v. E.R. Squibb and Sons, Inc. 405 Mich. 79, 83, 273 N.W.2d 476, 480 (1979). Actions alleging a breach of the manufacturer's duty to warn have thus been successfully brought under the various theories. See, e.g., Schenebeck v. Sterling Drug, Inc., 423 F.2d 919 (8th Cir. 1970) (negligence); Grinnell v. Charles Pfizer & Co, 274 Cal. App. 2d 424, 79 Cal. Rptr. 369 (Ct. App. 1969) (breach of warranty); Davis v. Wyeth Labs., Inc., 399 F.2d 121 (9th Cir. 1968) (strict liability). The Ninth Circuit Court of Appeals held that it was not error to present to the jury the issue of a manufacturer's duty to warn under warranty theory instead of strict liability because "[t]he difference is largely one of terminology." Davis v. Wyeth Labs., Inc., 399 F.2d 121 at 126 (9th Cir. 1968). For a good discussion of this area, see Adverse Drug Reactions, supra note 17.
risks and dangers involved, since the many benefits of their use far outweigh the disadvantages. In addition, today there is a federal regulatory agency which must decide in this "societal risk versus benefit" context, whether the product should be marketed. But, if there is a chance of injury, it is the informed consumer and not the drug manufacturer who should have the opportunity of weighing the risks involved in taking the drug.

The manufacturer's duty to warn extends to that class of people for which the drug was intended. This fact helps to define what is a "proper warning". The FDA is given responsibility for two types of drugs: prescription drugs and over-the-counter medications. In practice, both categories must be shown to be generally safe for the use intended, or their limitations must be so defined.

1. Prescription Drugs

A prescription drug is one that requires a licensed practitioner to prescribe it. Many of the same methods used by manufacturers to promote a product are also used to provide warnings of the product's dangers or side-effects. As such, the issue becomes whether a particular statement is a warning or advertisement. Where the manufacturer warns but his warning is lost in voluminous verbiage, or where the dangers are minimized within advertisements designed to sell the drug, the duty to warn is not satisfied. In fact, an inadequate or inaccurate warning may have the same result as no warning at all in many instances.

In the case of prescription drugs, the adequacy of the warning is a question of fact for the jury. The scope of material which the jury may consider in this determination sometimes extends beyond the warning material on the package insert. For example, in Love v. Wolf, the plaintiff's decedent died as the result of taking the drug Chloromycetin. An action followed against the drug manufacturer for negligent failure to properly warn. The California

265. The terms "licensed practitioner" and "prescription drug" contain special meaning under federal law. Although not well defined, the category of licensed practitioner includes medical doctors, osteopathic physicians, podiatrists, optometrists, chiropractors, naturopaths, nurse practitioners, midwives, and physicians' assistants. Many of these practitioners are given varying authority to prescribe drugs under various state licensing provisions. Id. at 5-11. A prescription drug under 21 U.S.C. § 353(b)(1) is defined as a "drug intended for use by man which—(A) is a habit-forming drug to which § 502(d) applies; or (B) because of its toxicity or potentiality for harmful effect . . . is not safe for use except under the supervision of a practitioner licensed by law to administer such drug . . . ." See infra notes 288-89.

266. See supra notes 255-60 and accompanying text. See also infra notes 268-76 and accompanying text.

court observed that the labels on the drug package insert were probably adequate to warn the physician of the side effect in question.268 The court then took notice that there were other more effective materials and methods that the drug manufacturer used to persuade physicians to prescribe the drug, stating, "[W]e must accept the evidence leading to justifiable inferences that Parke-Davis [the manufacturer] . . . had watered down its regulations—required warnings and had caused its detail men to promote wider use of the drug by physicians than proper medical practice justified."269 The court concluded that it was a proper question for the jury whether an otherwise adequate warning had been "watered down" by the manufacturer's promotional efforts, including detail men, reminder advertising, and the Physician's Desk Reference.270

A federal district court in Yarrow v. Sterling Drug, Inc.,271 determined that the drug manufacturer must effectively warn doctors of even rare or remote side-effects inherent in the use of the drug.272 The court then found that even though the manufacturer sent physicians a letter with the appropriate warning of the side-effects, this warning was not the most effective means of making physicians aware of the danger. Furthermore, the court found that to warn effectively, the manufacturer should use the same medium that it finds most effective in promotion of the drug, which in this case was the company's detail men.273
The failure to warn may not have actually caused the physicians to prescribe the drug if the physician learned of the inherent dangers in the drug's use from other independent sources and prescribed the medication anyway. This causation requirement has been raised as an effective defense by the drug manufacturer; if there is no causation, then there is no liability.\(^\text{274}\) In *Incollingo v. Ewing*,\(^\text{275}\) the court found that by overpromoting, the defendant manufacturer had breached its duty to warn the medical profession but found that the question of causation was proper to submit to the jury, holding causation a requisite to finding the manufacturer liable for the breach of its duty to warn properly.\(^\text{276}\) The consumer is most often presented with formidable barriers against recovery, not the least of which is the heavy burden of proving causation of this type. It should be remembered, though, that this difficult task involves but one kind of causation. As has already been discussed, proving the causal link between the drug and the injury itself is still another problem. This is especially true in the case of the child born with a serious birth defect. In such a case, the problems of proving causation are amplified by numerous other variables and influences (both environmental and genetic) present.

---


\(^\text{276}\) In *Incollingo*, the Supreme Court of Pennsylvania affirmed a lower court's judgment against a drug manufacturer on the grounds that sufficient evidence was presented to warrant going to the jury regarding the issue of whether the manufacturer's detail men caused a doctor to prescribe a dangerous drug indiscriminately. *Id.*
during pregnancy.277

Defendant-manufacturers have also argued that by complying with FDA regulations on labeling and testing, they, as a matter of law, have fulfilled their duty to warn. The court in Stevens v. Parke-Davis and Company278 summarily rejected this argument and held that such warnings are merely “minimal” in nature and do not necessarily satisfy the duty to warn.279 In approving a $500,000 recovery in favor of a brain-damaged infant, the court in Stromsodt v. Parke-Davis and Company280 observed: “Although all of the Government regulations and requirements had been satisfactorily met in the production and marketing of Quadrigen, the standards promulgated were minimal. The defendant still owes a duty to warn of dangers of which it knew or should have known in the exercise of reasonable care.”281 In a more recent decision, the court in Michael v. Warner/Chilcott,282 held that the manufacturer’s warning, which had been adopted verbatim from a regulation under the federal Food, Drug and Cosmetic Act, did not constitute an adequate warning as a matter of law.283 In another case, the Texas Supreme Court affirmed a lower court’s finding that the manufacturer’s warning was not adequate as a matter of law simply because it complied with FDA requirements, since such requirements set only minimum standards.284 In short, mere compliance with the FDA’s warning requirements and regulations will not be considered a complete defense.

277. See supra notes 64-77, 85 & 87-92 and accompanying text.
278. 9 Cal. 3d 51, 507 P.2d 663, 107 Cal. Rptr. 45 (1973).
279. The court in Stevens observed that even if the drug manufacturer placed a proper warning on package inserts as required by the FDA, the manufacturer could erode or even nullify the warning’s effect by utilizing various promotional devices including the company’s detail men. 9 Cal. 3d at 66, 507 P.2d at 662, 107 Cal. Rptr. at 54. The court concluded that: “The warnings [on package inserts] given in this case were not so clearly effective as to defeat, as a matter of law, the inference that they were nullified by overpromotion.” 9 Cal. 3d at 67, 507 P.2d at 662, 107 Cal. Rptr. at 54.
281. Id. at 997. In affirming the trial court’s decision, the court of appeals reviewed the Parke-Davis printed warning which stated under the headnote “Reactions” that: “When given in accordance with suggested methods, local and systemic reaction following the administration of Quadrigen are usually mild. The incidence is usually no greater than is normally experienced with trivalent vaccine.” Parke-Davis and Co. v. Stromsodt, 411 F.2d 1390, 1400 (8th Cir. 1969). The court stated, “This is simply not borne out of the evidence in this case . . . .” Id.
283. Id.
2. **Over-the-Counter Drugs**

In 1972, ten years after the statutory mandate to the FDA, a study was started to evaluate over-the-counter drugs to ensure that they were effective as required under the statute. Unlike prescription drugs, over-the-counter drugs are sold directly to the consumer. Thus, the packaging must contain information which includes adequate labeling instructions and directions for use as well as information concerning side-effects and other precautionary warnings. In a 1979 case, a New Jersey court noted that the duty of the manufacturer to warn consumers of the specific risks of over-the-counter drug use derives from the basic marketing principle within the industry that nonprescription drugs are purchased by consumers for the purpose of self-medication, typically without any intended or actual intervention by a physician.

This logical rationale compares with the concept that the "learned intermediary" acts for the consumer in making a decision about prescription drugs, with the physician in a better position than the ultimate layman consumer to make the best initial drug choice. As a result, regulations protect the manufacturer from a similar over-the-counter drug information requirement, so long as when it goes to the pharmacy, the prescribing and precautionary

---


286. Id. at 5-11 & 12. Under the 1962 amendments, drugs must be proven to be effective. The FDA is charged with implementing these provisions. In 1966, the Fair Package & Labeling Act was enacted to require that products be honestly and informatively labeled. Likewise, the FDA was expected to enforce the provisions affecting drugs. Id. at 5-6.


288. The rationale of the "learned intermediary" rule is well expressed in Reyes v. Wyeth Labs., 498 F.2d 1264 (5th Cir.), cert. denied, 419 U.S. 1096 (1974), where the court observed:

This special standard for prescription drugs is an understandable exception to the Restatement's general rule that one who markets goods must warn foreseeable ultimate users of dangers inherent in his products. See Restatement (Second) of Torts, Section 388 (1965). Prescription drugs are likely to be complex medicines, esoteric in formula and varied in effect. As a medical expert, the prescribing physician can take into account the propensities of the drug, as well as the susceptibilities of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individualized medical judgment bottomed on a knowledge of both patient and palliative. Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a "learned intermediary" between manufacturer and consumer. Id. at 1276 (emphasis added).
information is included on the packaging with a package brochure. The regulations permit the removal of these package inserts before they are given to the customer. Thus, although the regulations do not prohibit the manufacturer from providing direct information about the prescription drug to the consumer, they do allow the withholding of consumer information. One commentator asserts that the initial choice of a drug is a different decision than the decision to continue in the face of potentially serious side effects or adverse reactions. "The patient package insert should have a role in avoiding drug injuries. The patient is the only individual to become initially aware of the early signs which may herald a serious drug catastrophe." One reason for the suggestion that the "prescription consumer" be afforded the same consideration as his "over-the-counter counterpart" stems from the fact that the theory behind the prescription package insert is flawed. This theory suggests that by including it with the package, the package insert is therefore available to the physician to read, study, and ultimately use to protect the patient from the hazards listed. Unfortunately, the regulations do not require the package insert to leave the backroom of the pharmacy and to travel to the doctor's office or ward where the prescriptions are subsequently written. As the same commentator observed, "The pharmacist's time is, therefore, spent in removing the outer package and the package insert from the box . . . so that his own gummed label identifying the pharmacy, the doctor, the patient, . . . etc., can be placed on the container." Thus, there is no guarantee that the physician will ever read the drug's complete labeling or be able to keep up with revisions as they are made.

One critic of the FDA approved labeling practice observed that patients are "jeopardized" by its "frequent ineffectiveness." This is because a central assumption about FDA approval of a drug is that hazards can be minimized with instructions and warnings in the labeling. "This assumption in turn rests, obviously, on the supposition that physicians will read and follow the directions provided. But experience suggests that faith in the protections afforded by label information is often misplaced.

289. See supra note 289.
291. Id.
292. Id. at 6-33.
293. Merrill, supra note 16, at 23.
294. Id.
295. Id. at 23-24.
296. Id. at 24. Dr. James Goddard, as FDA Commissioner, described to a Congressional subcommittee the already discussed facts of life:

[T]he prescribing physician . . . is, frankly, under siege in my opin-
Warning: As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product.297

The new FDA labeling requirements represent one of the latest attempts at providing better protection for the American consumer. As has already been examined in this article, the realization of effective Government intervention between the drug manufacturer and the ultimate drug consumer has been painfully slow. Before discussing the warning regulations, it is appropriate to briefly reflect upon just how far government intervention has evolved.

On September 7, 1982, the proposed rules were published. In issuing the proposed rules, the FDA observed that it “believes that it is in the interest of the public health to require OTC drugs to bear a warning against use by pregnant or nursing women in the absence of professional advice.”298 From a consumer's perspective, the information accompanying the proposed warning provided significant language: “Although only a small number of drugs have been conclusively shown to have adverse effects on the developing human fetus or newborn, information of this type is inadequate to establish safety for most drugs.”299 This significance stems not from its scientific content, but from the fact that FDA sources have admitted that as many as 300,000 products sold over-the-counter may well be affected by the new regulations300

This willingness to recognize the need to better protect the unborn and newly born from devastating birth defects (even when extremely remote) is nothing short of a giant step forward in drug-related consumer protection. But should the consumer, placated

---

299. Id. (emphasis added).
300. FDA spokesman Ed Nida stated that as many as 300,000 products may be affected by the new warning. Drugs to Carry Warning Labels for Pregnant, Nursing Women, Omaha World Herald, Dec. 3, 1982, at 4, col. 3.
by this advance, sit back and revel in this progress? Clearly, the answer is “no.”

A. The New Warning: What It Is

In 1972, American jurisdictions unanimously recognized that one who intentionally or negligently injures an unborn fetus may be liable for damages. This unanimity finalized the reversal from the long-followed decision in Dietrich v. Northampton, which had denied a cause of action for injuries to the unborn. It has been nearly one hundred years since Dietrich was decided. Obviously, medical science and the law have both experienced expansive growth and change in the interim. On December 3, 1982, the rules and regulations for the new labeling requirement were published. On that date they also became effective, although the manufacturers of affected drug products will have until Decem-

---


303. Id.

ber 5, 1983, to comply. The final rules and accompanying information reiterate the FDA's stance that existing evidence establishing the "potential for some OTC drugs to have harmful effects on the fetus or nursing infant warrants warning pregnant and nursing women."

Stated in "twenty-five words or less," the warning applies only to over-the-counter drug products intended for "systemic absorption." Drugs that are not intended for systemic absorption need not bear the warning. The regulations also provide for exemptions from the pregnancy-nursing general warning requirements, where appropriate, upon petition, as well as for exemptions from the warning requirement for those drugs intended to benefit the fetus or nursing infant during the period of pregnancy or nursing.

The FDA noted that it selected the word "warning" as a signal word because it was more likely to attract the attention of consumers than the word "caution." The general warning was intended to cover those drugs for which the available evidence revealed neither that the product was unsafe nor that the product was safe for use by these women. The FDA further observed that "appropriate" general warnings "are an important means of educating the public about drug use."

---

306. Id.
307. See supra note 298 and accompanying text.
308. The FDA states that it does not intend to include drugs absorbed in amounts "sufficiently small as to have no pharmacological or toxicological significance." 47 Fed. Reg. 54,750, 54,751 (1982). For example, OTC drugs used topically, or mouthwashes regulated as OTC drugs, (which, due to their method of use are not intended to be systemically absorbed) will not be covered by the new regulation. Id.
309. Id. Cosmetic products were not covered by the original proposal, nor are they included in the final regulations. Id. at 54,752.
310. 21 C.F.R. § 201.63(d) (1982) provides for exemptions from the pregnancy-nursing general warning requirement "where appropriate" upon petition under 21 C.F.R. 10.30 (1982). For example, manufacturers who believe that available data demonstrates that their products, although intended for systemic absorption, are safe for use by pregnant and nursing women may petition for an exemption from the warning requirement. 21 C.F.R. § 201.63(d) (1982).
311. The FDA observed that such exemptions are reasonable "because such drugs would have been evaluated specifically for their effects on the fetus or infant and [would have been] demonstrated to be beneficial." 21 C.F.R. § 201.63(d) (1982). Drugs labeled exclusively for pediatric use are also exempted "because pregnant or nursing women would not be taking such products." Id.
313. Id. at 54,752.
314. Id. at 54,754. As the FDA stated, "An implicit assumption underlying most OTC drug labeling regulations is that consumers, in pursuing their own best interests, will read labeling that is appropriately designed and worded." Id.
B. The New Warning: What It Is Not

The new general warning is not an original concept on the part of the FDA. The State of California had already approved new requirements that were to become effective on November 18, 1982, which provided for the following warning to appear on over-the-counter drugs in that state: “Caution: If pregnant or nursing a baby, consult your physician or pharmacist before using this product.”\(^3\) Fearing perhaps that California's action would lead to a wide range of confusing or conflicting state warning labeling requirements, the FDA was spurred into action to provide the uniform national message. The agency acknowledged once again that warnings must be used “judiciously” so that they do not lose their effectiveness.\(^3\) But is the twenty-four word warning the most effective one that could have been chosen? Furthermore, is criticism of the FDA’s “central assumption,” that hazards can be minimized by instructions and warnings in the labeling, relevant to those over-the-counter drugs affected by the new regulations?

1. Other Suggested Warnings

On September 7, 1982, the FDA invited interested persons to file written comments regarding the proposed new rules (due on or before October 7, 1982). The alternative warnings received suggest the diverse interests that responded.\(^3\) One commentator proposed that the following language precede the warning: “CAUTION: This drug has not been proven safe for babies before or

---

315. Id. at 54,750. The FDA reiterated that a single national pregnancy-nursing warning with a specified text is necessary to ensure that OTC drugs are used safely and for their intended purposes. Id. at 54,756. “A single national warning will help ensure that consumers receive clear, unambiguous, and consistent information on the labeling of OTC drugs concerning use by pregnant or nursing women.” Id.

316. Id. at 54,753.

317. In response to the invitation for written comments about the proposed regulations, the FDA received comments from 19 drug manufacturers, two drug merchandisers, 11 health professional associations, five women's organizations, three state governments, 14 private individuals, and four consumer associations. Id. at 54,750. The comments reflect this “diversity”. For example, one commentator stated that the FDA did not provide studies to show that the general warning will actually cause women to consult with health professionals before using OTC drugs. “The implication was that the warning should not, therefore, be required.” Id. at 54,754 (emphasis added). Another contended that the general warning undermines the very concept of an OTC drug as one that can be used in the treatment of illnesses and disorders as diagnosed by the lay person. Id. at 54,755. Finally, it was contended that to the extent the general warning would encourage physician consultation for every set of symptoms experienced, it [the warning] could seriously disrupt the delicate balance that now exists in our nation's health care system. Id.
after birth. 318 The commentator further argued that the proposed warning statement failed to convey the most essential message: "that the risks of taking certain OTC drugs during pregnancy and nursing are either unknown or known to be dangerous." 319

Another commentator stated that the proposed warning needed to be strengthened and suggested that the following statement precede the warning: "USAGE IN PREGNANCY: The effect of this drug on the fetus and/or the subsequent development of the exposed offspring is unknown." 320 Another response observed that the FDA's proposed warning lacked grammatical preciseness and suggested the following alternative warning: "If you are pregnant or nursing a baby, you should seek professional advice before using this or any other drug product." 321 The proposed rule was also criticized for placing full responsibility "to discern the possible existence of harmful effects on the woman whose fetus is at risk." 322 The following alternative was offered: "If pregnant or nursing an infant, do not use this product without consulting a health professional." 323 The argument was raised that the proposed general warning would have absolutely no impact on the many women in this country who cannot read. 324 The FDA noted that in addition to the written warning, properly designed symbols could be used to attract the attention of those women. However, the agency refused to make such a symbol mandatory, stating that it would "permit voluntary use of such symbols by manufacturers." 325 This defacto rejection by the agency contradicts in part the FDA's own language that "[a]n explicit assumption underlying most OTC drug labeling regulations is that consumers, in pursuing their own best interests, will read labeling that is appropriately designed and worded." 326

318. Id. at 54,753.
319. Id.
320. Id.
321. Id.
322. Id. at 54,751.
323. Id.
324. Id. at 54,753.
325. Id.
326. Id. at 54,754.
2. Will the Warning Be Heeded?

Several commentators have observed that if the general warning is used when it is not necessary (e.g., on all systemically absorbed over-the-counter drugs) it would "dilute" the impact of important cautionary statements. Another commentator has contended that the general warning would "join other phrases that are so ubiquitous they are not read." Two of the best examples of warnings that go unread or unheeded by millions of American consumers each day are the saccharin warning: "Use of this product may be hazardous to your health. This product contains saccharin which has been determined to cause cancer in laboratory animals," and the warning that appears on all cigarette packaging and advertising: "Warning: The Surgeon General Has Determined That Cigarette Smoking Is Dangerous to Your Health." In the case of saccharin, the safety of this chemical was bitterly contested during the first five years after the enactment of the 1906 Act! The controversy continues today, over seventy-five years later. The case of the ineffectiveness of cigarette warnings is certainly difficult to dismiss. Recently, a Reagan administration official endorsed the idea of having even tougher warnings for cigarettes. Currently, a bill is being proposed that would require the use of three different warnings on a rotating basis:

327. Id. at 54,753.
328. Id.
329. Id.
330. This warning uniformly appears on millions of soft drink cans, bottles, and other assorted food containers.
331. The warning on packaging and advertising as it has appeared for the last two decades.
332. Hutt, supra note 92, at 131.
Warning: Cigarette-smoking causes lung cancer and emphysema, is a major cause of heart disease, is addictive and may result in death.

Warning: Cigarette-smoking by pregnant women may result in miscarriage, premature births or birth weight deficiencies.

Smokers: No matter how long you have smoked, quitting now greatly reduces the risks to your health.\textsuperscript{334}

But Americans smoked 634 billion cigarettes last year, despite the current warning.\textsuperscript{335} Dr. Edward Brandt Jr., assistant secretary of health, testified to a House subcommittee that, "[s]moking remains the major cause of premature death and disability," adding that "[i]t is well established that cigarette smoking is a drug dependence and that cigarette smoking is addictive to many people."\textsuperscript{336} A new Government pamphlet asserts that cigarette smoking is not just a habit, but represents the most widespread example of drug dependence in this country, with 56 million Americans presently smoking.\textsuperscript{337} However, Reginald Lester, a spokesman for the Tobacco Growers Information Committee, stated that he was not surprised that the government was not telling the true story: "It's quite an overstatement. There are no studies in existence which can prove a causal link between cigarettes and any disease."\textsuperscript{338} He further stated, "Ninety percent of all smokers already believe there could be a link, so continued government expenditures for pamphlets like this are wasteful and ridiculous."\textsuperscript{339} It would indeed be difficult to imagine a successful cause of action by a plaintiff who claimed to have developed health problems as a result of smoking cigarettes, given the current warnings. In a similar way, the manufacturers of the numerous over-the-counter drugs bearing the new label warnings can perhaps successfully defend against subsequent consumer claims of injury to their offspring or themselves. This may or may not be an unwelcome side effect of the labeling regulations.

VI. CONCLUSION

The credibility of regulatory agencies has been severely damaged by the mounting evidence, as the result of one form of scientific test or another, that indicates that some of the most popular items in our food supply are carcinogenic. As one commentator asserted, "The public is not prepared to give up charcoal-broiled

\textsuperscript{334} Id.
\textsuperscript{336} Tougher Cigarette Warning, supra note 333.
\textsuperscript{337} Smoking Called Worst Drug Dependency, Omaha World Herald, March 7, 1983, at 1, col. 2.
\textsuperscript{338} Id. at cols. 3 & 4.
\textsuperscript{339} Id. at col. 4.
steak or hamburgers, pepper, nutmeg, mustard, and coffee, much less the essential nutrients that have been implicated by this scientific evidence. As a group, American consumers are often willing to accept long-term risk on a voluntary basis if short-term benefits can be derived in the process. The examples of saccharin and cigarettes are indicative of this fact. But in terms of a lifetime, the tragic reality for a newborn baby damaged as the result of drugs taken by its mother is not a long-term risk, rather, it is an immediate one. Pregnant and nursing women are far too willing to ingest a variety of chemicals which are potentially harmful to their offspring, often erroneously assuming that because the drug can be purchased without a prescription, it must indeed be safe.

Whether the new general warnings on the labels of thousands of over-the-counter drugs go the way of the cigarette and saccharin warnings (and are likewise generally ignored) depends upon the actions of both the government and the drug industry in providing more complete information and better education for the American consumer. After all, if there is even a chance of injury, it is the consumer and not the drug company who should have the opportunity of evaluating the risk involved in taking the drug.

As has happened so often in the past, the government has finally taken a step in the right direction but has again stopped short. The new labeling requirement should provide, in addition to the warning, a symbol that will insure that the thousands of illiterate women may also be warned. This warning symbol should be made mandatory if the drug manufacturers do not voluntarily include it. If the present language of the warnings proves to be either unclear or ineffective, the warning should be revised and strengthened based upon feedback from consumers using the affected products. Finally, large scale public education campaigns informing consumers about the uses of all drugs during pregnancy should be considered by government and industry “working as partners” to protect the unborn American consumer.

David DeTar Newbert ’83

340. Hutt, supra note 92, at 129.
341. Id. See supra notes 331-40 and accompanying text.
342. See supra note 213 and accompanying text.