

THE BITTEREST PILL

*How Drug Companies Fail To Protect Women
And How Lawsuits Save Their Lives*



Center for Justice & Democracy

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**The Bitterest Pill - How Drug Companies Fail To Protect Women
And How Lawsuits Save Their Lives**

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Many thanks to Trevor Goring for donating this image.

*Co-author Joanne Doroshow gathered some research for this report while on staff at Public Citizen in 1997. The authors wish to thank Public Citizen for this invaluable research contribution.

Executive Summary

Women across the country have suffered tremendously as a result of defective and dangerous drugs and medical devices. History shows that many FDA-approved drugs and devices that have caused some of the most serious injuries and death have been marketed specifically for women. This is largely due to the number of products routinely prescribed to otherwise healthy women to control some aspect of their reproductive system. In addition, some drugs have had a disproportionate impact on pregnant women and their children.

Many drugs and devices were made safer only after women and their families filed lawsuits against those responsible. Sometimes, companies that have been hit with large verdicts or settlements act immediately to change their unsafe product or practice. Lawsuits also have had a tremendously beneficial role spurring medical research and alerting the public – and ultimately pressuring regulators – to act on larger health risks and problems. As a result, the lives of countless other women have been saved.

In addition, unlike the regulatory scheme, which provides no direct benefit to victims, civil cases hold companies directly accountable to those whom they have hurt, and provide their victims with compensation to help rebuild their lives. Drug company immunity would remove the most significant and effective financial consequence to a company for choosing to keep a dangerous drug or device on the market.

The following are some examples that illustrate these points:

Hazardous Birth Control:

- **Ortho-Evra Patch.** This weekly birth control patch, approved by the FDA in 2002 and marketed to young women with sexy television commercials and fashion runway shows, caused blood clots, heart attacks and strokes. Both the company and FDA knew of major problems with the patch but kept the information quiet until documents, including those produced in litigation, forced the information out.
- **Dalkon Shield IUD.** This IUD caused at least 17 American deaths and over 200,000 injuries including pelvic inflammatory disease, perforated uteruses, and infertility. The FDA suspended distribution of the IUD after three years but did not recall existing stock or require the company to tell doctors to remove them. For the next 10 years, the company continued to promote the device. It took several lawsuits and the threat of larger punitive damages awards for the company finally to urge women to have the Dalkon Shield removed and financed the removal.
- **Copper-7 IUD.** Like the Dalkon Shield, this IUD led to deaths and injuries. It was pulled from the market after numerous lawsuits, coupled with the company's inability to obtain products liability insurance. Actual injuries and deaths of women, which came years before the devices were withdrawn, never had that effect.

- **Ortho-Novum 1/80 Birth Control Pill.** This pill contained extremely high and dangerous levels of estrogen leading to blood clots and blood disorders. One woman suffered life-threatening injuries after taking this pill. As a result of this case, the manufacturer lowered estrogen levels in the pill.

Lethal Hormones:

- **DES** was a synthetic estrogen approved by the FDA to prevent miscarriages. DES did not work but instead caused cancer, infertility and other serious physical problems for the women who took it, and the children they carried. For almost two decades after the drug was proven ineffective, manufacturers continued to push the drug and expose hundreds of thousands of women and their offspring to risk. Until women started bringing lawsuits, many DES exposed women did not know about the risks they faced.
- **Estrogen replacement therapy (ERT) or hormone replacement therapy (HRT).** Hormones were approved by the FDA and heavily promoted by the pharmaceutical industry beginning in the 1960s to women experiencing menopause. Yet evidence had existed since the 1930s and 1940s that estrogen therapy caused cancer. After years of struggle by consumer groups and women's health organizations to bring attention to the cancer and other risks, in 2002 NIH researchers finally confirmed a significant increase in the risk of breast cancer, heart attacks, blood clots and strokes. By then, an untold number of women had been harmed or killed from being over-prescribed HRT.

Other Harmful Drugs and Devices:

- **High-absorbency tampons.** These tampons cause "toxic shock syndrome" resulting in many deaths. A woman died from toxic shock syndrome after using super-absorbent tampons, and her family sued. The company stopped making these tampons only after the jury's punitive damage award.
- **Parlodel.** The FDA approved this drug in 1980 to suppress lactation after birth. It caused heart attacks and strokes. The FDA requested the drug's five manufacturers to voluntarily take it off the market. One company refused and for the next five years, continued to promote the drug and persuaded hospitals to prescribe it. Only after a large jury award and petitions by consumer groups to force the FDA to act, did the company withdraw the drug from the market.
- **Accutane.** Accutane is an acne drug to which the FDA gave fast track approval despite knowing it caused severe birth defects as serious as Thalidomide if taken by pregnant women. As a result of the company's continuously failed policies to prevent women who were or became pregnant to take the drug, hundreds of severely deformed babies have been born. Juries have now started to hold the company accountable in these cases.

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By Amanda Melpolder, Amy Widman and Joanne Doroshow

INTRODUCTION

Before the 1960s, the topic of menopause was generally never discussed and certainly not publicly. But in 1966, a new book about menopause hit the bookstores and quickly became a best seller. It was called *Feminine Forever*.¹ The book's main purpose was to encourage women to take hormones, like estrogen, to prevent what it called the "tragedy" of menopause.² The book's author, gynecologist Dr. Robert Wilson, argued that when a woman goes through menopause she becomes a "castrate," "the equivalent of a eunuch," "a dull-minded but sharp tongued caricature of her former self,"³ and that "when she realizes she is no longer a woman she may subside into a stupor of indifference."⁴ Luckily for women, claimed Wilson, the pharmaceutical industry had a "cure" for this "disease" – estrogen replacement therapy (ERT) or as it was later called, hormone replacement therapy (HRT). Wilson strongly advocated for women to take estrogen so they would not have to "live as sexual neuters for half their lives."⁵

Dr. Wilson headed the Wilson Research Foundation, an organization set up in the 1960s with drug industry money⁶ to promote hormone replacement therapy.⁷ And while there is no definitive information about how much Wilson was paid to research and promote *Feminine Forever*, his son later spoke out, denouncing his own father for covering up the health risks associated with estrogen.⁸ But at the time, women's magazines and other media quickly picked up on Dr. Wilson's description of menopause and promoted the use of ERT.⁹ Wilson went on to extensively lecture medical professionals and women's groups around the country and was often quoted in such widely read publications as *Time* magazine, calling menopause the "castration of women."¹⁰ *Time* declared hormones "perfectly safe" stating "there is no evidence that the hormones can cause cancer" ... and in fact "there seems to be evidence that they guard against it."

Sales of HRT drugs shot up. Between 1963 and 1973, the sale of estrogen quadrupled.¹¹ By 1975, Premarin, an estrogen derived from the urine of pregnant mares, had become the fifth leading prescription drug in the United States, with more than 30 million prescriptions.¹² Over the years since then, menopause grew to be huge business for pharmaceutical industry. By 2001, Wyeth's hormone replacement treatments Prempro, an estrogen-progesterone combination drug, and Premarin, were the company's top-selling drugs, generating \$2.1 billion in sales, which amounted to 14 percent of the company's total revenue.¹³

What Dr. Wilson did not mention in the 1960s was evidence that had been around since the 1930s and 1940s that estrogen caused cancer.¹⁴ After years of struggle by consumer groups and

women's health organizations to force the FDA to act on the cancer risk, it wasn't until 2002 that steroidal estrogens, the type used in estrogen replacement therapies and oral contraceptives, were finally labeled as "known human carcinogens."¹⁵ By then, an untold number of women had been harmed or killed from being over-prescribed HRT for common menopause symptoms like hot flashes and night sweats, as well as osteoporosis and other health problems.¹⁶



The struggles by women's health groups and consumer advocates over the years to try to force the FDA to pay attention to cancer and other risks of HRT and the constant marketing push by drug companies to find new reasons to scare women into taking these hormones, devaluing the risks, tells a very common story. It is a story about the hyped marketing to women of a disproportionate number of unsafe drugs and devices and needless deaths and injuries to millions of women that have resulted.

The FDA has had a spotty history, at best, when it comes to recognizing and warning of a drug or device's potential dangers. Regulatory failings have had a great impact in the area of women's health because of the number of products routinely prescribed to otherwise healthy women to control some aspect of their reproductive system.¹⁷ As University of Buffalo Law Professor Lucinda Finley has written, "Reproductive or sexual harm caused by drugs and medical devices has a highly disproportionate impact on women, because far more drugs and devices have been devised to control women's fertility or bodily functions associated with sex and childbearing than have been devised for men."¹⁸

Fortunately, lawsuits have made a huge difference in preventing harm to women. Recently, the U.S. House Committee on Oversight and Government Reform held a public hearing examining the prospect of complete immunity for medical products manufacturers. Former FDA Commissioner David A. Kessler testified,

[M]any believe that the FDA lacks sufficient resources to protect the public health, and many worry that the FDA is not adequately monitoring the safety of drugs once they are on the market. The FDA has long been hamstrung by resource limitations. Even if FDA's funding were doubled or tripled, its resources and ability to detect emerging risks on the thousands of marketed drugs and devices would still be dwarfed by those of the drug and device companies who manufacture those products. For that reason, the tort system has historically provided a critical incentive to drug and device companies to disclose important information to physicians, patients, and the FDA about newly emerging risks.¹⁹

There are many ways lawsuits can – and have – led to safety improvements as the last line of defense against unsafe drugs. Often, companies that are hit with large verdicts or settlements act immediately to change their unsafe product or practice. Sometimes it may take several large verdicts before a company acts. Lawsuits also can have a tremendously beneficial role spurring medical research and alerting the public, and ultimately pressuring regulators to act on larger



health risks and problems. In addition, unlike the regulatory scheme, which provides no direct benefit to victims, civil cases hold companies directly accountable to those whom they have hurt, and provide their victims with compensation to help rebuild their lives.

The critical social and financial importance of these lawsuits lies not in their frequency, but in the “signals” they send to other potential wrongdoers, the essence of the civil justice system’s deterrence function. Many academic scholars have written that the influence of jury

verdicts in civil cases, of which there are relatively few, is vastly disproportionate to their number.”²⁰ A rare peek into how such signals actually work was provided by the industry-funded Conference Board in a 1987 study of 232 risk managers of large U.S. corporations. The Board found, “Where product liability has had a notable impact — where it has most significantly affected management decision-making — has been in the quality of the products themselves. Managers say products have become safer, manufacturing procedures have been improved, and labels and use instructions have become more explicit.”²¹

In other words, as important as lawsuits are in protecting women’s health and compensating injured women, the consequence of immunizing drug companies from all liability for FDA-approved drugs would be far greater than simply losing the ability to sue in some cases. It is hard to envision the catastrophe that would result.

Liability tells manufacturers that there is a potential financial cost for deaths and injuries caused by the unsafe product, and they must weigh that against the costs of taking the corrective action. Simply speaking, when injuring women becomes more expensive than not injuring them, drug companies stop injuring women.²² Establishing immunity would reduce the potential liability costs for harming and killing women to zero. It would remove the most significant and effective financial consequence to a company for choosing to keep a dangerous drug or device on the market.

Drug companies are now arguing in favor of this outcome in a case currently pending before the U.S. Supreme Court. There are many who believe that the U.S. Supreme Court may be disturbingly on the verge of granting drug companies what they want – complete immunity for deaths and injuries caused by FDA-approved drugs, absolving all drug companies of any liability and removing any financial incentive the legal system provides to remove or improve a dangerous drug.

It would be one thing if the FDA confidently could be relied upon to protect the public. But the FDA has had a mixed record when it comes to recognizing and warning of a drug or device’s potential dangers. Thus, the “regulatory compliance” argument suffers from numerous problems, including, as this paper shows, regulatory failures due to lack of resources and will, the tendency by drug companies to withhold important information from regulators, and in some cases, the FDA’s own decisions not to make the information public.

Recently U.S. Representative Henry A. Waxman, (D – CA), who chaired the U.S. House Committee on Oversight and Government Reform hearing on medical products manufacturer immunity, introduced the issue by saying:

For decades, FDA believed that state liability cases actually helped the agency regulate drugs and medical devices. But under the Bush Administration, FDA has reversed course. Now FDA advocates that once a product receives FDA approval, the manufacturers should be absolved of responsibility for injuries caused by their products. This is exactly the wrong time for FDA to be saying: “Trust us.”²³

This paper shows exactly why that is true for drugs and devices manufactured for women. It examines the disproportionate impact of drug company failures when it comes to women’s health and safety, and shows how critical litigation is to exposing pharmaceutical industry misconduct, saving women’s lives, and providing a vital check on the pharmaceutical industry’s damaging future actions.

THE ORTHO-EVRA PATCH – ALERTING WOMEN THROUGH LITIGATION

In the mid-1990s, while working as a surgeon and researcher at Brigham and Women's Hospital and Harvard Medical School, Dr. Andrew Friedman admitted he had been fabricating “80 percent of patient data” that he used in articles he had published in medical journals and he had also “alter[ed] files in three studies of hormonal drugs for women.”²⁴ For this, “he was banned for three years from government-funded research for ‘scientific misconduct,’ resigned from his post ... and lost his medical license in Massachusetts for a year.”²⁵ But in January 2000, Ortho-McNeil (a division of Johnson & Johnson which makes the Ortho-Evra Birth Control Patch) hired Dr. Friedman as their senior director of clinical research.²⁶ Calling his reputation in the medical community “excellent,”²⁷ Dr. Friedman was assigned to “designing and reviewing clinical trials for hormonal birth control.”²⁸ While Dr. Friedman’s background may have given some pause, he seemed to fit in with Ortho-McNeil.



Four years earlier, the company had decided to develop a drug industry marketing dream – a weekly birth control patch, which would be far more convenient for women than the once-a-day pill. The company told the FDA it believed the patch would expose women to less estrogen than the pill “so lower doses could be used to achieve contraception.”²⁹ This was important because higher doses of estrogen increased the risk for blood clots, heart attacks and strokes. In fact, over a decade earlier, at the FDA’s request, the last of the “high-estrogen” birth control pills containing more than 50 micrograms of estrogen were taken off the market.³⁰

Unfortunately for the company, its clinical trials seemed to get in the way. As the *New York Times* recently reported, “a clinical trial completed in 1999 showed that the patch delivered 30 to 38 micrograms of estrogen into the bloodstream each day... suggest[ing] that the patch delivered an amount of estrogen that could be as high as a pill containing 76 micrograms of estrogen.”³¹ So the study’s author, the now-retired Johnson & Johnson employee, Dr. Larry Abrams, made a decision. He decided to apply a “correction factor” to these results to say that “the patch actually delivered about 40 percent less estrogen than the trial results showed — about 20 micrograms a day.... [T]his adjustment was never part of the study protocol, a plan filed with the F.D.A.” The correction was buried in a mathematical formula in a large report submitted to the FDA and “[w]hen the study was published in 2002, there was no reference to the alteration.”³² In 2002, the FDA approved the patch, which the company marketed falsely as releasing 20 micrograms of estrogen to the blood every 24 hours.³³

While the FDA may not have been aware of the company’s manipulation of data, it certainly knew of problems. Prior to the patch’s approval, the FDA was aware that women wearing the patch were three times more likely than pill users to have a non-fatal blood clot. During the clinical trials, two out of the 3,300 women given Ortho-Evra were treated for blood clots in the lungs. Ortho insisted that the patch was not responsible but according to the *Associated Press*, one FDA reviewer looking at Ortho McNeil’s data wrote “using capital letters and underscoring his comments,... ‘THE REVIEWER DOES NOT AGREE WITH THE SPONSOR’S ABOVE CONCLU-

SIONS' [and that] 'the label should clearly reflect this reviewer's safety concern about a potential increased risk [and] '[i]t would be important to study users after the patch came on the market for clot problems.'"³⁴ However, the FDA required no such follow-up studies when it approved the patch.³⁵

The marketing launch of Ortho-Evra was impressive: scantily clad women in sexy television commercials, pushing the new birth control that was "on your body, off your mind."³⁶ *TIME* magazine called the patch one of the "coolest inventions of 2002."³⁷ And during the 2003 New York City Fashion Week, in some of the runway shows, swimsuit models were actually accessorized with placebo Ortho-Evra patches.³⁸

Yet the glamour surrounding the trendy new contraceptive device soon faded. In April 2004, an 18-year old college student Zakiya Kennedy died of pulmonary embolisms – blood clots. The medical examiner blamed her death on her use of the birth control patch.³⁹ Shortly thereafter, documents uncovered through Freedom of Information Act (FOIA) requests by the *New York Post* in 2004 and *Associated Press* in 2005 revealed that the FDA had known of major problems with the patch, but failed to alert the public.⁴⁰

The FOIA documents and subsequent news reports disclosed that since August 2002, the FDA had been aware there had been 17 deaths from heart attacks or strokes of patch users under the age of 30.⁴¹ *Associated Press* wrote, "[t]hrough the Food and Drug Administration and patch-maker Ortho McNeil saw warning signs of possible problems with the patch well before it reached the market, both maintain that the patch is as safe as the pill. However, the reports obtained by the *Associated Press* appear to indicate that in 2004, when 800,000 women were on the patch, the risk of dying or suffering a survivable blood clot while using the device was about three times higher than while using birth control pills."⁴²

Moreover, *Associated Press* wrote, "[A]n internal Ortho McNeil memo shows that the company refused, in 2003, to fund a study comparing its Ortho-Evra patch to its Ortho-Cyclen pill because of concerns there was 'too high a chance that study may not produce a positive result for Evra' and there was a 'risk that Ortho-Evra may be the same or worse than Ortho-Cyclen.'"⁴³

Shortly after the *Associated Press'* report, according to internal company emails and a memorandum entitled, "Ortho-Evra Interactive Programs: Defense Actions to Minimize Impact of Negative Presence," employees of Johnson & Johnson looked into purchasing at least 100 domain names of "negative URLs." Johnson & Johnson was willing to pay up to \$10,000 to purchase the domain names that included OrthoEvraKills.com, ThePatchTruth.com, and TheBirthControlPatchKills.com.⁴⁴ Around the same time, Ortho-McNeil began advertising the patch



with a more serious tone, removing the sexy commercials and replacing them with doctors talking about the dangers of blood clots and strokes.⁴⁵

Still, it took three years after the patch was approved for the FDA to finally admit publicly that the patch was more dangerous than the pill it was supposed to replace. At the end of 2005, the FDA finally ordered the company to change the patch's labeling to indicate that the patch exposed women to about 60 percent more estrogen than those using typical birth control pills.⁴⁶ As the *New York Times* reported, "the F.D.A. did not warn the public of the potential risks until November 2005 – six years after the company's own study showed the high estrogen releases. At that point, the product's label was changed, and prescriptions fell 80 percent, to 187,000 by last February from 900,000 in March 2004."⁴⁷

In February 2006, Ortho-McNeil released a study that showed women who wore the patch were twice as likely to get serious blood clots as women who take birth control pills.⁴⁸ In September 2006, the FDA required that Ortho-McNeil add a warning, but even that warning was qualified by confusing language about conflicting reports casting doubt on whether the patch increased risk.⁴⁹ Not until 2008 were these conflicting reports removed from the label after more studies confirmed the risk, and the FDA ordered the company to warn more strongly of a higher risk of blood clots for women using this type of birth control.⁵⁰

Through it all, health advocates like the National Women's Health Network (NWHN) and Public Citizen's Health Research Group tried to help women figure out what to do about patch. Public Citizen issued a November 2005 news release called "Do Not Use the Ortho-Evra Birth Control Patch."⁵¹ And in an 2006 article, NWHN pointed out,

Women want a safe contraceptive patch. The contraceptive patch offers advantages over other hormonal contraceptives that women appreciate, including eliminating the need to take a daily pill, and giving women greater control than they have with contraceptive injections or implants. But, women want a patch that is as safe as it can possibly be. Therefore, the NWHN urges Ortho McNeil not only to complete the studies that will inform women about the health risks of the currently available patch, but also to conduct the research to develop a lower-dose patch in the future. A patch that delivers an estrogen dose similar to the low-dose pill would be a valued advance for women....⁵²

In November 2006, Joel S. Lippman, a former Vice-President of two of Johnson & Johnson's subsidiaries filed a whistle-blower lawsuit against his former employer.⁵³ In his complaint he said that he was terminated in part because he had "raised serious health concerns about...the Evra patch, which released dangerously high levels of estrogen into patients...[and the company] disregarded [his] concerns and launched the product," and allegation that Johnson & Johnson denied.⁵⁴ Another unnamed Johnson & Johnson Vice-President chose to resign from his job "overseeing the benefit risk and safety evaluation of reproductive products, including the patch, after being unable to properly exercise this responsibility."⁵⁵

Johnson & Johnson, the parent company for Ortho-McNeil had already begun to settle some lawsuits brought by women and their families by April 2006.⁵⁶ The family of Zakiya Kennedy brought one of the first cases scheduled to go to trial; the case settled confidentially out of court in October 2007. The family of Alycia Brown, a 14-year-old girl from Wisconsin, settled their case

with Johnson & Johnson around the same time for \$1.25 million. Brown had died after suffering from two blood clots in her lungs in May 2004.⁵⁷ Ashley Lewis, a 17 year-old mother, died in late 2003. Lewis' grandmother sued and confidentially settled the case in February 2008.⁵⁸

Now, however, Johnson & Johnson is urging a U.S. District Court to find that they are immune from any liability for injuries from the patch because the FDA approved the drug.⁵⁹ Yet the importance of litigation to date cannot be overstated, and not just to compensate families who were wronged. Time and again, news reports have referred to documents uncovered in litigation – from the muckraking work of *Associated Press*⁶⁰ to recent accounts by the *New York Times*.⁶¹ Documents uncovered through litigation have helped uncover the short, untoward history of the



patch and the FDA's failure to alert women of health risks associated with it while in possession of studies that indicated differently. The patch stands as a great example of one of the most important functions of litigation - uncovering information about products and creating widespread publicity about their dangers, alerting an otherwise unsuspecting public that has been bombarded with conflicting information through massive corporate advertising and public marketing efforts by the pharmaceutical industry.

LAWSUITS AND THE SORDID, PARTIAL HISTORY OF UNSAFE DRUGS AND DEVICES FOR WOMEN

EARLY, DEADLY BIRTH CONTROL

There are many ways lawsuits can lead to safety improvements for women. Sometimes, companies that are hit with large verdicts or settlements act immediately to change or remove their unsafe product, or they do so because they can no longer obtain products liability insurance. Sometimes it takes more. It may take several large verdicts before a company acts, as in the case of some of the most dangerous birth control products ever put on the market.

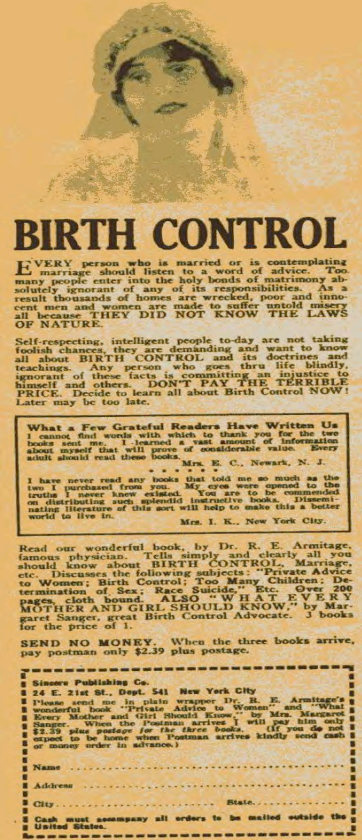
Dalkon Shield

From 1971 until 1974, A.H. Robins Co., Inc. sold a plastic intrauterine device (IUD), a form of birth control known commercially as the Dalkon Shield. The device had a tailstring and when correctly positioned, the tailstring passed from the uterus through the cervix and into the vagina. The Dalkon Shield tailstring consisted of a multifilament strand surrounded by a nylon sheath unsealed at both ends. This configuration allowed the tailstring to “wick” bacteria-containing vaginal fluid into the normally sterile uterus, thereby causing infection. As a result, many Dalkon Shield users suffered from pelvic inflammatory disease, perforated uteruses, and infertility. Those who became pregnant were in danger of suffering spontaneous septic abortion.⁶² At least seventeen American women died and over 200,000 were injured on account of the Dalkon Shield.⁶³ Many became sterile.⁶⁴

In August 1971, Robins was warned by a quality control supervisor that the tailstring could wick bacteria into the uterus and cause infection. However, the company's pharmaceutical research director instructed that no changes be made in the product.⁶⁵

In June 1972, Robins was alerted by one of its physician-consultants that, of the six women who became pregnant after he had fitted them with the contraceptive device, five suffered spontaneous infected abortions. He warned that “it is hazardous to leave the device in [pregnant women] and I advise that it be removed.” Nevertheless, the company made no attempt to warn Dalkon Shield users or their doctors of the danger.⁶⁶

Between June 1972 and November 1973, Robins received 22 reports of spontaneous infected abortions in women who became pregnant while using the Dalkon Shield, including one that resulted in death. The company failed to immediately inform the medical community.⁶⁷ Rather, in October 1972, Robins revised its patient brochure to state that, if a woman becomes pregnant while wearing the Dalkon Shield, “the bag of water pushes the IUD to one side and the develop-



BIRTH CONTROL

EVERY person who is married or is contemplating marriage should listen to a word of advice. Too many people enter into the holy bonds of matrimony absolutely ignorant of any of its responsibilities. As a result thousands of homes are wrecked, poor and innocent men and women are made to suffer untold misery all because THEY DID NOT KNOW THE LAWS OF NATURE.

Self-respecting, intelligent people to-day are not taking foolish chances, they are demanding and want to know all about BIRTH CONTROL and its doctrines and teachings. Any person who goes thru life blindly ignorant of these facts is committing an injustice to himself and others. **DON'T PAY THE TERRIBLE PRICE.** Decide to learn all about Birth Control NOW! Later may be too late.

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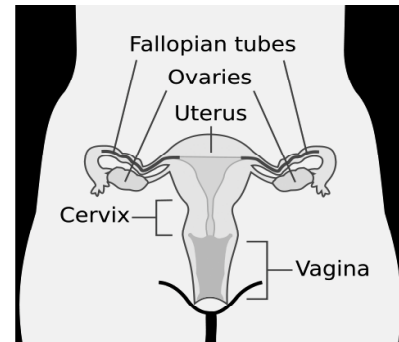
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ing baby is not really touching the device at all. There is no evidence that the frequency of abnormal births is any greater among women wearing IUDs than among women not wearing IUDs.”⁶⁸ Moreover, through at least April 1973, Robins continued to counsel physicians to leave the IUD in place if pregnancy occurred.⁶⁹



There was also evidence that Robins hired an advertising agency to encourage favorable publicity about the company's products, including the Dalkon Shield. This action “demonstrated a motive on the part of Robins to profit by making exaggerated statements regarding the safety and efficacy of its product.”⁷⁰

In 1974, a company document entitled “Status Report for Dalkon Shield” stated that “[i]t is the opinion of [Robins attorney Roger L.] Tuttle that if this product is taken off the market it will be a ‘confession of liability’ and Robins would lose many of the pending lawsuits.”⁷¹ That same year, the FDA suspended distribution of the Dalkon Shield in the United States.⁷² The FDA did not recall existing stock or require Robins to tell doctors and women to have the IUD's removed.⁷³ The company continued its distribution overseas.⁷⁴ For the next 10 years, Robins continued to promote and defend the device while concealing its hazards, thereby causing thousands of additional injuries.⁷⁵

In January of 1973, 24-year-old Carie Palmer was fitted with the Dalkon Shield. When she became pregnant in August, her doctor did not remove the device because he thought it could cause no harm. The pregnancy progressed normally until November, when Ms. Palmer became violently ill with flu-like symptoms. She suffered a miscarriage caused by a bacterial infection centered in the uterus and subsequently went into septic shock. In order to save her life, doctors removed her uterus, Fallopian tubes and ovaries. As a result of this total hysterectomy, she continued to suffer health problems.⁷⁶

A jury returned a verdict in Ms. Palmer's favor, requiring the company to pay \$6.2 million in punitive damages and \$600,000 in compensatory damages, and the trial court entered judgment thereon.⁷⁷ On appeal, the Supreme Court of Colorado affirmed the award, noting that there was “ample evidence” to support the punitive damage award.⁷⁸ Robins had accumulated gross revenues exceeding \$11 million from the Dalkon Shield; its net worth had doubled during the marketing period, reaching over \$157 million in 1974.⁷⁹

By 1984, more than 10,000 women had sued the company and several punitive damages awards had been assessed.⁸⁰ University of Buffalo Law School Professor Lucinda Finley wrote, “Robins’s post-marketing behavior with regard to the Dalkon Shield enraged juries and resulted in punitive damages verdicts. A.H. Robin's egregious behavior included: ignoring its own product safety staff who recommended an inexpensive change to the tail string that would have greatly reduced its tendency to ‘wick’ bacteria into the uterus; stonewalling and lying to doctors and the public about the product's dangers for over a decade; engaging in an active campaign to disparage those who did try to bring out evidence of the harms; and steadfastly refusing to order recalls or recommend removal for over a decade despite a mounting toll to the reproductive health, and in some cases life, of numerous women.”⁸¹

In one case, the Supreme Court of Kansas stated:

[T]here [was] substantial evidence to conclude that Robins fully comprehended, by 1974 at the latest, the enormity of the dangers it had created, but that it deliberately and intentionally concealed those dangers; that it put money into “favorable” studies; that it tried to neutralize any critics of the Dalkon Shield; . . . that it consistently denied the dangers of the Dalkon Shield for nearly fifteen years after its original marketing of the Dalkon Shield; that it commissioned studies on the Dalkon Shield which it dropped or concealed when the results were unfavorable; ... [and] consigned hundreds of documents to the furnace....⁸²

Robins finally urged women to have the Dalkon Shield removed and offered to pay for the removal.⁸³ The *Wall Street Journal* characterized the company's actions as “an apparent sign of Robins' growing concern about the rising tide of punitive-damages claims against the company,” noting a recent court filing in which Robins stated that “[t]he primary difficulty ... in the resolution of Dalkon Shield litigation is the possibility of an award of substantial punitive damages.”⁸⁴ Ultimately, over a period of 15 years, Robins incurred 11 punitive damage awards totaling in excess of \$24.8 million.⁸⁵ As Lucinda Finley put it,

Until it faced punitive damages, A. H. Robins had determined that it could weather the Dalkon Shield litigation and could avoid ordering a recall of the product. It was not until corporate executives realized that juries reacted adversely to the company's decision not to order removal of existing Shields, despite the overwhelming evidence of dangers to women of continuing to use them, that A.H. Robins finally wrote to physicians and advertised to women advising and offering to pay for removal. This step, which should have been taken ten years earlier, finally put an end to the carnage the Dalkon Shield caused to U.S. women.⁸⁶

The Dalkon Shield situation is also a good example of what Finley calls the “important synergistic relationship” between the tort system and the regulatory system. She wrote, “The Dalkon Shield litigation, and in particular the punitive damages judgments, were a powerful inducement to the FDA to investigate and assert its regulatory authority over the Dalkon Shield.”⁸⁷

It was also the Dalkon Shield disaster that prompted Congress to pass the Medical Devices Amendments of 1976, which required the FDA to test medical devices before they could be put on the market.⁸⁸ However, in a cruel twist this law – created to ensure more rigorous testing of medical devices – is now being used to preempt civil justice claims even if those products should later prove dangerous.⁸⁹

Copper-7 IUD

In 1974, G.D. Searle & Co. began marketing the Copper-7 IUD contraceptive device. It was eventually worn by an estimated 9 million women before it was taken off the market.⁹⁰ The device caused pelvic infections, ectopic pregnancies, perforation of the uterus and infertility in countless numbers of women. An FDA task force found, as early as 1975, “serious deficiencies in



Searle's operations and practices which undermine the basis for reliance on Searle's integrity."⁹¹ But the FDA never took action regarding the Copper-7.

By 1985, many personal injury lawsuits had been filed over the Copper-7.⁹² In early 1986, G.D. Searle pulled the device from the U.S. market.⁹³ As Law Professor Lucinda Finley wrote,

[A]n attorney for G.D. Searle Co., the manufacturer of the Copper-7 IUD, testified before the U.S. Senate that the first punitive damages verdict against this device, and the consequent withdrawal of coverage by the insurance carrier, led to the demise of this IUD. While it may well be true that this drastically changed the financial picture facing the Copper-7 and contributed to the decision to withdraw it, the punitive damages verdict was based on compelling evidence that the company had ignored and covered up evidence of risks, as well as irresponsibly promoted the device to a group of women for whom it was medically unadvised....

If G.D. Searle had been more responsive to this safety evidence than to cost considerations, then it may well have never had a liability and punitive damages problem. The overall irony of the argument that litigation costs drove some IUDs off the market is that "reports of injuries and deaths of women, which came years before the devices were withdrawn, never had that effect."⁹⁴

In 1988, a jury reached an \$8.75 million verdict against Searle after internal documents showed that company officials had expressed doubts about the safety of the Copper-7 design. The jury found that the manufacturer intentionally withheld this information from the public and continued to misrepresent the product, targeting young women even though it clearly was not appropriate for those who had never been pregnant.⁹⁵ Searle deliberately withheld this material from the FDA too. In one 1977 document unearthed by the litigation, a Searle employee reported that: "The group considered highest risk for infection and subsequent loss of fertility is that consisting of nulligravida, under 26, with multiple sex partners. It seems to be that the identification of such a group by the Food and Drug Administration, mishandled by the lay press, might have an impact on our marketing strategy."⁹⁶

Soon after this case, and these documents were unearthed, Searle settled all remaining lawsuits (as many as 350).⁹⁷

Ortho-Novum 1/80 Birth Control Pill

Ortho Pharmaceutical Corporation manufactured an oral contraceptive known as Ortho-Novum 1/80, which contained 80 micrograms of estrogen, as well as an oral contraceptive containing only 50 micrograms. It was suspected that products containing 75 micrograms or more of estrogen caused an increased incidence of thromboembolic disorders, which relate to blocked blood vessels.⁹⁸ By the early 1980s, there were 39 reported cases of women developing hemolytic uremic syndrome or HUS associated with the use of oral contraceptives.⁹⁹ Hemolytic uremic syndrome is a cluster of symptoms pertaining to the destruction of red blood cells and the toxic presence of urine in the blood.¹⁰⁰





Carol Lynn Wooderson started taking the oral contraceptive Ortho-Novum 1/80, as prescribed by her physician, in the fall of 1972. By January 1976, her blood pressure had increased and she was suffering from a cold; six months later she was also experiencing stomach pains, nausea, vomiting, dizziness, headaches, weakness, sore throat, cough, shortness of breath and aching legs. She was ultimately diagnosed as suffering from acute kidney failure secondary to HUS.¹⁰¹

Ms. Wooderson was forced to undergo dialysis and eventually removal of both kidneys. She had recurrent eye problems and a failed kidney transplant. By May 1981, she had developed

peritonitis and, after exploratory surgery, approximately one-third of her large intestine was found to be gangrenous and removed. A second kidney transplant was successful, making dialysis unnecessary. She continued to suffer from blind spots in one eye and was required to take steroids in connection with the donated kidney. Child-bearing was no longer an option because of the risk involved.¹⁰²

At the time of Ms. Wooderson's injury, there had been 21 reported cases of HUS associated with oral contraceptives and a number of scientific articles linked oral contraceptives to this serious condition. Nevertheless, Ortho did not warn physicians of the possible connection in its package inserts.¹⁰³

As early as 1970, the FDA had issued a letter warning about the relationship between oral contraceptives and certain thromboembolic diseases. The letter cited a British study indicating that only products containing 0.05 mg. or less of estrogen should be used because of the high incidence of such diseases associated with products containing 0.075 mg. or more. Ortho downplayed the British study, however, and sent a bulletin to its sales representatives urging the continued sale of the Ortho-Novum 1/80.¹⁰⁴ The bulletin suggested that concerned doctors should be told "Doctor, nothing in this British data offers enough sound evidence to cause you to switch patients who are on 100 gammas of mestranol [.1 mg. of estrogen]. ... [Y]ou may wish to move patients to low activity products such as ORTHO-NOVUM 1/80 or ORTHO-NOVUM 1/50."¹⁰⁵

Apparently, Ortho had determined that the continued manufacture and sale of Ortho-Novum 1/80 was important to its market position because other manufacturers were producing oral contraceptives at the 1/50 estrogen level.¹⁰⁶

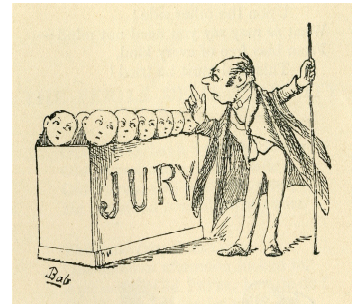
Carol Wooderson filed suit and a jury assessed \$2,000,000 in actual damages and \$2,750,000 in punitive damages against Ortho.¹⁰⁷ Ms. Wooderson's two gynecologists settled prior to trial.¹⁰⁸ On appeal, the Supreme Court of Kansas upheld the award, holding that there was sufficient evidence for the jury to find that Ortho was "grossly negligent and recklessly indifferent."¹⁰⁹

Ortho reduced estrogen levels after this case.¹¹⁰

SUPER-ABSORBENT TAMPONS

In the early 1980s, several brands of tampons, including Kotex, Playtex and Tampax, were made of polyacrylate fibers, which encouraged the growth of staphylococcus-aureus bacteria. The bacteria produce toxins that can enter, infect and ultimately poison a person's system within a few days -- a condition commonly known as "toxic shock syndrome" or "TSS".¹¹¹ Over 2,000 women developed TSS associated with use of these tampons, and approximately 100 of them died between 1979 and 1995.¹¹²

On the weekend of March 26-27, 1983, while using Playtex tampons during her menstrual period, Betty O'Gilvie developed a sore throat and a vaginal infection. By Wednesday, March 30, she was suffering from vomiting and diarrhea. That evening her temperature rose to 105 degrees and she had more or less lost consciousness. On Thursday her condition continued to deteriorate and by early afternoon her fingers had turned blue and she was having difficulty speaking. Betty O'Gilvie died on Saturday, April 2, of toxic shock syndrome.¹¹³



Her family filed suit and won. A jury assessed \$1,220,000 in actual damages and \$10 million in punitive damages against Playtex.¹¹⁴ The trial judge stated that "the amount of the verdict does not ... shock my conscience" and that punitive damages in the amount of \$20 million would not have surprised him.¹¹⁵ Nevertheless, he reduced the punitive damage award to \$1.35 million in response to remedial measures taken by Playtex, including removing the polyacrylate fibers from its tampons and removing all tampons containing such fibers from the market.¹¹⁶

On appeal, the 10th Circuit Court of Appeals reinstated the jury's award of \$10 million in punitive damages because the trial court lacked authority to reduce the award on the basis of Playtex's subsequent conduct. In so doing, the appellate court noted that "[t]he trial court here rewarded the company for continuing its tortious conduct long enough to use it as a bargaining chip" for reducing punitive damages.¹¹⁷

In the O'Gilvie case, the 10th Circuit noted that there was "abundant evidence" that Playtex:

[D]isregard[ed] studies and medical reports linking high-absorbency tampon fibers with increased risk of toxic shock at a time when other tampon manufacturers were responding to this information by modifying or withdrawing their high-absorbency products. Moreover, there is evidence that Playtex deliberately sought to profit from this situation by advertising the effectiveness of its high absorbency tampons when it knew other manufacturers were reducing the absorbency of their products due to the evidence of a causal connection between high absorbency and toxic shock. This occurred in the face of Playtex' awareness that its product was far more absorbent than necessary for its intended effectiveness.¹¹⁸

Moreover, Playtex knew that its super deodorant tampon was "exceptionally overabsorbent" -- more absorbent than necessary for its intended use. In an internal memorandum, a Playtex employee admitted: "In being obsessed with 'absorbency' we lost sight of the fact that 'leakage'

complaints did not decrease as the tampon absorbency potentials were increased.”¹¹⁹

Playtex stopped making tampons containing the polyacrylate fibers within two weeks of the jury's punitive damage award and the trial judge's suggestion that he might reduce or eliminate it if the company took corrective action.¹²⁰ As law professor Lucinda Finley put it,

Manufacturers of super-absorbent tampons have been subject to punitive damages, because they ignored the compelling evidence of toxic shock syndrome, brushed off the medical reports of injured women, failed to engage in any further testing or product modification to make the devices safer, and failed to withdraw them from the market when it became clear the risk was simply too high... Punitive damages brought a demise to the deadly marketing adventure of super-absorbent tampons.”¹²¹

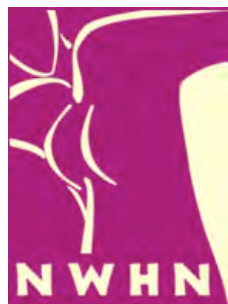
PARLODEL

Parlodel was a drug originally developed for Parkinson's disease, tumors and other disorders, but was approved by the FDA in 1980 to suppress lactation after birth.¹²² The drug caused heart attacks and strokes. The drug was manufactured by five companies and in 1989, the FDA requested they voluntarily take it off the market because of these severe health concerns. Four companies agreed. One company, refused. Instead, this company:



[I]gnored the FDA's request to withdraw it from the market and continued to promote the drug to doctors despite proof that it could cause maternal death, disabling strokes, and heart attacks. Sandoz, the manufacturer, also persuaded hospitals to prescribe it automatically to all non-breast feeding postpartum patients, even though the company's warning literature acknowledged it was not safe for all women. In response, the FDA took no stronger action than an appeal to the manufacturer's conscience, despite the FDA's awareness of the drug's deadly propensities.¹²³

Five years later, the National Women's Health Network and Public Citizen asked a court to order the FDA to force Sandoz to withdraw the drug. The groups said there was evidence that "at least 19 women have died and many others have suffered strokes, heart attacks and seizures after taking Parlodel since F.D.A. began wrestling with the drug in 1989," that since 1980, 32 women had died," and that "531 women reported to have suffered serious adverse reactions to the drug, including 36 strokes and 14 heart attacks."¹²⁴ Two days later, Sandoz announced that it was withdrawing the drug.¹²⁵



Just a few months before Sandoz's action, a Kentucky jury awarded substantial punitive damages against the company in a case involving 31-year-old Rosemary Roberts, who took Parlodel and a few days later suffered a severely disabling stroke. Other lawsuits were pending at the time. Cindy Pearson of the National Women's Health Network, said, "Any sensible doctor will stop prescribing Parlodel, now that there's been a verdict in Kentucky."¹²⁶ Professor Finley similarly wrote, "[t]he growing threat of lawsuits seeking punitive damages was also instrumental in eventually prompting Sandoz to cease marketing Parlodel as a lactation suppressant five years after the FDA had first requested that it take this action."¹²⁷

LETHAL HORMONES

DES

DES (diethylstilbestrol) was a synthetic estrogen created in 1938 and “marketed using hundreds of brand names in the mistaken belief it prevented miscarriages and premature deliveries. ... It was considered the standard of care for problem pregnancies from the late 1940s well into the 1960s in the U.S. and was widely prescribed during that time.”¹²⁸ Estimates are that it was prescribed to at least five million pregnant women.¹²⁹ The FDA eventually banned DES in 1971.



Not only did DES not work, it increased the risk for cancer, elevating the risk of vaginal and breast cancer and caused malformations of the reproductive tract, infertility and other serious health problems for not only the women who took it, but also the children they carried.”¹³⁰ The drug continued to be marketed for 18 years after it was determined to be ineffective. As University of Buffalo Law Professor Lucinda Finley has written,

After the drug DES was proven ineffective in preventing miscarriage in 1953, the drug companies continued to promote it for that purpose and expanded their efficacy claims to include the completely unproven assertion that DES would promote bigger healthier babies. Thus, for almost two decades after the drug was proven ineffective, the manufacturers continued to expose hundreds of thousands of women and their offspring to needless risk. In addition, after the connection between DES and cancer was established, the FDA took no remedial action for months and the manufacturers continued to promote the drug without warning physicians about the cancer risk until the FDA finally ordered it off the market.¹³¹

It took much effort and persistence by DES mothers and children to sue successfully over DES. Eventually the perseverance paid off but it has been difficult for a few reasons. First, some DES claims were declared “time-barred” by a state’s statute of limitations, which in some states required that a case be brought within a short time after the actual injury, instead of the date the injury was discovered. In other words, some judges were deciding to penalize women – particularly DES children - for the latent nature of their injuries or because they had not learned earlier of health risks that the company had covered-up.

Indeed, in a 1984 New York case, two women – a young Queens woman with cervical cancer, whose mother had taken DES years before, and a Long Island woman, also with cancer - sued. However, their cases were dismissed because at the time, New York law required that such cases be brought within three years of the date the women would have been initially exposed to DES. At the time, New York was in the minority of states with such a restrictive rule and New York shortly thereafter changed the law to correct such an unfair result for DES victims.¹³²

Another problem some DES victims faced was the biased view of some judges at the time about the significance of the damage caused by DES. Specifically, some viewed harm to the reproductive system “as purely emotional in nature” and therefore not involving significant economic loss

for women, or conversely, financial consequences for the company. As Professor Finley wrote,

For example, in the contemporary case of *Payton v. Abbott Labs*, in which a class of women sought compensation for a variety of injuries caused by the drug DES, the court held that the plaintiffs could not seek damages for their “purely emotional” harm because they had no accompanying physical injury. The court ruled in this manner despite the fact that many DES daughters have malformations of their cervixes and uteruses, as well as cellular changes to the vaginal and cervical lining. Moreover, gynecologists recommend as a practice that women exposed to DES undergo regular medical monitoring and far more extensive internal exams than non-exposed women.¹³³

Eventually, many lawsuits were successful, which were important for a number of reasons. Wrote Finley, “Until women started bringing and winning lawsuits, many DES exposed women did not know about the risks they faced.”¹³⁴ Moreover, “[u]ntil the first wave of successful lawsuits, little follow up research had been done to learn about the health effects of DES exposure. As such research has been done, more and more adverse health effects have come to light.”¹³⁵

Cows, Mares And Guinea Pigs – The Story Of Hormone Replacement Therapies (HRT)

In the mid 1800s, prior to the creation of the FDA,¹³⁶ doctors began giving women “ovarian extracts” for everything from anxiety to aging, as well as for the symptoms of menopause. In 1899, drug manufacturer Merck was producing a powder called Ovariin made from cow ovaries, which was prescribed for menopause and other “ills” of the ovaries.¹³⁷ Gynecologists were particularly enthusiastic about the results of these treatments in their patients. However the extracts were prepared in a haphazard manner and drug companies did not frequently disclose the list of ingredients.¹³⁸

But clearly, hormone research was becoming a new frontier and by the 1920’s, many drug manufacturers began focusing research on female hormones - especially estrogen.¹³⁹ Once scientists were able to identify and extract estrogen hormones,¹⁴⁰ estrogen was marketed¹⁴¹ and gynecologists and endocrinologists “dispensed [it] freely to their patients...[in] a trial-and-error approach.”¹⁴² There was no careful assessment of the risks and benefits of estrogen use, instead as one Dutch physician said, “We can only learn by experience whether female sex hormones therapy will be of any value.”¹⁴³



European and North American companies brought many estrogen products onto the market in the late 1920’s and early 1930’s.¹⁴⁴ In 1930, in Canada, Ayerst Labs¹⁴⁵ introduced an estrogen called Emmenin that was extracted from the urine of pregnant women. Due to the high cost, and problems with the taste and smell, the company looked for another source. Eventually the company settled on the urine of pregnant mares, which lent its name to the product, Premarin.¹⁴⁶

In 1933, the Council on Pharmacy and Chemistry, established by the American Medical Association to review products, was concerned about how little was known about the benefits and risks associated with estrogen use. "Great caution is necessary in the use of these preparations...and greater caution in making deductions from it. The indiscriminate use is likely to do more harm than good...The clinical use has kept far ahead of the laboratory data...Most of the basic facts should first be tried out in the laboratory before they are tried in the clinic."¹⁴⁷ In the same year, Emil Novak, a member of the Gynecology Department at John Hopkins, "acknowledged that estrogenic substances administered in large doses and for prolonged periods in certain experimental animals, ha[d] been shown to produce cancer."¹⁴⁸



In 1933, the U.S. Senate introduced legislation to overhaul the existing drug law.¹⁴⁹ The legislation was stalled until 1937, when over 100 people died after taking a liquid antibiotic, Elixir Sulfanilamide, which was made with a highly toxic chemical analogue of antifreeze. Many who died were children.¹⁵⁰ Following this tragedy in 1938, Congress passed the Federal Food Drug and Cosmetic Act, which, for the first time, required drug manufacturers to prove somewhat that their drugs were safe before they were allowed on the market.¹⁵¹ Drugs were required to be registered with the FDA, however, the new law did not require drug labels to include the drug's ingredients nor include any warnings as it was assumed that doctors would already know the drug's contents and side effects.¹⁵²

By the late 1930's, doctors were generally aware that "at least some researchers had a high suspicion" that estrogen use probably caused cancer even though "the data was not conclusive."¹⁵³ These findings were published in major medical journals. The *Journal of the Medical Association* (JAMA) published an editorial in 1940, which discussed the fact that researchers were able to induce cancer in the mammary glands and uteri of rodents and mentioned a case study of a woman who had developed breast cancer after a "prolonged use of estrogens."¹⁵⁴ In April 1941, Dr. Edgar Allen, the chair of the anatomy department at Yale Medical School, published an article in the journal *Cancer Research* that concluded that estrogen was a carcinogen and had the propensity to cause cervical cancer in animals.¹⁵⁵ Yet at the time many doctors dismissed these findings in animal tests claiming that the doses given to animals were excessive and that physicians only needed to be cautious in prescribing estrogen to women who were predisposed to cancer.¹⁵⁶

In May 1942, the FDA approved Premarin, becoming one of the first drugs it approved under the new Federal Food, Drug, and Cosmetic Act.¹⁵⁷ Bill McKenna was the chairman of Ayerst Labs, makers of Premarin, at the time. According to one author, McKenna was also connected to Carson P. Frailey, a drug industry lobbyist who helped instruct him on how to smoothly get approval by the FDA and how to obfuscate the cancer connection.¹⁵⁸ McKenna took the position that animals that developed cancer during trials were being given overdoses of estrogen.¹⁵⁹

Following FDA approval, safety warnings about estrogen continued to come from the scientific community. For example in 1947, Dr. Saul Gusberg, a cancer researcher at Columbia University, reported that he observed an increase in the number of endometrial cancers in women who were taking Premarin and described the use of estrogens as "a human experiment."¹⁶⁰

Although the cancer risks were being dismissed by the FDA and many doctors, at least at that time, HRT was not widely prescribed. It was generally accepted by the medical community and confirmed in medical journals that only a small number of women needed estrogen therapies to relieve menopausal symptoms, and the hormones should only be used for a short amount of time and in small doses.¹⁶¹ That was soon to dramatically change.¹⁶²

In 1957, gynecologist William Masters, later of the famed human sexuality research team Masters and Johnson,¹⁶³ presented a paper on menopausal hormone loss in a speech at the Washington University School of Medicine in St. Louis. His radical suggestion was that this hormone loss could and should be “corrected” and he advocated for all postmenopausal women to take HRT for life.¹⁶⁴ According to Masters, “the ageing woman was a victim of ‘steroid starvation’ that turned her into a ‘neutral gender’ [and that] the ‘failing reproductive powers of the gonads’ rendered her a ‘former female’”¹⁶⁵ This characterization of menopause as a deficiency “disease” rather than a natural process in a woman’s life, started to spread.¹⁶⁶

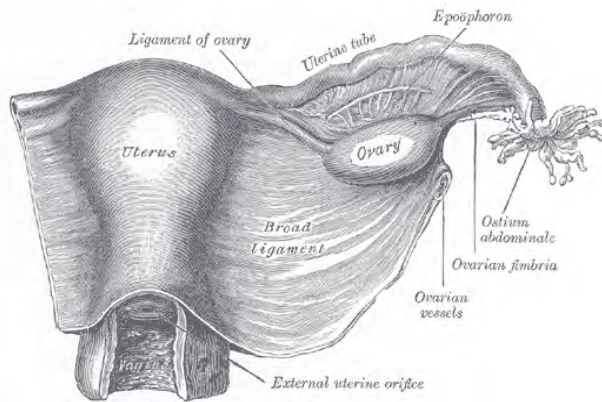
Not surprisingly, the pharmaceutical companies were quite willing to help hormone therapies, especially estrogen, gain in popularity. In 1963,¹⁶⁷ Dr. Robert Wilson, later credited with bringing HRT “to the attention of the American public,”¹⁶⁸ created the Wilson Research Foundation to promote hormone replacement therapy to the medical community and to the general public.¹⁶⁹ The Wilson Research Foundation, a “publicity machine and clearinghouse” that promoted the “anti-aging properties of estrogen”¹⁷⁰ received early funding from the makers of Premarin, Provera and Envoid, some of the HRT drugs on the market at that time.¹⁷¹ In 1966, Dr. Wilson, authored the book *Feminine Forever*,¹⁷² which was his “collection of personal observations and anecdotes” of his patients’ miserable experiences with menopause, calling post menopausal women “sexual neuters” and “no longer women.” To avoid this fate, Dr. Wilson recommended taking estrogen as the “cure” for menopause.¹⁷³ Wilson strongly defended the use of estrogen by saying, “estrogen therapy doesn’t change a woman...it keeps her from changing, that is, from suffering ‘living decay.’” Otherwise, he believed, a woman “will ‘be condemned to witness the death of her own womanhood.’”¹⁷⁴

Throughout his career, Dr. Wilson continuously dismissed evidence of the dangers associated with estrogen, even calling the reports about an increase risk for cancer associated with estrogen use “the worst lie in the world.”¹⁷⁵ According to later news accounts, Dr. Wilson’s youngest son, Ron, “believe[d] that his father hid evidence that the drugs were harmful to women,”¹⁷⁶ and that his parents were paid by drug companies to promote *Feminine Forever* across the country, including speaking appearances before women’s groups.¹⁷⁷ Ron “said he ha[d] suspected for years



that [hormone treatments] harmed women, including his own mother, who died of breast cancer in 1988.”¹⁷⁸ Ron said that his mother, Thelma Wilson, had battled breast cancer several times in her life and had undergone a mastectomy years before her death but she kept her illness a secret to protect her husband’s reputation. Ron reportedly said, “Wyeth urged his parents to hide his mother’s sickness. ‘If word ever got out that Dr. Wilson’s wife had cancer, there goes the drug,’ [Ron] said, adding that he believes his father was complicit: ‘Obviously, he wanted her to be a shining example.’”¹⁷⁹

After the publication of *Feminine Forever*, women's magazines and other media began to aggressively run articles (mostly positive) that advanced Dr. Wilson's description of menopause and promoted the use of estrogen.¹⁸⁰ Wilson was quoted in such widely read publications as *Time* magazine, calling menopause the "castration of women."¹⁸¹ *Time* declared hormones "perfectly safe" stating, "there is no evidence that the hormones can cause cancer" and, in fact, "there seems to be evidence that they guard against it."



As one author wrote, "As a pundit in the popular press, [Wilson] assured readers of *Look* and *Vogue* that ERT would prevent 26 symptoms of menopause, including hot flashes, melancholia, loss of memory, backaches and anxiety. Even more, estrogen would make women 'romantic, desirable, vibrant.' They would grow visibly younger day by day until they are transformed into exciting vibrant females they were before the 'change.' All they had to do was telephone the Wilson Foundation and obtain the name of a physician who prescribed ERT."¹⁸²

In 1962, a few years before Wilson's book was released, Congress had passed the Harris-Kefauver amendments to the Food, Drug, and Cosmetic Act, which required previously approved drugs to be reviewed for effectiveness.¹⁸³ In 1972, the National Academy of Sciences – National Research Council evaluated Premarin to review its safety and effectiveness for the FDA. After its review the FDA permitted Ayerst to list all of the FDA indications for Premarin in medical journals, which included treatment for menopausal symptoms and that it was "probably effective for estrogen deficiency-induced osteoporosis."¹⁸⁴ HRT treatments continued in popularity. Between 1963 and 1973, the sale of estrogen quadrupled.¹⁸⁵ By 1975, Premarin had become the fifth leading prescription drug in the United States, with more than 30 million prescriptions.¹⁸⁶

But estrogen's popularity soon waned. At the end of 1975, the *New England Journal of Medicine* published two studies linking estrogen with an increase risk of endometrial cancer (cancer of the lining of the uterus).¹⁸⁷ At the same time the California Cancer Registry showed an 80 percent increase in endometrial cancer cases between 1969 and 1974.¹⁸⁸ A few months later, the *New England Journal of Medicine* published another article confirming the increased risk for endometrial cancer by women taking estrogen.¹⁸⁹

Coinciding with the release of the *New England Journal of Medicine* reports, the FDA's Bureau of Drugs' Obstetrics and Gynecology Advisory Committee held its quarterly meeting in December 1975, and discussed the endometrial cancer issue.¹⁹⁰ Consumer advocates, government officials, pharmaceutical representatives and physicians and scientists attended the FDA's meeting. Dr. Sidney Wolfe, head of Public Citizen's Health Research Group, asked that all labels for estrogen products include information about the increased cancer risk.¹⁹¹

The pressure from consumer advocates came from outside the meeting as well. While the FDA conducted its meeting, the newly formed National Woman's Health Network (NWHN) protest-

ed in front of the steps of the FDA's offices in Rockville, Maryland "to bring national attention to the FDA for not adequately protecting the millions of women using estrogenic drugs" because, "[t]he FDA had failed in its core purpose."¹⁹² This was the first time in the FDA's history that an organization protested outside its building. The demonstration included a memorial service "for all the women who'd died from unnecessary estrogen products."¹⁹³ According to Barbara Seaman, co-founder of the NWHN, the head of the FDA Bureau of Drugs, Dr. Richard Crout was moved to tears by testimonials given by estrogen victims at the demonstration. Dr. Crout promised to get "mandated warnings on estrogen drugs."¹⁹⁴ The pressure worked. The FDA mandated that all estrogen drugs be required to include a warning that was given directly to patients. Until then, warning labels were only required to be given to physicians. Nothing had been given directly to patients.¹⁹⁵

In January 1976, the U.S. Senate held a joint hearing of the Senate Subcommittee on Health and the Senate Subcommittee on Administrative Practice and Procedure, to discuss estrogen and its use in menopause treatments.¹⁹⁶ The hearings resulted in a push for the FDA to "develop and maintain a system for continued surveillance of drugs after they earned approval to be marketed."¹⁹⁷

Initially the FDA did attempt to increase its oversight of the pharmaceutical industry because of doubts the agency had about the industry's ability to "self police."¹⁹⁸ In July 1977, the FDA announced that drug manufacturers were required to provide an informational brochure to be given with each prescription warning women of the increased cancer risk associated with the drug.¹⁹⁹ The Pharmaceutical Manufacturers Association (PMA) sued the FDA to prevent the distribution of the information to patients claiming that the FDA's regulation was "an unconstitutional interference with the practice of medicine." But PMA lost its case, with the judge ruling that the FDA did have the authority to require information and warnings to go directly to the patients.²⁰⁰



This was a great victory for consumers. Since the 1930's, medical professionals had been the "consumers' purchasing agents" giving the consumers little ability to calculate the risks and benefits about their prescription drugs.²⁰¹ But the victory was short-lived. In the early 1980's under the Reagan Administration, and under the encouragement of the new FDA commissioner Arthur Hull Hayes, Jr., the FDA revoked the mandate for patient package inserts "leaving the initiative to inform patients about prescription drugs to the private sector."²⁰²

Prior to the mid-1970's, most women taking HRT were doing so to alleviate menopausal symptoms (and staying eternally youthful) but as the cancer risk became more widely known by the 1980s, prescriptions for estrogen drugs fell 50 percent.²⁰³ Drug companies and some doctors decided to add progesterone to the drug regime in order to minimize the endometrial cancer risk,²⁰⁴ but as one author has written, "The endometrial cancer crisis created a need to find some additional reason to woo women onto hormones."²⁰⁵ Osteoporosis, or bone loss, became that reason.²⁰⁶ In 1978, Ayerst began to heavily push Premarin as a drug to prevent osteoporosis.²⁰⁷

In 1979, Dr. Lila Nachtigall finished a 10-year prospective study between the relationship of hor-

more therapies (by chance Dr. Nachtigall had given her patients both estrogen and progesterone) and osteoporosis.²⁰⁸ The results were dramatic; the study found that the patients not taking the HRT drugs had lost significantly more bone mass (some had developed osteoporosis) than the patients taking HRT, none of which developed the disease.²⁰⁹ Other studies had similar results.²¹⁰

In April 1984, the National Institute of Health (NIH) announced that women in menopause should be given HRT to prevent osteoporosis.²¹¹ By 1985, since Ayerst could not yet directly advertise drugs to the public, the maker of Premarin did what they could to educate the public about osteoporosis using images of older women hunched over encouraging their audience to “talk to your doctor” about the existing treatments.²¹² In 1986, the FDA permitted drug companies to “include prevention of bone loss in the indications for the use of estrogen.”²¹³

However, three years later, in 1989, a study in Sweden linked HRT with breast cancer.²¹⁴ In 1991, the Centers for Disease Control (CDC) conducted an analysis that showed the risk of breast cancer doubled for women taking HRT, and women with a family history of breast cancer were at an even greater risk.²¹⁵

In February 1990, the FDA’s Fertility and Material Health Advisory Committee met to discuss the links between HRT and breast cancer and decided that the existing data did not prove enough of a correlation.²¹⁶ They claimed the issue warranted additional study.²¹⁷

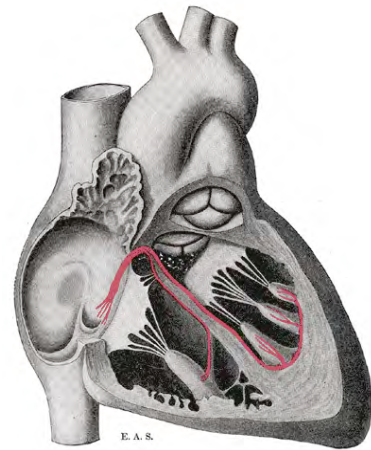
In the meantime, in the early 1990’s the company applied for FDA approval to sell Premarin as a drug to protect against heart disease, which would allow it to market the drug to an even wider audience. A few months after they met to discuss the breast cancer risk, the same FDA committee met to discuss the cardio-protective benefits that estrogen use might offer.²¹⁸ The advisory committee indicated it was likely that estrogen offered a benefit to the heart²¹⁹ but groups like the National Women’s Health Network fought this and ultimately, the FDA overruled the advisory committee, saying better data were needed.²²⁰

In response, Wyeth-Ayerst announced in October 1993, that it was funding a national study, the Heart and Estrogen-Progestin Replacement Study (HERS) “to determine the impact of estrogen replacement therapy on post-menopausal women.”²²¹ This included the correlation between heart benefits and estrogen use. The company had recently developed the estrogen-progesterone combination drug, Prempro, and to save money the company pushed for the study to only include Prempro and not Premarin. Since Prempro was simply Premarin with progesterone added, the company contended that any cardio-benefits found in Prempro could be generalized to Premarin as well.²²²



Two years into the HERS study, the National Institutes of Health (NIH)’s Data and Safety Monitoring Board noticed that the Prempro group had an “excess of blood clots and an excess of cardio-vascular events (e. g. heart attacks)” but allowed the study to be completed.²²³ In 1998, the results of the HERS study concluded that taking HRT offered no benefit for women who already had heart disease.²²⁴

But that was not the only bad news for HRT. Aided by some “political savvy, good coalition-building, and other factors that included just plain good luck,” women health activists and consumer groups finally made progress in their struggle to get HRT health issues comprehensively addressed when NIH and its first female director announced plans in 1991 to conduct the largest study ever of health problems in post-menopausal women.²²⁵ The Women’s Health Initiative (WHI) was a 10-year, government funded multi-million dollar study with over 140,000 participants that was intended to “redress...the years of neglect of women’s health issues,” and, in part, study HRT use and the prevention of bone loss and heart disease.²²⁶ The study, the first of its kind (because all other studies had relied on “circumstantial evidence, comparing women who chose to use hormones to those who didn’t”²²⁷) began in 1993, and was expected to conclude in 2005.



But three years earlier than expected, in July 2002, the NIH’s National Heart, Lung and Blood Institute (NHLBI) that had been conducting the WHI announced that it was stopping the trials.²²⁸ The researchers had noticed a significant increase in the risk of breast cancer, heart attacks, blood clots and strokes in the participants taking Prempro, the HRT drug being tested.²²⁹

Finally, in December 2002, in its biennial *Report on Carcinogens*, the U.S. Department of Health and Human Services added steroidal estrogens, the type used in estrogen replacement therapies and oral contraceptives, to the official list of “known human carcinogens.” The National Institutes of Health said, “A number of the individual steroidal estrogens were already listed as ‘reasonably anticipated carcinogens’ in past editions, but this is the first report to so list all these hormones, as a group.... The report cites data from human epidemiology studies that show an association between estrogen replacement therapy and a consistent increase in the risk of endometrial cancer (cancer of the endometrial lining of the uterus) and a less consistent increase in the risk of breast cancer.”²³⁰

In July 2002, only weeks after the announcement that the WHI study was being stopped, women who had developed cancers, blood clots and had heart attacks while taking Prempro began to file lawsuits against Wyeth.²³¹ By the following year, even more information was released from the WHI trials linking the drug to additional medical problems, like dementia²³² and an increase in breast density making mammograms less reliable.²³³

June Bloch, a Pennsylvania woman, sued the company because she said, “I’m unhappy that they didn’t do further research or at least tell us about any hints that had that it might be harmful...I would like to see it investigated. Someone has to be held accountable.”²³⁴ By the following year an estimated 5,000-6,000 women had filed individual as well as several class action lawsuits.²³⁵ These cases are meeting with mixed results. Some breast cancer claims have been declared “time-barred” because the injured women did not file their case until after the 2002 breast cancer study was published. In other words, some judges were deciding to penalize women for not learning of health risks that the company and FDA had covered-up, saying they should have filed their case before knowledge of the breast cancer study was made public.²³⁶ This is another way companies are benefiting from having covered-up serious health risks involving HRT.

In other cases, juries have ruled in favor of women who have sued, only to have the judge throw out the case for reasons that are perplexing. In another Pennsylvania case to go trial against Wyeth-Ayerst, jurors found that Prempro and Premarin caused Jennie Nelson's breast cancer and awarded her \$1.5 million in damages during the first phase of the case in October 2006.²³⁷ But the judge declared a mistrial without explanation and sealed the records for the case.²³⁸ Eventually a second jury awarded her \$3 million in damages,²³⁹ but the judge overturned the award. This case is currently under appeal.²⁴⁰ According to one Pennsylvania attorney, "only four of about 1,500 cases pending in Philadelphia have gone to trial. Each time, a jury sided with the plaintiff only to have the judge reverse the verdict."²⁴¹

In February 2008, a federal jury awarded an Arkansas woman \$2.75 million in her case against Wyeth; the second phase of the case is ongoing.²⁴² And in a 2007 Nevada case, a jury awarded \$134 million to three Nevada women who sued, although a judge reduced the amount to about \$58 million total -- \$23 million in compensatory and \$35 million in punitive damages. Wyeth appealed and during the appeal, Wyeth acted in bad faith during settlement talks resulting in the judge formally charging them with bad faith and ordering them to post a \$58 million bond and pay attorneys fees.²⁴³ The Nevada judgment is the largest award to date against Wyeth, which faces about 5,300 similar lawsuits across the country in state and federal courts.

DRUGS WITH DISPARATE IMPACT - ACCUTANE

There is perhaps no drug more associated with formation of severe birth defects than Thalidomide, the morning sickness drug widely prescribed in Europe in late 1950s that severely deformed 8,000 babies. Thankfully, Thalidomide was never approved for general sale in the United States.²⁴⁴ But when the *New England Journal of Medicine* called the acne drug Accutane so dangerous that it “puts the drug in a class with Thalidomide,”²⁴⁵ one might expect a swift and immediate FDA response to greatly restrict young women’s access to this drug. One would be wrong.

Accutane, made by Hoffman-La Roche, is an ingested acne drug to which the FDA gave fast track approval in May 1982; it was available to the public by September 1982. The drug company called Accutane a “medical breakthrough” and former FDA Commissioner Arthur Hull Hayes, Jr. said, at the time of its approval, “it [held] promise for the many sufferers of this physically and psychologically debilitating disease cystic acne.”²⁴⁶ But at the time it was approved, Accutane was known to cause severe birth defects in animals and was suspected of doing the same to humans. In fact, during the human trials, women were first given pregnancy tests to ensure that no pregnant women took the drug.²⁴⁷

When Accutane was being developed a decade before, a Hoffman-La Roche official and dermatologist wrote, “[I]n the psychological climate engendered by the Thalidomide tragedy, it would have been inconceivable to develop an agent with teratogenic properties [causing birth defects] for the treatment of such a common complaint as acne.”²⁴⁸ But not only was it developed and put on the market, “the company did not recommend and the FDA did not insist upon labeling that emphasized the importance of contraception or abstinence while under treatment with the drug.”²⁴⁹

Not surprisingly, many women who were prescribed the drug were or became pregnant. In 1983, news reports surfaced about the drug causing severe birth defects in babies and spontaneous abortions linked to the drug. Under pressure from Public Citizen’s Health Research group, the FDA announced that it would review Accutane for possible additional action.²⁵⁰ Public Citizen “cited FDA’s own data showing that the drug was linked with five severe cases of birth defects, eight spontaneous abortions, 12 cases of impaired vision and other side effects” and “blamed those problems on doctors’ prescribing the drug for patients who suffered mild forms of acne that could be treated with other drugs and on their prescribing unnecessarily large doses.”²⁵¹

An FDA advisory board of dermatologists met to consider removing it from the market. They didn’t.²⁵² Instead, they recommended new warnings to medical professionals as a reminder to discourage women from taking the drug during pregnancy.²⁵³ In March 1984, Hoffmann-La Roche again sent a letter to doctors warning about the risk to pregnant women who took the drug. This didn’t work either. By then, at least 18 cases of severe birth defects and 21 miscar-



**DO NOT
GET PREGNANT**

riages had been linked to Accutane.²⁵⁴ The company also suggested that women take a pregnancy test before beginning the drug regime.²⁵⁵ The FDA also told blood banks not to accept blood from people who were taking the drug.²⁵⁶

The Centers for Disease Control (CDC) also warned against the drug's use for pregnant woman.²⁵⁷ According to the CDC, one third of the pregnant women taking the drug miscarry in the first trimester and at least 30 percent of the babies are born with severe birth defects.²⁵⁸



In 1985, the *New England Journal of Medicine* published a new study on Accutane. The researchers found that not only were pregnant women taking the drug, but also that, “of 154 pregnant women who took the drug inadvertently, 12 had miscarriages, 21 delivered babies with birth defects, and 26 had normal infants. The other 95 chose to have abortions after learning of the risk.... Birth defects included malformations of the head, face, heart, central nervous system and thymus -- a gland that regulates growth.” Moreover, despite warnings, 10,000 new women of childbearing age were receiving the drug every month.²⁵⁹

In 1988, another FDA advisory committee met “to discuss the high level of pregnancy exposure to Accutane and the overuse of the product and its contribution to the pregnancy exposure problem.”²⁶⁰ A confidential FDA memo leaked to the *New York Times* said that “Accutane has caused hundreds, perhaps more than 1,000, babies to be born with severe birth defects in the past six years” and despite warnings, “thousands of women have taken Accutane in their pregnancies.”²⁶¹

At that time, a former Hoffman-La Roche dermatologist who became chief of dermatology at Children's Hospital of Columbus, Dr. Frank W. Yoder, came forward to say that the company was “negligent and wrong” for over-promoting the drug, “which resulted in its being put in the hands of doctors who were not dermatologists.”²⁶² He said that “while testing Accutane before it received FDA approval, Hoffman-La Roche placed severe restrictions on researchers to ensure that pregnant women did not get the drug. The restrictions included the requirement that women not be included in the study, or that they submit to a pregnancy test to prove they were not pregnant before being given the drug. ... But when the drug was sold to the public, the company did not require such pregnancy tests. ‘This was very, very wrong,’ Yoder said. ‘It is incredible to require that in a study, but not in a mass market situation.’”

Moreover, Dr. Yoder claimed, “It was only later, after reports of birth defects began trickling into the FDA and as pressure increased from consumer groups, that the company began to recommend that doctors give women pregnancy tests before prescribing the drug.”²⁶³ The company disputed Yoder's charges, but according to scientists with the FDA's Division of Epidemiology and Biostatistics, “All efforts to date have been unsuccessful at protecting against pregnancy exposure and the sequelae of birth defects and abortion” and these facts “warrant active consideration of removal of Accutane from the market.”²⁶⁴

Despite this evidence, the agency again refused to pull the drug from the market or follow the “critical control measure” of requiring doctors “to promise in writing that they will prescribe Accutane only for severe, otherwise untreatable acne”,²⁶⁵ instead issuing another warning – this time including a picture of a severely deformed child on its label.²⁶⁶ This led Dr. David Graham, the lead FDA epidemiological researcher on Accutane to say, “Those (recommendations) are simply not going to successfully eliminate pregnancy exposure for Accutane users.”²⁶⁷ Dr. Sidney Wolfe of Public Citizen’s Health Research Group, which had asked the FDA to allow only dermatologists to prescribe Accutane and “make doctors sign statements saying that they are prescribing it according to FDA rules,” said, “the FDA is choosing not to use its legal authority to stop an epidemic of birth defects that is preventable.”²⁶⁸ A June 1988, *New York Times* editorial outlined the “failed policies of the [FDA] in regulating the acne medication Accutane.”²⁶⁹

In September 1988, the company began a “Pregnancy Prevention Program (PPP),” which involved have sale reps deliver kits to dermatologists that instructed them on advising their patients.²⁷⁰ By this time, dozens of lawsuits had been filed against Hoffmann-La Roche.²⁷¹ While some cases were not succeeding,²⁷² in July 1989, a Mississippi jury awarded a woman \$1 million in damages after “the company failed to warn [the woman’s] doctor adequately about Accutane’s potential side effects when it was prescribed in 1984.”²⁷³



Between 1989 and 1991, “several advisory committee meetings were held to monitor the progress of the PPP.”²⁷⁴ However, “[i]t was clear from these meetings that the majority of women taking Accutane were not volunteering to participate in the PPP, that even in the group that did volunteer, pregnancy testing was infrequently performed and that pregnancy exposure to Accutane was still occurring at a high level.”²⁷⁵

Not until September 2000 was another FDA advisory committee meeting held, and,

At this meeting, it was shown that enrollment in the PPP was low and falling, that pregnancy testing was still often not being performed and that recommendations about contraception or abstinence were often not adhered to. Even more alarming, the use of Accutane in women had increased 3-fold during the preceding 10-year period when one would have expected it to decline substantially because of successful treatment of prevalent cases of severe nodular acne. The committee’s response to this evidence was to declare the PPP a failure and to recommend that a comprehensive risk management program that included patient and physician registration as well as mandatory pregnancy testing be established.²⁷⁶

In 2005, Accutane’s manufacturers agreed “to construct a system that required doctors, pharmacists, wholesalers and patients to participate in a tightly controlled distribution system mostly operated on the Internet. The system, called iPledge, requires female patients to take pregnancy tests and birth control. But doctors say that is inconvenient, cumbersome and sometimes impossible to manage.”²⁷⁷ Public Citizen’s Dr. Sidney Wolfe told the *New York Times*, “There is this never-ending whimpering coming from many dermatologists that someone is cramping their style and making it more difficult to prescribe something.... The reason there are all these failed efforts to limit pregnancies is that dermatologists are prescribing Accutane to way too many peo-

ple." In response, the FDA did the opposite, instead making it "a little easier" for women to fill their Accutane prescription.²⁷⁸

At the end of 2007, University of Pittsburgh Medical Center researchers studied half a million women who were taking a variety of medications, including Accutane, and found that nearly half "didn't get counseling from their doctor about using contraceptives or other birth control measures".²⁷⁹ They noted, "Anyone taking Accutane or one of its generic competitors is required to use birth control, pass a pregnancy test before each monthly refill and enroll in a national registry. Despite that program, administrators in July reported that more than 120 women became pregnant in the previous year."

As the *New York Times* put it, "The federal government has undertaken more than 40 efforts over the last 23 years to prevent women from becoming pregnant while taking Accutane. Nothing has worked."²⁸⁰

It should also be noted that additional health concerns have arisen surrounding Accutane that do not pertain just to women. There has been extended public discussion about the drug's link to suicide after the suicides of B.J. Stupak, the teenage son of U.S. Representative Bart Stupak, (D-Mich.) who shot himself in 2000, and Charles J. Bishop, the 15-year old who flew a plane into a Florida building in January 2002.²⁸¹ A congressional oversight committee's two-year investigation into the health effects and regulatory control of Accutane concluded in 2002 that the drug had frequently been associated with suicide.²⁸²

Juries have also ruled against Hoffmann-La Roche in cases that have included inflammatory bowel disease²⁸³ with additional cases from people across the country claiming that Accutane caused their colon problems.²⁸⁴ In April 2008, a New Jersey state-court awarded a young woman \$10.5 million in punitive damages in her case against Hoffmann-La Roche over inflammatory bowel disease.²⁸⁵

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