

How Far We've Come

A PHARM EXEC TIMELINE

In 1981, pharma was a more innocent industry. It stood on the brink of an AIDS epidemic that science had yet to name or understand. Hazards of generics, product lifecycles, and off-label marketing lay years ahead. There were no embryonic stem cells to fight over—nor euphemisms like “overactive bladder syndrome” and “erectile dysfunction” to ease conversations or kick off ad campaigns. Who knew what awaited us? To remember—and to reflect on what shaped modern pharma—we invite you to page through the most significant events of the past quarter century.

1981

AIDS first detected

On June 5 the Centers for Disease Control's *Morbidity and Mortality Weekly Report* publishes the details of five patients with symptoms that later would be identified as AIDS. The publication date is known as the official onset of the HIV/AIDS epidemic.



First ACE inhibitor

Squibb's Capoten (captopril) is approved to treat hypertension and congestive heart failure. It's one of the first effective oral hypertensives, the first angiotensin-converting enzyme inhibitor, and an important breakthrough in structure-based drug design.

First DTC advertisement

UK-based Boots Pharmaceuticals runs a print ad for Rufen, its American subsidiary's prescription ibuprofen product. The Boots ad kicks off a series of drug promotions aimed at consumers. FDA responds the next year by asking the industry for a voluntary moratorium on all DTC drug advertising so it can research the issue.

Package inserts spiked

An FDA pilot program to require “more useful” information on patient package inserts is stopped by the new Reagan administration in the wake of protests by doctors and pharmacists.

1982

Oraflex recalled

In a preview of recent safety controversies, Eli Lilly voluntarily suspends sales and distribution of its anti-arthritis drug Oraflex (benoxaprofen), following reports of 61 deaths in Britain and nine in the United States. The move comes just 10 weeks after the product's US launch.

HEADACHE

Tylenol tampering

[September 29, 1982]

Extra-strength Tylenol laced with cyanide kills seven people on the west side of Chicago and touches off a nationwide panic. Johnson & Johnson quickly determines that the poisoned pills come from two different plants, suggesting that the tampering occurred after the bottles arrived in Chicago, but recalls the drug nationwide. A textbook public-relations campaign that is still studied today restores the public's faith in the company and the brand. The incident also leads to new FDA regulations requiring tamper-proof containers. In months, the product returns to the shelf in new, safer packaging. No perpetrator is caught.



First recombinant product

FDA approves Eli Lilly's Humulin, insulin identical to that produced by the human body and the world's first drug created using recombinant DNA technology.

New aspirin side effect

Four long decades after aspirin was synthesized, research links the common drug with increased likelihood of Reye's Syndrome, a rare brain and liver disorder that often occurs during recovery from the flu or chicken pox.

1983

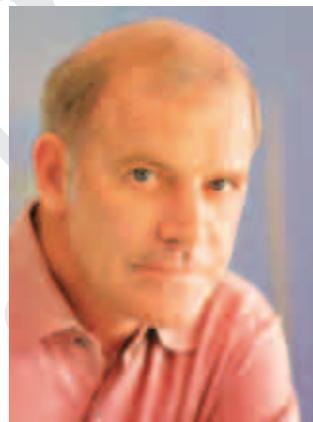
Orphan Drug Act

Designed to stimulate R&D of products that treat rare diseases, the act grants seven-year exclusivity to companies that make drugs for "orphan" diseases (those that affect fewer than 200,000 people in the United States), and allows them to tax-deduct a portion of clinical-trial costs.

TRANSPLANTATION

Cyclosporin approved

[1983] After 30 years of kidney transplants, patients still face an obstacle: Their immune systems attack the new organ. That changes radically when Novartis' Sandimmune (cyclosporin) is introduced. Derived from soil fungus, the drug selectively suppresses T-cells—fueling almost two decades of revolutionary surgery.



1984

Hatch-Waxman Act



Named for Sen. Orrin Hatch (left) and Rep. Henry Waxman, the act provides incentives and privileges for generic drug manufacturers—essentially creating the modern generic industry.

1985

FDA lifts DTC moratorium

Print ads resume, but full prescribing info is required, so broadcast ads are still out.

NOBEL PRIZE

Polymerase chain reaction discovered by Kary Mullis at Cetus

[1983] Polymerase chain reaction (PCR), a technique of amplifying DNA, is discovered by Kary Mullis at Emeryville, California-based Cetus Corporation (taken over by Chiron in 1991). Mullis goes on to win the 1993 Nobel Prize in Chemistry for his method of rapidly multiplying one DNA sequence into many. PCR has been described as being to genes what the Gutenberg press was to words: The process can turn a single sequence into a million identical copies in about an hour. PCR opened up a world of possibilities, from paternity testing and DNA fingerprinting to genome mapping and DNA-based diagnosis of diseases.

“Without being asked, [J&J] quickly withdrew extra-strength Tylenol at considerable expense. J&J chose to take a large loss rather than expose anyone to further risk.”
WSJ, October 1982

APPROVED: Protropin

Genentech's human growth hormone is an important drug, but so is the fact that for the first time a biotech company is manufacturing and marketing its own product. It's a turning point for Genentech, and the industry.

NIH approves guidelines for gene therapy experiments in humans

1986

APPROVED: Prozac

Eli Lilly's revolutionary anti-depressant, the first selective serotonin reuptake inhibitor, receives its first regulatory green light in Belgium; US approval follows in 1987.

APPROVED: Orthoclone OKT3

FDA gives Ortho Biotech the go-ahead for the first therapeutic monoclonal antibody, which prevents kidney transplant rejection.

APPROVED: Intron A and Roferon A

Schering and Hoffman-La Roche introduce the first biotech-derived interferon drugs: Intron A and Roferon A (now marketed by Biogen and Genentech, respectively) for leukemia. In 1988, the drugs are approved to treat Kaposi's sarcoma, a complication of AIDS.

Merck-Chiron receive license for first recombinant vaccine

Recombivax for hepatitis B becomes the first vaccine that relies on genetic sequencing of the virus protein.

1987

APPROVED: AZT

Burroughs Wellcome gets the go-ahead for the first AIDS treatment.

October 19: Black Monday stock market crash



APPROVED: Cipro

FDA approves Bayer's fluoroquinolone

antibiotic for a number of infections, including skin, lower respiratory track, bone, and joint. It becomes a textbook example of lifecycle management.

WASHINGTON

The Prescription Drug Marketing Act



[April 22, 1988] This controversial piece of legislation was Congress's attempt to protect the drug supply from products that were counterfeit, contaminated, or simply expired. The PDMA requires

licenses for wholesalers, mandates pedigree tracking, and prohibits the re-sale of drugs by hospitals or charity groups. But certain provisions angered secondary wholesalers, which fought parts of the law, arguing that they were at an unfair disadvantage against bigger players. They successfully prevented its full implementation until this year, when new technology, particularly RFID, renewed interest in pedigree tracking.



THE FIRST STATIN

Mevacor launched

[September 1, 1987] Merck's introduction of the world's first statin was not without a major educational effort to tell patients why lowering their cholesterol mattered. The company spent millions building a campaign around the tagline "know your number," taking advantage of the recently available cholesterol-measuring tests. Less than a decade later, HDL and LDL were household terms, the pill was a blockbuster for Merck, and next generation Zocor was seeing similar billion-dollar success. A crowded group of follow-ons would soon join Mevacor to vie for best in class.

1988

APPROVED: Losec (Prilosec) launched in Europe

AstraZeneca launches its proton-pump inhibitor in Europe and Asia, with US approval following a year later. The pill, one of the world's largest sellers, goes OTC in 2003, laying the groundwork for price debates over next-generation Nexium.

\$539.9 billion US healthcare expenditures

Pharma/biotech partnership sets model for the future

Hoffman-La Roche and Cetus negotiate a licensing agreement for two anti-cancer drugs, interleukin-2 and PEG-modified IL-2, after their patents come into conflict. The deal becomes the standard for cross-licensing between companies.

60% amount of Rx drug spending paid out of pocket

1989

APPROVED: EPO

After a tough patent fight, Amgen wins the race to bring its epoetin alfa product to market. First aimed at dialysis patients, Epo goes on to improve the lives of cancer and AIDS patients suffering from drug-induced anemia.

1990

International Conference on Harmonization

The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) brings together regulators and industry representatives from Japan, Europe, and the United States to break down barriers to free global trade in medicines. A key result: the Common Technical Document.

1991

APPROVED: Neupogen

Amgen's Neupogen (filgrastim), launched in the United States and Europe, is a recombinant version of a human protein that selectively stimulates the production of infection-fighting white blood cells, called neutrophils.

1992

APPROVED: Paclitaxel

Virtually the only survivor of a program that screened 114,045 plants for activity against cancer, taxol is derived from the Pacific yew. BMS' version of the drug goes on to become a blockbuster anti-cancer agent.

229

Number of generic versions of new drugs approved



PDUFA

The Prescription Drug User Fee Act offers pharma quicker decisions from FDA in exchange for industry financial support.

Amgen is the first biotech to make the Fortune 500

1993

APPROVED: Betaseron

Chiron receives approval for Betaseron, the first treatment for multiple sclerosis in 20 years. The drug initially was distributed using a lottery-style allotment system.



BIO launched

Two biotechnology trade organizations merge to create the Biotechnology Industry Organization (BIO). The goal was to achieve a balance of power within the organization between the handful of firms that launched the first wave of biotechnology products.

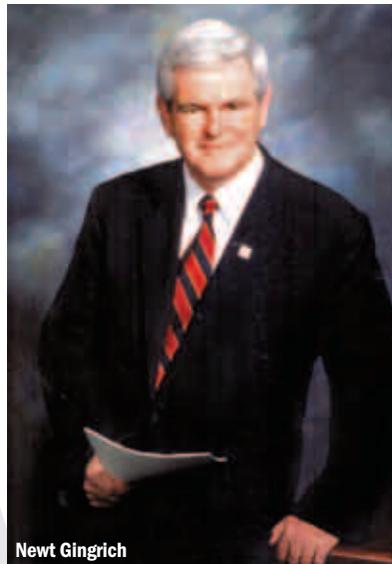
LEGAL

Washington Legal Foundation fights for off-label rights



Judge Royce C. Lamberth

[1994] Doctors are allowed to prescribe medications for uses not mentioned in the product label. But FDA, in the early 1990s, goes after companies that provide physicians with information about off-label use—even when that information comes from peer-reviewed scientific journals. That policy comes under fire as the pro-business Washington Legal Foundation (WLF) files a lawsuit arguing that FDA is interfering with the First Amendment right of free speech. In July of 1998, Judge Royce C. Lamberth rules in favor of WLF. In the meantime, though, Congress has passed the FDA Modernization Act of 1997 (FDAMA), which includes new provisions permitting the distribution of off-label information. The catch: The rules are cumbersome, and require companies to file an application for the new use before they are allowed to distribute information about it. The stage is set for 2001 and 2002, when HHS's Office of the Inspector General launches its campaign against pharma, arguing in part that off-label communication about a drug covered by Medicare is *de facto* Medicare fraud.



Newt Gingrich

1994

Newt speaks

Soon-to-be House Speaker Newt Gingrich calls FDA “the number-one job-killer in America,” and commissioner David Kessler “a thug and a bully.” He goes on to back privatization of many regulatory functions.

APPROVED: Nutropin

Genentech receives approval to begin marketing its second human growth hormone, Nutropin, for the treatment of growth failure in children. The drug is later used to treat adults suffering from growth deficiency caused by Turner syndrome.

APPROVED: Cerezyme

Genzyme's recombinant version of glucocerebrosidase—the human enzyme

whose lack causes Gaucher's disease—is a striking example that a successful business can be built around orphan drugs.

“The court considered the underlying policies in evaluating the constitutionality of FDA's position on manufacturer-sponsored dissemination of medical information.”
Judge Royce C. Lamberth

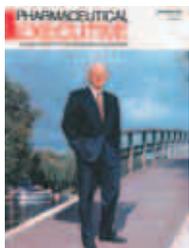
1995

EMA founded

The European Medicines Agency finally gives pharmaceutical manufacturers the ability to obtain marketing approval for all of the EU with a single application.

First protease inhibitor

Hoffman-La Roche's Invirase (saquinavir) is the first major breakthrough in AIDS therapy in a decade, and the new class of protease inhibitors go on to revolutionize AIDS treatment.



Pharm Exec November 1996

Pharmacia, Upjohn merge

In a \$6-billion deal, Sweden's Pharmacia and Kalamazoo-based Upjohn both strengthen their global capacities. Two years later, Pharmacia acquires Monsanto/Searle.

CLONING

Dolly the sheep is born

[July 5, 1996] The first mammal cloned from an adult cell, Dolly, is born in July 1996, though it isn't announced until February 1997. Heralded as one of the most significant scientific breakthroughs ever, Dolly's birth aroused controversy over the ethics of human cloning. Dolly is eventually euthanized in 2003 because of progressive lung disease.

Ebola outbreak kills hundreds in Zaire

1996

DDMAC established

FDA creates the Division of Drug Marketing, Advertising and Communications (DDMAC) within the Center for Drug Evaluation (CDER), in response to a growing need to regulate prescription drug advertising and promotion.

Mad cow disease hits Britain

APPROVED: OxyContin

Purdue Pharma's blockbuster time-release formulation of oxycodone, with sales eventually topping \$1.5 billion, becomes controversial, as would-be abusers learn how to defeat the time-release mechanism and obtain pure oxycodone.

"There are a number of genetic diseases for which there is no cure. This will enable us to [find] causes of those diseases and perhaps develop methods to treat them."
CNN.com, February 1997



Pharm Exec February 1997

Sandoz/Ciba-Geigy merge to create Novartis

The two Swiss-based, chemical/life sciences giants approach their record-breaking \$30.9-billion merger with an unusual idea: Rather than integrate two companies, they'll build an entirely new one, new name and all. Dan Vasella becomes CEO.

APPROVED: Avonex

Produced by Biogen Idec, Avonex (interferon beta) is approved as an intramuscular injection to treat multiple sclerosis. It becomes the most prescribed MS therapy worldwide.

M&A

Glaxo acquires Wellcome

[1995] After several months of boardroom tussles, Glaxo's £9-billion takeover of Wellcome, the largest merger in British history up to that point, creates a top-10 drug company. The 39.5 percent owner of Wellcome, the Wellcome Trust, had first turned Glaxo down, but relented after failed attempts to find other buyers. Less than five years later, Glaxo Wellcome and SmithKline Beecham merge in a £114-billion deal that creates the largest pharmaceutical company of the time (with a seven-percent global market share), and the largest corporation in Britain, GlaxoSmithKline.

APPROVED: Lipitor

Pfizer's statin, the fifth to reach market, goes on to become the best-selling drug ever.

1997

FDA issues draft guidelines for broadcast DTC

The document details ways in which pharma companies can provide, in less detail, the risks associated with drugs in TV and radio ads.

APPROVED: Rituximab

Genentech wins approval for the first therapeutic monoclonal antibody for cancer.

Fen-phen withdrawal

A popular weight-loss drug combination is found to cause heart-valve disease. American Home Products (now Wyeth) is quickly embroiled in one of the largest product-liability cases of all time. By 2006, the company has paid more than \$20 billion to cover its costs.

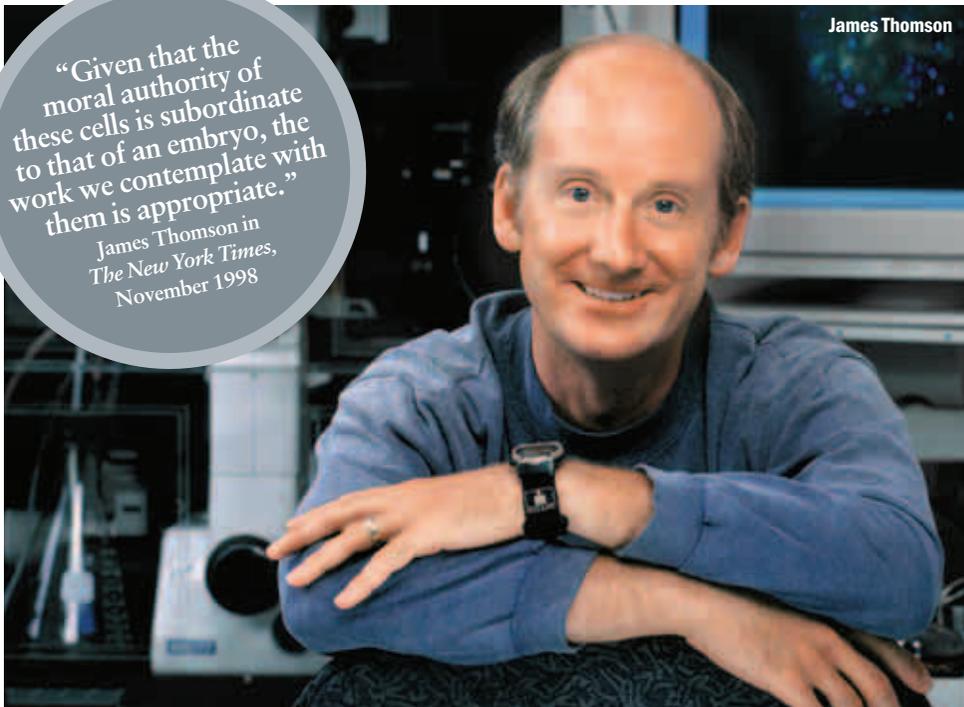
FDA Modernization Act

A sprawling law covers pediatric drug research, fast-track development, post-marketing studies, and communication of off-label information, to name just a few.

21 CFR Part 11 released

FDA's rules on electronic signatures and data integrity prove to be far harder to implement than anticipated. Final guidance takes almost six years to arrive.

"Given that the moral authority of these cells is subordinate to that of an embryo, the work we contemplate with them is appropriate."
James Thomson in *The New York Times*, November 1998



BREAKTHROUGHS

James Thomson isolates human embryonic stem cells

[1998] James Thomson of the University of Wisconsin in Madison, along with John Gearhart of Johns Hopkins University, becomes the first scientist to isolate and culture human embryonic stem cells. This is a major advance for its ability to aid in organ transplantation, gene therapy, and treatment of such ailments as paralysis, diabetes, and AIDS. But similar to the controversy that surrounded the birth of Dolly the cloned sheep, conservative groups raise a number of ethical considerations over the nature of where the cells were taken from—in one instance, a man and a woman were asked to use their sperm and egg, but in another experiment, cells were taken from aborted fetuses. Anti-abortion groups contend that the ball of cells (blastocysts) that eventually becomes the stem cells is considered human life.

1998

APPROVED: Viagra

"Vitamin V" and "the Blue Pill" become common nicknames for Pfizer's blue and diamond-shaped pill to treat male erectile dysfunction. It is widely advertised to consumers and famously endorsed by Bob Dole.

First bird-to-human transmission of bird flu

In Hong Kong, 18 people are hospitalized and six die from the flu. DNA tests prove that the disease is H5N1 influenza, caught from contact with birds. A million-and-a-half chickens, Hong Kong's entire supply, are killed.

Pfizer's sales force exceeds 4,000 representatives

The pharma sales force arms race begins in earnest. By 2005, Pfizer will hit its peak, when it employs a reported 38,000 sales reps.

Combivir, the first combination AIDS pill, is approved





OBESITY
Body Mass Index cut-off is lowered

[June 17, 1998] The federal government issues new guidelines on the identification, evaluation, and treatment of overweight and obese adults. According to the new guidelines, adults with a Body Mass Index (BMI) of 25 to 29.9 are considered "overweight;" those with a BMI of 30 are considered "obese." Previously, the BMI cut-off for overweight was 27.8. The new guidelines, by creating a new definition of healthy weight, redefine approximately 30 million Americans as technically overweight and also bump up significantly the number of obese adults living in the United States.

Craig Venter founds Celera

The genetic scientist, in announcing his new company, Celera Genomics, declared that it would sequence the human genome within three years, for \$300 million.

NICE established

National Institute for Clinical Excellence decides the cost effectiveness of therapies in the UK. NICE delays numer-

ous life-saving drugs from reaching the market in the UK, yet remains a potential cost-containment model.

Astra and Zeneca merge

Astra AB of Sweden and Zeneca Group PLC of the UK announce in December that they will team up to form a \$67-billion company. The deal, completed in April 1999, is one of Europe's largest-ever mergers.

1999

West Nile virus arrives in US

The virus, named after the West Nile District of Uganda, where it was first discovered in 1937, makes its first US appearance, in New York City.



2000

Congress passes Medicine Equity and Drug Safety Act

Legislators, appalled by rising prices, vote to allow importation of drugs from abroad. But the law contains a clause that allows HHS to ban imports if the Secretary finds that they would be unsafe or ineffective—a finding both Donna Shalala and Tommy Thompson make.

DTC advertising spending breaks the \$2-billion mark

2001

New cholesterol guidelines

NIH issues the first major update in decades on the prevention and management of high cholesterol. A key change: use of a lipoprotein profile as the first test for high cholesterol.

OIG begins anti-fraud steps

In October, TAP Pharmaceutical agrees to pay a record \$875 million to settle charges of illegally marketing and manipulating the cost of prostate cancer drug Lupron. It's the first of several blockbuster settlements resulting from OIG's crackdown.

George W. Bush limits federal funding of stem cell research

Human genome published

The Human Genome Project consortium publishes a working draft of the genome mapping in the February 15 issue of *Nature*. Celera, Craig Venter's company, publishes its draft a day later, in *Science*.

Pediatric patent law passed

Pharma is incentivized to focus on children, when Congress grants six-month patent extensions on drugs whose efficacy is proven (through clinical trials) in pediatric patients.

APPROVED: Gleevec

Novartis' drug for chronic myeloid leukemia is unique not only for its efficacy, but for the level of patient involvement in development and speed of approval. Turnaround at FDA is less than three months, a new record.

PERSONALIZED MEDICINE

Herceptin approved



[September 25, 1998] After receiving fast-track designation, Genentech's biologic is approved in combination with paclitaxel for the first-line treatment of HER2-positive metastatic breast cancer, and as a second- and third-line therapy as a single agent. Herceptin (trastuzumab) is the first therapeutic antibody targeted to a cancer-related molecular marker to receive FDA approval. In 2006, Herceptin is approved in Europe for early-stage HER2-positive breast cancer.



PART D

Rx discount card program

[July 12, 2001] In his first step toward controlling drug costs for seniors, President Bush announces a prescription discount card program that he hopes to implement without Congressional approval. Pharmacists object to the plan, arguing that most of the discount comes out of the gross profit margin of pharmacies and drug stores. Later, a federal district court blocks the president's plan, noting in its ruling that the president had "acted without legal authority" and violated the law by skirting a requirement to solicit public comment on a new regulation. Eventually, like the Medicare Part D program that replaces the cards, private insurers and pharmaceutical companies offer a confusing array of plans for the 40 million seniors with Medicare but no drug coverage.

2001

Baycol withdrawal

Bayer withdraws its statin after cases of rhabdomyolysis, a rare muscle disorder, is reported among patients taking higher doses.



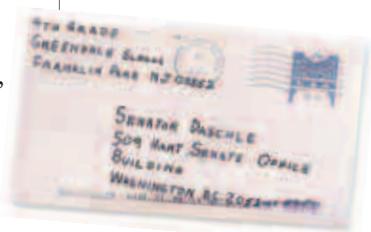
Robert Tools receives first implantable artificial heart

On June 20, doctors at Jewish Hospital in Louisville implant a two-pound plastic and titanium heart in the chest of a 58-year-old diabetic man diagnosed with end-stage heart disease. He lives another 151 days.

9/11 terrorist attacks

Anthrax letters

Anthrax spores arrive via US mail at the offices of NBC, the *New York Post*, and two US Senators. No suspects are arrested; 22 people fall ill.



2002

Women's Health Initiative halts HRT study

A 10-million-patient study of hormone replacement therapy is stopped when data show slight increases in risk of breast cancer, stroke, and heart disease. HRT instantly becomes controversial.

PhRMA Code

The trade association's new guidelines allow drug reps to offer items only for the benefit of a doctor's patients or practice, provided that the gifts are worth \$100 or less.

HHS issues privacy rules

The rules fulfill requirements of the 1996 Health Insurance Portability and Accountability Act. They put strict limits on how patient information—not just medical records, but data such as name, address, birth date, and social security number—can be shared.

"The real payoff will come only if Congress can assemble a drug plan that provides a permanent, equitably determined benefit while controlling costs."
The New York Times, July 2001

American Home Products changes name to Wyeth

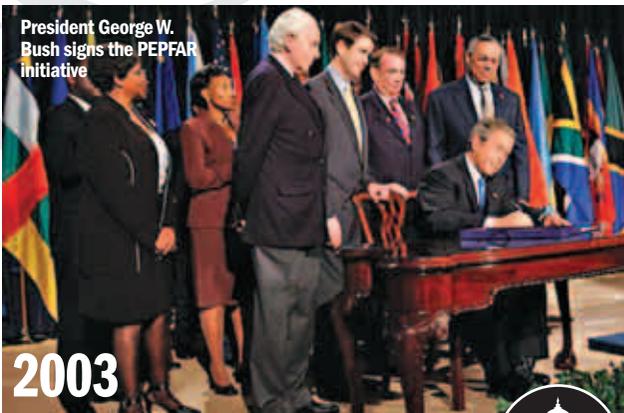
The name change helps erase memories of the fen-phen debacle after the lawsuits reach a settlement in January.

Claritin goes OTC

Schering Plough's prescription allergy medication goes over-the-counter at about \$1 a pill after WellPoint petitions FDA for a change in status. For insured patients, who formerly paid a small co-pay, it's a price hike.

FDA Office of Combination Products

FDA establishes the office to better manage applications from a growing number of medical products that combine drugs, biologics, and/or medical devices.



2003

President George W. Bush signs the PEPFAR initiative

PHOTOGRAPH BY TINA HAGER

AIDS

PEPFAR launched



[January 28, 2003] In his State of the Union address, President Bush announces the President's Emergency Plan for AIDS Relief (PEPFAR), a five-year, \$15-billion initiative to fight HIV/AIDS in Africa. By January of 2004, Congress earmarks \$2.4 billion for year one. PEPFAR increases the volume of branded ARV drugs going overseas, which helps create a regulatory pathway for approving generic AIDS drugs that are used in government programs for the 15 countries targeted by the initiative.

2003

ACCME's new guidelines

The accrediting body for CME sets rules for commercial support.

For the first time, biotech surpasses Big Pharma in NMEs



Mad cow disease in the US

Bovine spongiform encephalitis appears in Washington State, sparking fears of contamination of the food supply.

Pfizer and Pharmacia merge

The world's largest drug company purchases Pharmacia for \$67 billion. Pfizer's new estimated market share is 11 percent.

2.8 billion
Box procedure

REGULATORY AFFAIRS

OIG targets drugmakers with new guidance

[April 28, 2003] The Office of the Inspector General releases its Compliance Program Guidance (CPG) for pharmaceutical companies, targeting gifts, financial incentives, and other drug marketing activities.

The politically charged code lays groundwork for laws

later enacted in states

such as California.

Although the measure is voluntary, some

companies report a

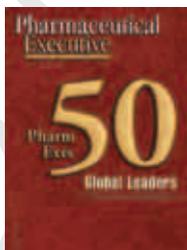
chilling effect on their interactions with doctors.

The CPG follows a

similar marketing code

released by PhRMA in 2002.

"Labeling and advertising can convey... benefits, side effects, and the like, but if doctors aren't committed to the idea of analyzing risk, it's unlikely that patients will make good decisions."
Pharm Exec, May 2003



Pharm Exec May 2003



First gene therapy is approved in China

LAWSUITS

Pfizer pleads guilty, pays \$430 million

[May 13, 2004] Pfizer

pleads guilty to two felonies involving the marketing of its epilepsy drug Neurontin (gabapentin).

According to a whistleblower suit filed in 1996, sales reps from Warner-Lambert (acquired by Pfizer in 2000) promoted

Neurontin for unapproved uses, such as pain relief. The drug

giant is ordered to pay \$430 million in

criminal and civil

penalties, and signs

a corporate integrity

agreement giving the

government oversight

of its marketing and

employee training

practices.

Medicare drug cards

Criticism of the drug discount cards—a temporary measure before the start of Part D—is a harbinger of things to come, especially complaints of confusion.

2004

Senate passes Medicare Rx benefit

The Medicare Modernization Act provides the first prescription drug benefit to Medicare beneficiaries in the most significant overhaul of Medicare since 1965.

APPROVED: Avastin

Genentech's antiangiogenesis product is the first to treat tumors by "starving" them of their blood supply.

Critical Path report

FDA outlines a goal to modernize the scientific process of bringing drugs to market. The new initiative eventually will cover risk communication, clinical-trial data collection, and adverse-events reporting.

HIV Fuzeon approval

[March 13, 2003] Roche's AIDS treatment receives accelerated approval from FDA as the first in a class of drugs known as fusion inhibitors. Working in combination with older therapies, the drug is hailed for its ability to prevent the fusion of viral and cellular membranes—protecting the immune system from infection, rather than treating the disease after the fact. Fuzeon also provides new hope to patients who have developed a tolerance to their current treatments. Although criticized for its high price tag, the drug is also credited for helping to transform a sure death sentence into a chronic condition.

IMPORTATION

States rebel against industry on importation

[August 26, 2004] In a suit filed

by 19 California pharmacies, 15 major drug companies are accused of inflating US prices while prohibiting pharmacies from buying their drugs outside the country for less. The action in California is one of many taken by states against industry and FDA for their refusal to allow drug importation from Canada and other countries, where drugs are cheaper. The state revolt against federal policies is seen as a sea change in how the two bodies relate on health matters.



The Project BioShield Act

The law provides \$5.6 billion to stockpile vaccines and authorizes the government to expedite R&D on anti-terror medicine.

Lipitor hits \$10 billion

Pfizer's cholesterol-lowering drug finishes 2004 with \$10.8 billion in sales, making it the first drug ever to surpass \$10 billion in annual sales.

Flu vaccine shortage

Manufacturing problems at a Chiron factory cuts drastically the number of available flu shots in the United States, leaving to Aventis Pasteur the

task of producing the nation's vaccine supply. Roche and MedImmune are called upon to increase production of Tamiflu and FluMist, respectively. Federal officials urge healthy people to defer shots so they'll be available for those at most risk.

Vioxx withdrawal

Merck announces the voluntary worldwide withdrawal of its COX-2 painkiller Vioxx (rofecoxib). Less than one year later, a jury rules against Merck on all major counts in the first Vioxx-related trial, awarding the plaintiff \$253.4 million.

Journals say register trials, or forget about publishing

The International Committee of Medical Journal Editors announces that member journals (including some of the most prestigious) will no longer publish studies unless sponsors first register all trials related to the product in a clinical trials registry.

"Honest reporting begins with revealing the existence of all clinical studies, even those that reflect unfavorably on a research sponsor's product." ICJME's announcement

2005



New heads at PhRMA and BIO



Longtime colleagues Billy Tausin and James Greenwood retire from the House of Representatives and take the helms of the pharmaceutical industry's most influential advocacy organizations.



Pharm Exec March 2005

Pargluva misses the mark

A much anticipated diabetes drug gets an approvable (not approval) letter from FDA. As a result, Bristol-Myers Squibb ceases development. The incident is seen by many as a sign that safety concerns are making it harder to get needed drugs to market.



Drug Safety Board

FDA establishes its Drug Safety Board and reorganizes its drug safety offices. But agency critics continue to call for more stringent review of safety concerns.



PhRMA's Guiding Principles

In August, PhRMA releases a voluntary set of Guiding Principles on direct-to-consumer advertising.

Launch of Part D

Referred to within industry as "D-Day," November 15 is the first day of enrollment for Medicare's new prescription drug plan.

2006

APPROVED: Exubera

The January approval brought to market the first inhaled form of insulin, and the first insulin option that does not need to be administered by injection. The drug, manufactured by Pfizer, is considered a major step forward for the nearly 21 million Americans who suffer from diabetes.

APPROVED: Omnitrope

Sandoz's human growth hormone product is widely perceived as the first generic biologic. Not so, says FDA, which calls it a "follow-on protein," similar to several previous drugs.

Zocor patent expires

At \$4.4 billion, Merck's cholesterol-lowering drug is the biggest seller to go generic—and just one of a series of blockbuster patent expirations to take place this year.

APPROVED: Gardisil

Merck's product, the first-ever vaccine designed to prevent a cancer, works by building immunity against the sexually transmitted human papillomavirus (HPV). Because the vaccine needs to be administered before the virus is present, public health groups are pushing for mandatory vaccinations for young girls, causing an uproar among some social conservatives.

J&J tops the charts

With its June purchase of Pfizer's consumer health business, Johnson & Johnson becomes the largest pharmaceutical company. (Pfizer remains the largest on the basis of prescription drug sales.)