

The Cost to Society of Pharmaceutical Mass Tort Litigation

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Bridging the gap between academia and policymakers



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Distinguished colleagues and friends, it is an honor for me to address you today. I want to thank especially John Adams, Denis Galligan, and Chris Hodges and colleagues, for their outstanding work with the Foundation for Law, Justice and Society, Wolfson College, and the Centre for Socio-Legal Studies, in advancing an understanding of the role that law plays in society. I will address the cost to society of pharmaceutical mass tort litigation, on the eve of the 15th anniversary of the voluntary withdrawal of Vioxx[®] (rofecoxib) from markets worldwide.

Merck & Co., Inc. of the United States, with scientists in its labs, in academia, in government, and collaborators around the world, brought us streptomycin for tuberculosis; cortisone for rheumatoid arthritis; indomethacin for the relief of pain and inflammation; vaccines for measles, mumps, rubella, and other diseases; carbidopa levodopa for Parkinson's disease; antiretrovirals for HIV; a series of new antibiotics; and more breakthrough treatments for hypertension, cholesterol lowering (lovastatin and simvastatin), and glaucoma.² It commercialized losartan for hypertension; alendronate for osteoporosis, a recombinant HPV vaccine for cervical cancer; and sitagliptin for type 2 diabetes.³ Today, Merck's anti-PD-1 therapy, pembrolizumab, first in a new class of immunotherapy treatments for cancer, is studied in more than 1,000 clinical trials across more than 30 cancer types.⁴

This is the company that returned exclusive patent rights for streptomycin, acquired under a collaboration agreement, to Rutgers University for non-exclusive licensing to fight tuberculosis and other diseases in the 1940's.⁵ It gave us The Merck Index, The Merck Manual, The Merck Gene Index; and The Merck Genome Research Institute.⁶ In 1987, Merck committed to donate ivermectin for as long as needed to eliminate river blindness, now eliminated in at least four countries in Latin America, with promise continuing for others in Africa.⁷ Merck's Access pricing to more than 60 low income countries helps antiretrovirals reach as many HIV/AIDS patients in those countries as possible.⁸ The USD 500 million Merck for Mothers initiative aims to end preventable deaths from complications of pregnancy and childbirth.⁹

Last week we observed the 75th anniversary of D-Day, June 6, 1944. Before that battle, Merck and other US pharmaceutical companies rapidly scaled up pilot plant processes in development for the commercial large-scale production of penicillin, and rushed billions of doses of penicillin to the battlefields of World War II.¹⁰ You will know that penicillin was invented in the UK by Dr. Fleming and its therapeutic potential initially was recognized at the Sir William Dunn School of Pathology here at the University of Oxford.¹¹ Drs. Florey and Heatley of that school traveled to the US with the support of the Rockefeller Foundation to interest US companies, including Merck (at which Heatley spent six months in 1942) in developing formulations and manufacturing processes for penicillin, and in large scale production.¹² Dr. Florey observed after the war, "too high a tribute cannot be paid to the enterprise and energy with which the American manufacturing firms tackled the large-scale production of the drug. Had it not been for their efforts there would certainly not have been sufficient penicillin by D-Day in Normandy in 1944 to treat all severe casualties, both British and American."¹³

Had it not been for these and other successful collaborations among scientists, philanthropists, academia, industry, and governments, some of us might not be here today.

That brings us to rofecoxib, a selective COX-2 inhibitor from Merck & Co., Inc.

No drug for the relief of pain and inflammation has the safety profile of placebo. Long-term use of traditional non-steroidal anti-inflammatory pain relievers (t-NSAIDs), such as diclofenac, ibuprofen, and naproxen, is limited by serious gastrointestinal side effects including bleeds that can be fatal.¹⁴ Those t-NSAIDs inhibit both COX-1 and COX-2. COX-1 mediates the synthesis of prostaglandins responsible for protecting the stomach lining. COX-2 mediates the synthesis of prostaglandins responsible for pain and inflammation. Scientists reasoned that selectively inhibiting COX-2, sparing COX-1, would relieve pain and inflammation with reduced gastrointestinal toxicity compared to t-NSAIDs.¹⁵ They were right.

After years of research and development including clinical trials in more than 10,000 patients, Merck's selective COX-2 inhibitor, Vioxx, was approved by the FDA in May 1999 for certain indications including relief of osteoarthritis, and by regulatory authorities worldwide. By the end of 1999, Vioxx was the fastest growing prescription medication for arthritis in the United States and had been launched in 47 other countries.¹⁶

In March 2000, an outcomes research trial, VIGOR, reported the gastrointestinal benefit of rofecoxib over naproxen in rheumatoid arthritis patients.¹⁷ VIGOR, however, reported more thrombotic cardiovascular events in patients on rofecoxib than in patients on naproxen.¹⁸ Merck provided these reports to regulatory authorities, scientists, and clinicians, and issued a press release.¹⁹ Scientists analysing the available data, including clinical trial data, concluded that "the weight of the evidence was most consistent with a cardioprotective benefit of naproxen and no prothrombotic effect of rofecoxib;"²⁰ the data continued to support their interpretation that "rofecoxib did not increase the risk of cardiovascular thrombotic events in comparison either to placebo or non-naproxen NSAIDs."²¹ There was robust public scientific debate over whether the protective effect of naproxen was the best explanation for the findings. Meanwhile, regulators approved updated prescribing information that included the VIGOR study results.²²

Then, in late September 2004, interim results of the Merck-sponsored placebo-controlled APPROVe study²³ became available: the risk of thrombotic events in patients taking rofecoxib 25mg began to diverge from placebo beginning after 18 months of daily therapy, and over time the difference became significant.²⁴

Whether a similar increased risk would be seen with non-naproxen t-NSAIDs, such as diclofenac and ibuprofen, was "an as yet unanswered question."²⁵ We will come back to that.

Although the relative risk seen in APPROVe did not appear elevated during the first 18 months of use, and Vioxx could have remained on the market with appropriate prescribing information, on September 30, 2004, Merck voluntarily withdrew Vioxx from markets worldwide because it believed withdrawal would "best serve the interests of patients" and was "the responsible course to take," given the questions raised by the data and the availability of alternative therapies without similar placebo-controlled data.²⁶

At that point, Vioxx was available in more than 80 countries with worldwide sales in 2003 of USD 2.5 billion, about 11% of Merck's \$22.5 billion in sales for that year.²⁷ In the US alone, an estimated 105 million prescriptions had been written and about 20 million patients had taken Vioxx.²⁸ Outside the US, comprising some 80 or more other countries, Vioxx was the best selling arthritis and pain medicine,²⁹ taken by millions more patients.

Shares in Merck & Co., Inc. dropped at the opening bell on the NY Stock Exchange and were down USD 12.07, or 26.78 percent on the day; the company's capitalization consequently was reduced some USD 25 billion on September 30, 2004.³⁰ The US Securities and Exchange Commission, the US Department of Justice, and US Congressional Committees, among others, launched investigations that would last for years.³¹ Lawyers filed court actions in the US, Australia, Canada, European countries, and other countries around the world.³² Physicians prescribed alternative treatments for disappointed patients.³³ Journalists, critics, partisans, and politicians launched narratives and campaigns. Any short sellers were delighted. Scientists, though, as we will see, would illuminate the entire field of NSAIDs over fifteen years.³⁴

As Merck prepared for a first trial by jury in the United States, US lawyers had filed at least 850 court cases in which 2,425 individuals alleged use of the drug caused personal injuries, 90 putative class actions alleging different types of product liability, and 32 shareholder actions.³⁵ The company already had reserved USD 675 million solely for its future legal defense costs.³⁶

On August 19, 2005, a lay jury in Angleton, Texas³⁷ returned a verdict for one claimant in a case about an arrhythmia, which is not a thrombotic event, in the amount of USD 253.4 million.

"Respect us, that's the message," said Derrick Chizer, a juror. "Respect us."³⁸

The evidence did not support that verdict, and Merck announced its appeal would be "about fundamental rights to a fair trial."³⁹ The FT reported:

"another shocker, causing the shares to tumble nearly 8 percent."

"might cause some to upgrade their assessment of Merck's potential for litigation costs. ... AG Edwards, for instance, had reckoned total litigation costs could range between \$10bn and \$20bn over many years. ... Merck can afford what the US legal system produces, especially if the thousands of cases it faces drag on for many years."⁴⁰

Although that unsupported verdict would be overturned nearly three years later for lack of evidence, lawyers promptly filed thousands more court actions, activated hundreds of others, advertised for claimants, and discussed litigation strategies with journalists:

*Vioxx Britons queue up to sue*⁴¹

ROME — Outraged patients around the world ... are lining up to sue..."

"Lawyers are collecting data on thousands of cases, trying to assess whether they should try to sue Merck in the United States, where rewards are likely to be higher, or in their home countries, where there are likely to be fewer legal hurdles. ..."

“lawyers in Italy, France, Britain and Australia are working on cases. In each of those countries, the number of people who took the drug was in the hundreds of thousands.”⁴²

"Patients taking prescription

PAIN KILLERS

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By the end of 2005, US lawyers had filed nearly 10,000 court cases in which more than 19,000 individuals alleged use of the drug caused personal injuries, and 190 class actions alleging different types of product liability. In thirteen of the putative class actions, claimants from other countries sought to represent hundreds of thousands of Vioxx users “throughout the world,” all users “residing in Europe,” or all users residing in each of 11 countries on four continents. Hundreds more from other countries filed individual actions throughout the United States. Others, comparatively more reasonably, filed or activated more than 70 class or representative actions in home countries on four continents and hundreds of individual actions in more than 20 countries.⁴⁴ One year later, US lawyers had filed at least 27,400 court cases in which 46,100 individuals alleged use of the drug caused personal injuries, and 264 class actions alleging different types of product liability. Numbers also continued to rise outside the US.

By November 2007, juries in the United States had decided for Merck 12 times and for plaintiffs five times; two of the five plaintiffs’ verdicts later would be overturned for insufficient evidence and judgment entered for Merck.⁴⁵ About 50,000 cases remained to be tried in the US, however, and Merck already had spent USD 1.2 billion of USD 1.9 billion reserved solely for its own defense costs; there is no cost-shifting in the US for these cases. For pragmatic business reasons, and without admitting liability or causation, Merck agreed to resolve the US heart attack and ischemic stroke personal injury claims for USD 4.85 billion, a deal said to be “favourable” to the company and “clearly at the low end of general expectations.”⁴⁶ On the news Merck’s shares rose 5% in New York lunchtime trading.⁴⁷ US claimant lawyers would take home some 32% of USD 4.85 billion, i.e. more than USD 1.55 billion, plus reasonable litigation expenses.⁴⁸ Medicare, Medicaid, other government insurers or providers, and private insurers would take their shares of the remaining USD 3.3 billion under liens.⁴⁹ Qualifying claimants would realize reduced amounts. The FT wrote:

“The drug may well be remembered best in years to come for its effect on the entire pharmaceuticals industry – not just on Merck. Two-long term effects of Vioxx are clear: a new and more cautious handling of drug risks by US regulators, drugmakers, doctors and patients; and a more aggressive defence posture by drugs companies facing mass litigation. Vioxx became one of the biggest pharmaceuticals controversies ever, particularly in the US, where there were about 20m users.”⁵⁰

The US agreement, however, applied only to certain US claims⁵¹ and US federal and state courts dismissed the actions filed by persons domiciled outside the US, on the basis of *forum non conveniens*.⁵² Many of those claimants filed actions in their home countries; those claimants and others with actions already underway in their home countries were energized by media reports of the US settlement, hoping for quick, large, comparable, settlements in their home countries.

In Australia, *The Age* reported:

“THOUSANDS of Australians who suffered heart attacks and strokes after taking the painkiller Vioxx are expected to join a class action against its manufacturer following a multibillion dollar settlement in the United States. ...

“About 1000 claimants have joined a Federal Court class action ... [Their lawyer] yesterday predicted thousands more would join the class action and that Merck would feel pressure to join mediation talks. ‘We believe this will now lead to discussions and resolution of the international claims by Vioxx victims.’”⁵³

Merck did not “feel pressure to join mediation talks,” nor would its litigation strategy be influenced by media releases and stories. It continued to prepare and defend the international cases based on the evidence, in court. In March 2010, following a 43-day trial during 2009 of a class action against Merck and its subsidiary MSD Australia (MSDA), a Justice of the Federal Court of Australia published his 459-page Reasons for Judgment, in which he dismissed, on a class wide basis, all claims against Merck, finding, after extensive review and analysis:

“Merck had done everything that might reasonably be expected of it in the discharge of its duty of care.”⁵⁴

The Justice also dismissed, on a class wide basis, all statutory product defect claims, finding in the company’s favor on its state of art defense and, for want of causation evidence, all claims involving stroke, unstable angina, transient ischemic attack, and peripheral vascular disease. He then found against MSDA in favor of the individual applicant, on his personal claim only, under two sections of the Australian Trade Practices Act.⁵⁵

In the aftermath, the claimants’ lawyer focused in the media on the award to the applicant on his personal claim, but not on the significance of the class-wide rulings in the company’s favor.

“Lawyers representing Mr Peterson said yesterday ... *the damages bill for Merck [in Australia] could run up to \$300 million*

....

Peter Gordon, chairman of law firm Slater & Gordon, ... said it was time Merck afforded their Australian "victims" the same justice as American consumers.

"Enough is enough. Time has come for Merck to do justice to these people," he said. "(Merck should) accept this judgment and the important findings it makes about the dangers of Vioxx and compensate these people who took their drug in good faith, and let them get on with the rest of their lives."⁵⁶

The applicant, the group members, and MSDA appealed. In October 2011, a Full Court of the Federal Court of Australia published Reasons for Judgment, granted MSDA's appeal and dismissed the applicant's personal claims, rejected the applicant's and the group's appeals, affirmed the class-wide rulings for MSDA, and awarded full costs to MSDA.⁵⁷ In May 2012, the High Court refused the claimants' applications for special leave to appeal the Full Court's orders and awarded costs to MSD Australia.⁵⁸ The claimants' law firm, listed on the Australian Stock Exchange, announced an AUD 10.5 million loss on its investment in the case.⁵⁹

About three years later, the Federal Court of Australia approved an agreement resolving and dismissing all claims of the remaining 1,660 registered group members for a total payment by MSDA of AUD 542,000 to be distributed among qualifying group members.⁶⁰

These Australian judgments in Merck's favor would influence outcomes in other countries, given the Federal Court's thorough and well-reasoned dismissal of the claims sounding in negligence and of the claims made under a statute modeled on the European Product Liability Directive.⁶¹

When Merck withdrew Vioxx based on an increased relative risk seen in APPROVe in "the interests of patients" and "as the responsible course to take," the company's stock dropped nearly 27%; it took a charge of more than USD 726 million to effect the withdrawal; physicians prescribed alternative NSAIDs that did not have rofecoxib's GI safety data; governments investigated the company; and lawyers launched more than 50,000 claims and class actions in the US and hundreds of jurisdictions across six continents. Although Merck won most of the cases heard in the United States and prevailed in jurisdictions around the world, the company spent more than USD 2 billion on its own legal defense and nearly USD 7 billion more for the resolution of Vioxx litigation and investigations through the end of 2016.⁶²

When the interim results of APPROVe were received, "no other non-aspirin NSAIDs or selective COX-2 inhibitors had been studied in this large a patient group for this duration,"⁶³ and no one knew whether a similar increased relative risk would be seen with non-naproxen t-NSAIDs, such as diclofenac and ibuprofen.⁶⁴ That question would be addressed here in Oxford: "the whole field of NSAIDs has been illuminated during the past 15 years."⁶⁵

In 2006, Drs Kearney, Baigent, and colleagues published a meta-analysis of randomized trials showing that "selective COX-2 inhibitors are associated with a moderate increase in the risk of vascular events, as are high dose regimens of ibuprofen and diclofenac, but that high dose naproxen is not associated with such an excess."⁶⁶

In 2013, the CNT Collaboration published meta-analyses of individual participant data from randomised trials, showing, with regard to vascular risks of NSAIDs, "clearly that the vascular risks of diclofenac, and possibly ibuprofen, are similar to coxibs, but that naproxen is not associated with an increased risk of major vascular risks."⁶⁷

In 2015, after reviewing the CNT Collaboration publication, based on a comprehensive review, and with recommendations from its advisory committees, the FDA issued a Drug Safety Communication "strengthening an existing warning that NSAIDs increase the chance of a heart attack or stroke" and "requiring updates to the drug labels of all prescription NSAIDs."⁶⁸

It now appears that all of the non-aspirin NSAIDs, with the possible exception of naproxen, have a similar cardiovascular safety profile to Vioxx. Merck scientists achieved what they aimed to create and develop in the 1990s: a new anti-inflammatory pain reliever with a similar safety profile to traditional NSAIDs but with an improved GI safety profile.

Merck spent approximately USD 10 billion in connection with withdrawing Vioxx and defending and resolving litigation and investigations.⁶⁹ From drug discovery through FDA approval, developing a new medication takes ten to 15 years on average, and costs an average of USD 2.6 billion.⁷⁰ Let us reflect on the eve of the 15th anniversary of the withdrawal that about USD 10 billion spent to defend and resolve litigation was not available to fund the discovery and development of up to four or more new breakthrough life-saving, life-sustaining medications.

“We try to remember that medicine is for the patient. We try never to forget that medicine is for the people. It is not only for the profit. The profits follow. And if we have remembered that, they have never failed to appear.” - George W. Merck.⁷¹ → Merck & Co., Inc. today is one of the most valuable companies included in the Dow Jones Industrial Average.

Thank you for the opportunity to speak here today. I look forward to your questions and to continuing debates and discussions on these topics.

¹ Special Counsel, Hughes Hubbard & Reed LLP. Previously Executive Director & Senior Counsel, Merck & Co., Inc. Views expressed are my own and do not necessarily reflect the views of Hughes Hubbard & Reed LLP or any of its clients, Merck & Co., Inc., or of any other person, entity, or institution. I dedicate this lecture to Merck & Co., Inc. scientists past and present.

² Values & Visions, A Merck Century, Merck & Co., Inc., Jeffrey L. Sturchio (ed.) 1991 (“Values & Visions”), pp. 27, 34-35, 68, 71-72, 78, 80, 83, 85-86, 90-91, 93, 95-96, 98; www.merck.com/about/our-history/home.html. Dr. Salman Waxman of Rutgers University, with whom Merck collaborated, received the 1952 Nobel Prize in Physiology or Medicine for his discovery of streptomycin. Values & Visions, pp. 74-76; 70. By the early 1950s, “the company had contributed to two major projects that had produced Nobel Prizes – to Kendall and ... Hench for cortisone and to Waxman for streptomycin.” Values & Visions, p. 91. For an interesting review of indomethacin, an early non-steroidal anti-inflammatory drug (NSAID), see FD Hart and PL Boardman, *Indomethacin: A New Non-Steroid Anti-Inflammatory Agent*, *BMJ* 1963; pp. 965-970.

³ Values & Visions, p. 32 (losartan partnership with DuPont); <https://www.merck.com/about/our-history/home.html>.

⁴ Merck & Co., Inc. Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2019, May 8, 2019.

⁵ Values & Visions, pp. 73-76. With the production and distribution of streptomycin, “tuberculosis, the ‘white plague,’ was on its path to extinction ...” Values & Visions, p. 76.

⁶ Values & Visions, p. 33; www.merck.com/about/our-history/home.html.

⁷ Values & Visions, pp. 35-36, 89 and 91 (Dr. William Campbell, to whom a 2015 Nobel Prize in Physiology or Medicine (1/4) would be awarded, describes the multi-team effort leading to ivermectin); Values & Visions, p.154 (Dr. Mohammed Aziz, “one of the heroes of the company,” championed the seven-year worldwide clinical program for ivermectin which succeeded in 1987; in 1987, the Merck & Co., Inc. Board of Directors recognized

Dr. Aziz with its Scientific Award; he died that year from cancer at 58); <https://www.merck.com/about/our-history/home.html>.

⁸ Merck & Co., Inc. offers its lowest access price for antiretrovirals to countries based on a combination of highest disease burden and lower country income (gross national income per capita), as defined by the World Bank. See Corporate Responsibility Report 2017/2018 at <https://www.msdrresponsibility.com/access-to-health/infectious-diseases/hiv aids/> and <http://s3.amazonaws.com/msd18-assets/wp-content/uploads/2018/09/11153102/Isentress-Access-Countries-20181.pdf> (visited May 15, 2019). Merck also established a low cost supply chain for an antiretroviral in low-income and sub-Saharan countries, reducing its price for raltegravir to \$1.85 per day for these countries; and granted nonexclusive licenses to several generic companies for the manufacture and commercialization of a formulation of raltegravir in low income and sub-Saharan countries. Corporate Responsibility Report 2017/2018, <https://www.msdrresponsibility.com/access-to-health/infectious-diseases/hiv aids/>

⁹ See, e.g., Merck & Co., Inc. Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2019, May 8, 2019; www.merckformothers.com.

¹⁰ Values & Visions, pp.76-77; S Aldridge, J Parascandola, and JL Sturchio, *The discovery and development of penicillin 1928-1945*, a booklet commemorating the designation of the development of penicillin as an International Historic Chemical Landmark, The Alexander Fleming Laboratory Museum, London, UK, the Royal Society of Chemistry and the American Chemical Society November 19, 1999 (“Penicillin Booklet”); “The large-scale development of penicillin was undertaken in the United States of America during the 1939-1945 World War, led by scientists and engineers at the Northern Regional Research Laboratory of the US Department of Agriculture, Abbott Laboratories, Lederle Laboratories, Merck & Co., Inc., Chas. Pfizer & Co. Inc., and E.R. Squibb & Sons.” Penicillin Booklet, p.10, Commemorative Plaque Inscription; www.merck.com/about/our-history/home.html. Production increased from 21 billion units in 1943 to 1,663 billion units in 1944, to more than 6.8 trillion units in 1945. Penicillin Booklet, p.8.

¹¹ Penicillin Booklet, pp.3-4. Alexander Fleming discovered penicillin in 1928 at St. Mary’s Hospital in London. Howard Florey at the University of Oxford, working with Ernst Chain, Norman Heatley, and Edward Abraham, “successfully took penicillin from the laboratory to the clinic as a medical treatment in 1941.” Penicillin Booklet, p.10, Commemorative Plaque Inscription. Drs. Fleming, Florey, and Chain were awarded the 1945 Nobel Prize in Physiology or Medicine for their “discovery of penicillin and its curative effect in various infectious diseases.” Penicillin Booklet, p.8; The Nobel Prize in Physiology or Medicine 1945, nobelprize.org.

¹² Penicillin Booklet, pp.4-6.

¹³ Penicillin Booklet, p.9.

¹⁴ In the US alone, “[a]n estimated 15,000 Americans die each year from gastrointestinal bleeding associated with NSAID use.” Remarks of Raymond V. Gilmartin, Chairman, President, and Chief Executive Officer of Merck & Co., Inc., Ex. 99.1 to Merck & Co., Inc. Report on Form 8-K, December 14, 2004.

¹⁵ FDA Advisory Committee Background Information, January 2005 (“2005 Background”), p.42.

¹⁶ Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 1999, filed March 22, 2000.

¹⁷ 2005 Background, p.30.

¹⁸ 2005 Background, p.30.

¹⁹ 2005 Background, p.78.

²⁰ 2005 Background, p.32.

²¹ 2005 Background, p.32.

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- ²² See, for the United States, 2005 Background, p.106.
- ²³ APPROVe was a large placebo controlled outcomes study evaluating the effect of rofecoxib on recurrence of colon polyps in patients with a history of colorectal adenoma. The study began screening patients in 1999 and enrolling patients in February 2000. 2005 Background, p.24.
- ²⁴ 2005 Background, pp.34 and 133-148.
- ²⁵ 2005 Background, p.30. As of late September 2004, “no other non-aspirin NSAIDs or selective COX-2 inhibitors had been studied in this large a patient group for this duration.” 2005 Background, p.34.
- ²⁶ Merck Press Release issued September 30, 2004. The term “relative risk” has been defined as “the cumulative risk in the treatment group (e.g., number of events per the number of individuals in this group) divided by the cumulative risk in the control group.” Memorandum, JK Jenkins and PJ Seligman through S Galson to NDA files 20-998, 21-156, 21-341, 21-042, *Analysis and recommendations for Agency action regarding non-steroidal anti-inflammatory drugs and cardiovascular risk*, April 6, 2005.
- ²⁷ Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005.
- ²⁸ Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005.
- ²⁹ Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005.
- ³⁰ *Merck Pulls Vioxx from Market, and Stock Plunges*, Terence Neilan, New York Times, Sept. 30, 2004. See Merck & Co., Inc. Press Release issued October 21, 2004 (3Q 2004 Earnings Per Share of 60 cents included negative impact of 25 cents per share associated with voluntary withdrawal of Vioxx: “The voluntary withdrawal of VIOXX, with sales of \$2.5 billion last year, represents a significant financial loss for us, but clearly was the right course of action.”).
- ³¹ Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005, and Annual Reports on Form 10-K for the years 2005 through 2016. See, for example, *The Lessons of Vioxx – Drug Safety and Sales*, HA Waxman, N Engl J Med 352:25, June 23, 2005 (“The testimony we heard [in hearings before the Government Reform Committee of the U.S. House of Representatives] indicated that Merck’s marketing practices may be less aggressive and more ethical than those of many of its competitors. What is needed is a broad assessment of the ways in which all new drugs are promoted and prescribed in the United States.”); *How Vioxx is changing US drug regulation*, Todd Zwillich, The Lancet, Vol. 366, Issue 9499, p1763-1764; *Guest Editorial, The Institute of Medicine Report on the FDA: Where is the Science?*, Tomas Philipson, Anupam B. Jena, Eric Sun, Health Econ. 16:219-221 (2007).
- ³² Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005.
- ³³ For example, celecoxib, diclofenac, ibuprofen, or naproxen, sometimes prescribed with a proton-pump inhibitor. Interestingly, a study reported “prescription of opioids increased from 31% to 40% from 2003 to 2009,” and “most of the increase was observed between 2003 and 2006, when overall opioid usage showed a relative increase of 24%.” *Trends in prescription of Opioids from 2003-2009 in Persons with Knee Arthritis*, Arthritis Care Res. (Hoboken), 2014 Oct;66: 1489-1495.
- ³⁴ *Nonsteroidal Anti-Inflammatory Drugs and the Heart*, Carlo Patrono and Colin Baigent, Circulation. 2014; 129: 907-916, at 907 (“the whole field of NSAIDs has been illuminated during the past 15 years.”).
- ³⁵ Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005.
- ³⁶ As of February 2005. Merck & Co., Inc. Annual Report on Form 10-K for the year ending December 31, 2004, filed March 11, 2005.

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- ³⁷ See www.angleton.tx.us, the official website of Angleton, Texas. According to the US Census Bureau, as of April 1, 2010, 18,862 people lived in the town. The estimated per capita income in the past 12 months (in 2017 dollars), 2013-2017, was USD 27,689, and an estimated 12% of the population was living in poverty. See <https://www.census.gov/quickfacts/fact/table/angletoncitytexas/PST045218>.
- ³⁸ *Jury Calls Merck Liable in Death of Man on Vioxx*, Alex Berenson, The New York Times, Aug. 20, 2005.
- ³⁹ Plaintiff's lawyer waited until June 16, 2006, nearly one year after the USD 253 million jury verdict, to move for entry of a judgment that lawyers knew would be greatly reduced by operation of Texas state law. On June 23, 2006, the trial judge reduced the exemplary damages portion of the USD 253 million award as required by the Texas Code, and entered judgment against Merck in the amount of USD 26.1 million. Merck's appeal from that judgment would not be decided until nearly two years later (nearly three years after the verdict) in May 2008: the Court of Appeals of Texas, an intermediate appellate court, found the evidence legally insufficient to support a jury finding of causation, reversed the judgment in its entirety, and gave judgment for Merck. *Merck & Co., Inc. v. Ernst*, 296 S.W.3d 81 (Ct. App. Texas 2009). On 16 December 2011, the Texas Supreme Court, the state's highest court, declined to review the decision of the Texas Court of Appeals. On April 12, 2012, the Supreme Court of the United States denied Ernst's petition for a writ of certiorari to review the Texas judgment. *Ernst v. Merck & Co., Inc.*, No. 11-1144, petition for writ of certiorari to the Court of Appeals of Texas, Fourteenth District, denied.
- ⁴⁰ *Lex: Merck*, Financial Times, Aug. 19, 2005.
- ⁴¹ *Vioxx Britons queue up to sue*, Amelia Hill, The Guardian, Aug. 21, 2005.
- ⁴² *Claimants worldwide line up to sue Merck*, Elisabeth Rosenthal, The New York Times, Aug. 26, 2005 (emphasis added).
- ⁴³ Advertisement, Scotland's Daily Record, 20 Sept. 2005 and 27 Sept. 2005 (emphasis added).
- ⁴⁴ In Australia: *Class action filed over arthritis drug Vioxx*, Catherine Best, The Sydney Morning Herald, Dec. 15, 2005 ("Slater & Gordon launched a class action in the Supreme Court of Victoria on 15 December 2005. On behalf of more than 400 victims, including relatives of up to 50 people believed to have died while using the anti-arthritis drug, Slater & Gordon are seeking damages from Merck."); in Canada: plaintiffs' lawyers filed carriage motions and would battle over control of some 40 class actions in ten provinces, see, for example, *Setterington v. Merck Frosst Canada Ltd.*, 2006 CanLII 2623 (ON SC), [2006] O.J. No. 376, 145 A.C.W.S.(3d) 566 (S.C.J.) (Winkler, J.) (granting plaintiffs' 19-law firm consortium carriage of Ontario multijurisdictional class proceedings; staying parallel action filed in Ontario by Saskatchewan counsel).
- ⁴⁵ By November 2007, lay juries in the United States had decided for Merck 12 times and for plaintiff five times. One Merck verdict was set aside and not retried. Another Merck verdict was set aside and retried, leading to one of the five plaintiff verdicts. There were two unresolved mistrials. Merck filed appeals or sought review in each of the five cases with plaintiff's verdicts. Two of the five plaintiff verdicts, including the Angleton, Texas verdict, later were reversed on appeal for insufficient evidence, and judgment entered for Merck.
- ⁴⁶ *Merck Agrees \$4.85bn Vioxx Settlement*, Christopher Bowe, Financial Times, Nov. 9, 2007 ("Barbara Ryan, analyst at Deutsche Bank, said: 'We believe the company's aggressive and successful defence strategy has given it a heavy hand in the bargaining process and produced a favourable outcome in the Vioxx settlement at a cost that is clearly at the low end of general expectations.'"); Merck News Release, November 9, 2007 ("This agreement also makes sense for the Company because since 2004, we have reserved approximately \$1.9 billion for defending VIOXX litigation and, absent this agreement, could anticipate that the litigation might stretch on for years.").
- ⁴⁷ *Merck Agrees \$4.85bn Vioxx Settlement*, Christopher Bowe, Financial Times, Nov. 9, 2007.
- ⁴⁸ *In re Vioxx Prods. Liab. Litig.*, 574 F. Supp. 2d 606 (E.D. La. 2008) (capping contingent fee arrangements at 32% of the total settlement amount plus reasonable costs); *In re Vioxx Prods. Liab. Litig.*, 670 F. Supp. 2d 549 (E.D. La. 2009) (confirming cap decision; allowing court to deviate from the 32% cap in rare circumstances); *In re Vioxx Prods. Liab. Litig.*, 760 F. Supp. 2d 640 (E.D. La. 2010) (common benefit fee award of 6.5% of the total

settlement amount assessed against the capped contingent fee recoveries of all primary plaintiffs' attorneys; a total award of attorneys fees of USD 1,552,000,000, of which USD 1,236,750,000 was awarded to plaintiffs' primary attorneys, and USD 315,250,000 was awarded to plaintiffs' common benefit attorneys). To this would be added "reasonable costs," i.e. reasonable expenses that were incurred by plaintiffs in addition to their attorneys' fees.

- ⁴⁹ US Products Litigation Settlement Agreement Section 12.1; *In re Vioxx Prods. Liab. Litig.*, MDL No. 1657 (E.D. La. Dec. 4, 2012).
- ⁵⁰ *Vioxx storm to have lasting effects*, Christopher Bowe, Financial Times, Nov. 12, 2007.
- ⁵¹ The US agreement applied only to U.S. citizens, U.S. legal residents, and those who alleged that their heart attack or ischemic stroke occurred in the United States.
- ⁵² *In re Vioxx Prods. Liab. Litig.*, 448 F. Supp. 2d 741 (E.D. La. 2006) (dismissing *forum non conveniens* the putative class actions filed by French and Italian residents); *In re Vioxx Prods. Liab. Litig.*, 2009 WL 1636244 (E.D. La. Feb. 10, 2009) (dismissing *forum non conveniens* the individual actions by remaining residents of other countries who were not eligible for the US settlement); *Adams v. Merck & Co., Inc.*, No. 09-30260 (5th Cir. Nov. 30, 2009) (affirming *forum non conveniens* dismissal of individual actions of plaintiffs living in England, Scotland, Wales, Northern Ireland, and Ireland); *In re Vioxx Litig.*, 395 N.J. Super. 358 (App. Div. 2007) (affirming *forum non conveniens* dismissal of ninety-eight plaintiffs residing in England and Wales represented by a consortium of three firms including Leigh Day and Co of London, England, holding, among other things, that claimed inadequacies of litigation funding and the rules imposing costs upon the losing party in the UK system do not render the UK an inadequate forum; and noting "we observe that [plaintiffs'] counsel's concern that the litigation [in England] not bankrupt the plaintiffs, while laudable, suggests an apparent lack of confidence in the ultimate merits of at least some of their claims."), *certif. denied*, 193 N.J. 221 (2007).
- ⁵³ *Painkiller victims look set to join class action*, Carmel Egan, The Age, Nov. 11, 2007. See Slater & Gordon Media Release, *Vioxx Class Action Numbers Surge*, Nov. 13, 2007 ("We are keen to talk with the other side").
- ⁵⁴ *Peterson v Merck Sharp & Dohme (Australia) Pty Ltd* [2010] FCA 180, March 5, 2010, ¶811 ("Merck had done everything that might reasonably be expected of it in the discharge of its duty of care."). In a summary he read in court, the Justice stated: "It was an important element of the applicant's case that, well before September 2004, the respondent knew, or ought to have known, that the consumption of Vioxx increased the risk of cardiovascular disease. In my reasons to be published today, I have rejected that allegation."
- ⁵⁵ Implied warranty claims under sections 74B and 74D of the Trade Practices Act. The Justice found that Vioxx, at a population level, increased the risk of a heart attack "by a factor of about 2" ("taken as a whole, the data referred to warrant generalisation that, over a population, the consumption of Vioxx increased the risk ... of myocardial infarction by a factor of about 2"); and that, on the balance of probabilities, Vioxx made a "material contribution" to the heart attack in the applicant's own circumstances; but he did not find that the applicant's heart attack would not otherwise have occurred ("I do not find that the heart attack would not otherwise have occurred: there is no way of knowing whether it would have"). March 5, 2010 Reasons for Judgment ¶¶ 475; 772-773. The finding in the applicant's favor in his personal case was overturned on appeal. *Merck Sharp & Dohme (Australia) Pty Ltd v Peterson* [2011] FCAFC 128, 12 October 2011 (findings of fact not sufficient as a matter of law to sustain determination of causation in the applicant's favor).
- ⁵⁶ *Vioxx maker urged to pay all victims*, Melinda Rout, The Australian, Mar. 5, 2010 (emphasis added). *Vioxx ruling gives hope for payouts to British 'victims'*, Kathy Marks, The Independent, 6 Mar. 2010; *Australian court findings on Vioxx may have global ramifications*, 16 Mar. 2010; BMJ 340 doi:10.1136/bmj.c1485; *Australian court finds Vioxx increased risk of heart attack*, 20 Mar. 2010; BMJ 2010;340:c1485 ("The lead lawyer for the plaintiffs, Peter Gordon, told the BMJ that the Australian court's judgment will have 'enormous global ramifications,' including in the United Kingdom.").
- ⁵⁷ *Merck Sharp & Dohme (Australia) Pty Ltd v Peterson* [2011] FCAFC 128, 12 October 2011.

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- ⁵⁸ *Peterson v Merck Sharp & Dohme (Australia) Pty Ltd* [2012] HCAB 05, refusing the applicant's and the group members' requests for special leave to appeal the Full Court's orders to the High Court of Australia, with costs awarded to the company.
- ⁵⁹ *Failed Vioxx action hits Slaters' profit*, Stephanie Quine, Lawyers Weekly, 28 Aug. 2012. The firm's managing director told Lawyers Weekly: "While it was very disappointing, I think the important thing to emphasis [sic] is it's very much a once-off situation and certainly not indicative of what's in the portfolio of cases we have in the future, most of which, in the class action area, are funded by third party litigation funders now."
- ⁶⁰ *Peterson v Merck Sharp & Dohme (Australia) Pty Ltd (No 7)* [2015] FCA 123 (approving class settlement in *Peterson* and related representative action *Reeves*; resolution, release, and dismissal of all claims in Australia including claims of 1,660 registered group members in *Peterson*, for the sum of AUD 542,500.)
- ⁶¹ Ironically, shortly after publication of the March 5, 2010 Reasons for Judgment in the Australian action, "[t]he lead lawyer for the plaintiffs, Peter Gordon, told the *BMJ* that the Australian court's judgment will have 'enormous global ramifications,' including in the United Kingdom." *Australian court finds Vioxx increased risk of heart attack*, *BMJ* 2010;340:c1485. That prediction would not be to plaintiffs' advantage. In England and Wales, the Legal Services Commission turned down applications to fund cases and appeals to the Funding Review Committee were unsuccessful. No other funders appeared; the claimant law firms did not invest in the litigation and abandoned the multi-party actions filed in the High Court. Instead, they pursued actions in the United States which were dismissed *forum non conveniens*, leading one New Jersey judge to observe: "[plaintiffs'] counsel's concern that the litigation [in England] not bankrupt the plaintiffs, while laudable, suggests an apparent lack of confidence in the ultimate merits of at least some of their claims." *In re Vioxx Litig.*, 395 N.J. Super. 358 (App. Div. 2007), *certif. denied*, 193 N.J. 221 (2007). In Scotland, on the eve of trial in a lead case alleging a stroke, the parties resolved all claims pending in the Court of Sessions (the scientific evidence does not support a claim that Vioxx is capable of causing stroke). Likewise, all claims were resolved in The Netherlands. Several hundred cases in other countries on the continent were decided in Merck's favor; in a significant number of these cases, court-appointed experts recognized that individual risk factors, not the medication, were responsible for claimants' alleged conditions. In Canada, after more than seven years of procedural litigation involving some 40 class proceedings in early stages in ten provinces, the parties resolved all claims nationwide, obtaining approval orders in three provinces and recognition and enforcement orders in seven provinces.
- ⁶² Merck's Annual Reports on Form 10-K for the years 2004 through 2018.
- ⁶³ 2005 Background, p.34 (As of late September 2004, "no other non-aspirin NSAIDs or selective COX-2 inhibitors had been studied in this large a patient group for this duration.").
- ⁶⁴ 2005 Background, p.30 (Whether a similar increased risk would be seen with non-naproxen t-NSAIDs, such as diclofenac and ibuprofen, was "an as yet unanswered question.").
- ⁶⁵ Nonsteroidal Anti-Inflammatory Drugs and the Heart, Carlo Patrono and Colin Baigent, *Circulation*. 2014; 129: 907-916, at 907 ("the whole field of NSAIDs has been illuminated during the past 15 years.").
- ⁶⁶ Kearny PM, Baigent C, Godwin J, Halls H, Emberson JR, Patrono C, *Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomised trials*, *BMJ* 2006; 332:1302-1308.
- ⁶⁷ Coxib and traditional NSAID Trialists' (CNT) Collaboration, Bhala N, Emberson J, Merhi A, Abramson S, Arber N, et al. *Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials*. *Lancet* 2013;382:769-79.
- ⁶⁸ FDA Drug Safety Communication: *FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes*, Jul. 9, 2015; see also FDA Briefing Information for the February 10-11, 2014 Joint Meeting of the Arthritis Advisory Committee and Drug Safety and Risk Management Advisory Committee.

⁶⁹ Merck's Annual Reports on Form 10-K for the years 2004 through 2018.

⁷⁰ DiMasi JA, Grabowski HG, Hansen RA. *Innovation in the pharmaceutical industry: new estimates of R&D costs*. *Journal of Health Economics* 2016;47:20-33.

⁷¹ Audio recording of George W. Merck, available at www.merck.com/about/our-history/home.html. Merck & Co., Inc. today is one of the most valuable companies included in the Dow Jones Industrial Average.