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03 Jan 2024 | **Obituary**

Advocacy For Drug Safety And Public Health Loses Passionate And Effective Leader Sidney Wolfe

Sidney Wolfe, Iconic Advocate For Drug Safety, Dies

by Brenda Sandburg

Wolfe is lauded by former colleagues for his fierceness in pushing to get dangerous drugs off the market, his rigorous scientific approach, and mastery of the press.

Sidney Wolfe, a prominent pharmaceutical industry critic whose work led to the US Food and Drug Administration withdrawing more than two dozen drugs from the market and requiring warnings on aspirin labels about the risk of Reye's syndrome in children with chicken pox or flu, has died of a brain tumor.

Wolfe died on 1 January. He was 86 years old.

Wolfe for more than 40 years was the director of the Health Research Group in Ralph Nader's Public Citizen public safety and health advocacy organization. He founded HRG in 1971 and stepped down as director in 2013 to became senior advisor. He remained active on cases and continued to speak at FDA advisory committees against the approval of drugs he deemed to lack sufficient efficacy or safety.

Allison Zieve, director of Public Citizen Litigation Group who worked with Wolfe on numerous suits against FDA, said he was an outstanding client.

"He was a super demanding person, demanding a lot of himself, pharmaceutical companies and FDA," Zieve added. She noted that an obituary referred to Wolfe as a foe of the FDA, but she agreed with a colleague who said this was inaccurate.

“He didn’t see FDA as an enemy. He had tremendous respect for the agency and wanted it to live up to its potential as a guardian of public health,” she said. “He was unafraid to call it out when he felt it was not doing so.”

Douglas Throckmorton, deputy director for regulatory programs in the FDA's Center for Drug Evaluation and Research, expressed appreciation for Wolfe’s commitment.

“Everyone I know within the FDA who interacted with him respected his passion and dedication. Even when we disagreed about the course to take on a matter the FDA was working on, he was thoughtful and focused on public health,” Throckmorton said in a statement.

Public Citizen president Robert Weissman said Wolfe saved the lives of tens of thousands of people by helping to get 28 medications off the market, limiting the use of 10 other drugs and adding strong warnings to dozens of others.

“Sid was brilliant (he won a MacArthur ‘genius’ grant) and fearless in his advocacy. But what was most singular about him professionally was his passion for advancing health justice,” Weissman said in a statement. “There was a distinctive fierceness and fury to his work. Everyone who knew or encountered Sid – allies and adversaries alike – experienced his intensity.”

SIDNEY WOLFE, A COLLEAGUE SAYS, "DID NOT EQUIVOCATE” ABOUT A DRUG’S RISK AND WAS WILLING TO CALL FOR IMMEDIATE ACTION AND WAS IMPATIENT WHEN THE GOVERNMENT DID NOT ACT AND WITH DRUG COMPANIES WHEN HE FELT THEY WERE TRYING TO PROTECT THEIR PROFITS. *Source: Source: Public Citizen*

In addition to being an advisory committee member and speaking at the panels' meetings, Wolfe was with Public Citizen when the group in 1999 sued the FDA under the Federal Advisory Committee Act and the Freedom of Information Act to increase transparency in the advisory process by making committees' brieng materials ahead of their meetings. The agency began the practice in 2007. (Also see "*FDA Aims To Boost Transparency Through Earlier Release Of Panel Materials*" - HBW Insight, 5 Mar, 2007.)

Master Of The Press

William Schultz, who worked at the Public Citizen's Litigation Group for 14 years and is a former general counsel at the Department of Health and Human Service, said that at his core Wolfe was a scientist and spent much of the day reading scientific papers, often learning about a product’s risks before regulators and others.

“Unlike most scientists, once he reached a decision, he was willing to be definitive,” Schultz said. “He did not equivocate” about a drug’s risk and was willing to call for immediate action and was impatient when the government did not act and with drug companies when he felt they were trying to protect their profits.

Shultz, a partner at Zuckerman Spaeder, also noted that Wolfe was a master at working with the press and used it to urge government officials to take action.

He recalled working with Wolfe on a case against the University of Chicago and *Eli Lilly and Company* over a study of DES, a drug found to cause birth defects in pregnant women, in university students. He said three days after the *Washington Post* ran a front-page story about the case, the cartoonist Herbert Block published a cartoon depicting a witch’s brew with skeletons emerging from university research.

But Wolfe would also stand behind a drug if the science supported it. Schultz recalled an instance in which the television news show “60 Minutes” put together a story critical of a product and called Wolfe to get his take on it. Wolfe told them that the science did not support their conclusions.

Wolfe earned a McArthur Foundation “genius” fellow award and $320,000 in 1990 for his ability to use the political/media/regulatory system to question the safety and use of pharmaceuticals.

Public Interest Doctor

Alan Morrison, who founded Public Citizen Litigation Group shortly after the HRG's launch, said there aren’t many public interest lawyers and fewer public interest doctors. “Sid was the one,” he said. “There was nothing Sid wouldn’t go after if he thought it was wrong,” noting that in addition to FDA drug and device cases, Wolfe also worked on occupational safety and Medicare for All.

Morrison, who spent 32 years at Public Citizen and is now the Lerner Family Associate Dean for Public Interest and Public Service Law at Georgetown Washington University Law School, said Wolfe was a skillful advocate who made medical matters simple and understandable.

Wolfman noted that while Wolfe did not spend time practicing medicine he remained an impressive physician. "He was just a great person to know. He cared about you and the people in your life," he added.

He recalled that after Wolfe appeared on the Phil Donahue show to talk about his book “Worst Pills, Best Pills: A Consumer’s Guide to Avoiding Drug-Induced Death or Illness,” 15 or 20 huge sacks of mail arrived at Public Citizen’s office. Morrison said the staff was unprepared to process all the checks for the book, noting that about 500,000 books were sold in a month.

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Schultz said Donahue had announced on the show that people could get a copy of the book by sending five dollars to a post office in Maryland.

The income from the books enabled Public Citizen to purchase its current headquarters at 1600 20th St. NW in Washington, DC, a former mansion off Dupont Circle. "We called it the House that Pills Built," Morrison said.

Brian Wolfman, former director of Public Citizen Litigation Group and now director of the Appellate Courts Immersion Clinic at Georgetown University Law Center, said Wolfe was his hero. "If you had to describe someone with unshakable persistence and integrity it would be Sid," Wolfman said. "There were a lot of wrongs to be righted but he would stick with something until he got it right or could go no further."

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From NIH To Nader Ally

Wolfe began his career at the National Institutes of Health doing research on aspects of blood clotting and alcoholism. In an interview in 2013, Wolfe said he joined NIH in 1966 to avoid the Vietnam War since those in the public health service couldn't be drafted. While at NIH he met Ralph Nader, co-founder of Public Citizen, and through this association with Nader he received a call in early 1971 from a physician at the Centers for Disease Control who told him that hundreds of patients who had received *Abbott*'s intravenous fluids had developed severe bacterial infections and that dozens had died.

> ***"If you had to describe someone with unshakable persistence and integrity it would be Sid. There were a lot of wrongs to be righted but he would stick with something until he got it right or could go no further." – Brian Wolfman, former director of Public Citizen Litigation Group***

Wolfe said that when the government did not recall the fluids because it feared there would be a shortage, he called other manufacturers of the fluids and found they had stockpiles. Wolfe and Nader wrote a letter to FDA calling for the immediate withdrawal of Abbott's products and told the media about the contamination. Forty-eight hours later the agency recalled the fluids.

Wolfe then began getting calls from people at FDA and elsewhere telling him about other problems. In November 1971, he filed a petition with the FDA to ban the use of Red Dye No. 2 as food coloring, citing its links to cancer and birth defects. He then decided to leave NIH and establish HRG as an arm of Public Citizen where he sought to warn people to stay away from products without a unique advantage that are unequivocally dangerous.

The drugs that he succeeded in getting pulled from the market include Eli Lilly's nonsteroidal anti-inflammatory Oraflex (benoxaprofen), *Johnson & Johnson*'s NSAID Suprol (suprofen) and *Pfizer Inc.*'s NSAID Bextra (valdecoxib); Wyeth's Redux (dexfenfluramine) and Abbott Laboratories Inc.'s Meridia (sibutramine) weight loss drugs; Parke-Davis/Warner Lambert Co.'s Rezulin (troglitazone) and Ciba-Geigy Corp.'s phenformin diabetes drug; *GlaxoSmithKline Pharmaceuticals Ltd.*'s Lotronex (alosetron) for irritable bowel syndrome (which was subsequently approved for a restricted indication); and *Xanodyne Pharmaceuticals, Inc.*'s opioid pain reliever Darvon (propoxyphene).

Lilly voluntarily withdrew Oraflex from the market in August 1982, four months after its approval for treatment of arthritis, following reports of severe liver toxicity in patients who took the drug. Wyeth agreed to stop marketing Redux, as well as its weight loss drug Pondimin (fenfluramine), in 1997 after findings suggested they were the likely cause of heart valve problems.

In other significant achievements, Wolfe obtained a court order that FDA require label warnings that high-absorbency tampons are more likely to cause toxic shock syndrome, and succeeded in efforts to get FDA to require warnings on aspirin labels about the risk of Reye's Syndrome in children with chicken pox or flu.

In addition, a lawsuit it filed against the agency resulted in a settlement in which FDA agreed to make materials provided to members of CDER advisory committees available to the public prior to the meeting, a huge boon for reporters and others who struggled to follow the scientific data presented at these meetings.

More recently, HRG was critical of the FDA's review of *Biogen, Inc.*/*Eisai Co., Ltd.*'s Alzheimer's disease drug Aduhlem (aducanumab-avwa), which prompted the agency to conduct an internal review of the review process.

A week after completing the review, the FDA approved Aduhelm over the objections of its Peripheral and Central Nervous System Drugs Advisory Committee. HRG subsequently asked HHS Secretary Xavier Becerra to request the resignations or seek the removal of the three FDA officials most responsible for the approval decision, including FDA Acting Commissioner Janet Woodcock, CDER Director Patrizia Cavazzoni, and CDER's then director of the Office of Neuroscience Billy Dunn. (Also see "*US FDA's Post-Aduhelm Reforms Include Updated Alzheimer's*

Development Guidance, Record-Keeping On Sponsor Meetings" - Pink Sheet, 2 Jan, 2023.)

Wolfe also signed a letter by a group of 30 organizations opposing Woodcock becoming a nominee for FDA commissioner. (Also see "*Campaign Against Woodcock's US FDA Commissioner Bid Has Begun*" - Pink Sheet, 28 Jan, 2021.)

In 2022. he was among multiple public health advocates who submitted comments to the FDA saying expanding access to nonprescription drugs and improving public health aren't likely to result from the agency's proposed "additional conditions for nonprescription use" rule. (Also see "*Public Health Groups Doubt FDA's ACNU Proposal Will Expand OTC Access, Benefit Public Health*" - HBW Insight, 17 Jan, 2023.)

He wrote in his comment that additional information available online won't be enough to safely guide consumers to self-selection of drugs for which indications, warnings and directions won't fit on a container label. "Pharmacists are the only health professionals who could theoretically ensure appropriate self-selection or appropriate actual use," Wolfe stated.

He also doubted making statins available OTC would be safe for consumers. He told HBW Insight in 2012, when he was the consumer representative on FDA's Drug Safety and Risk Management Advisory Committee, that easing hepatic monitoring requirements on statin labels didn't sway his opinion on whether statins should be available without prescriptions. (Also see "*Statin Label Change Stirs OTC Switch Discussions*" - HBW Insight, 5 Mar, 2012.)

Consumers' safe self-selection of a statin therapy is the primary question, regardless of label statements on liver enzyme tests, he said, noting that "hundreds of thousands of healthy people" who do not have high cholesterol levels and are not at risk of cardiovascular problems "needlessly" use statins without evidence of any benefit while increasing their risks for muscle damage, memory loss and diabetes. Conversely, as many or more people should be candidates for statins but are not diagnosed and do not use the drug.

Career Highlight

In an interview after turning over the leadership reins, Wolfe said his tenure on FDA's Drug Safety and Risk Management Advisory Committee from August 2008 to May 2012 was one of the highlights of his career. (Also see "*Public Citizen's Health Group Changes Leadership, But Wolfe Remains On Prowl*" - Pink Sheet, 10 Jun, 2013.)

In four years, Wolfe cast only two votes in favor of approval of a new drug application. He sat on 16 panels where a vote was taken on approvability of an NDA and voted against approval 14 times. He also sat on a number of post-marketing safety reviews, and consistently called for stricter post-marketing controls and reconsideration of the marketability of products up for review. (Also see "*Lone Wolfe: Drug Industry Critic Ends Tenure As Advisory Committee Member*

With Rare Decisive Vote" - Pink Sheet, 25 Jun, 2012.)

Wolfe said that a number of times people at the agency did not like that he was being critical of a drug. He noted that when the committee was considering *Jazz Pharmaceuticals plc*'s Rekinla (sodium oxybate) for an additional indication, he read a passage from the government's complaint against Jazz, which resulted in the company pleading guilty to off-label marketing and paying a criminal fine. He said the chair tried to stop him, but he continued reading and FDA cut his microphone off.

In another instance, the agency said Wolfe could not participate in the review of oral contraceptives containing drospirenone because he had an intellectual conflict of interest as HRG was advising in its newsletter that people not use them.

Wolfe was succeeded as director of HRG by Michael Carome, who retired last year and was succeeded by Robert Steinbrook in July.

Steinbrook said he first met Wolfe in 1985 during his residency as a medical writer at the *Los Angeles Times*. Wolfe was seeking to get a mechanical heart valve manufactured by Bjork-Shiley off the market. The defective device was linked to 100 deaths worldwide. Steinbrook said Wolfe's advocacy put the problem on the public agenda and led to its withdrawal.

Wolfe has been "a towering figure, an iconic figure, by the force of facts and personality," Steinbrook said. "He's been an inspiration to generations of physicians and the public who care about drug and medical device safety."

An earlier version of the article was reported and published by Citeline's Pink Sheet newsletter.