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Dr. Jonathan Fishbein's Fight for Medical Ethics in AIDS Medicine

By Liam Scheff

In December 2005, I spoke with NIH whistleblower Dr. Jonathan Fishbein. In an exclusive interview, Fishbein discussed the controversial African AIDS drug trials he exposed, his firing and reinstatement and how medical ethics and the public trust are violated when profit and politics rule the day.

“Science has become so severely politicized that one has to be skeptical of nearly every research result that is reported.” Says Dr. Jonathan Fishbein, once and future NIH employee.

He should know. Fishbein just fought a two-year battle with the nation’s medical authority, his former employer, the National Institutes of Health (NIH), for what he feels was no less a goal than restoring integrity to science.

Dr. Fishbein had a nearly 20 year work history in medicine, specializing in pharmaceutical safety and oversight, when he was hired at the NIH in July, 2003, as Director of the Office for Policy in Clinical Research Operations. His job was “to create, implement, and enforce research policy in the Division of AIDS,” to ensure studies were being conducted according to ethical research standards.

The agency had some recent failures in maintaining ethical research guidelines, both in the United States and abroad. In 2004, I broke a story of NIH clinical trial abuse in a New York orphanage. The Associated Press took the investigation national, and in 2005, Fishbein helped bring it to Congress.

But when Fishbein first arrived at the NIH, his attention was on an African drug trial completed in 1999, called HIVNET 012 – a study of the drug Nevirapine in pregnant women in Uganda.

Fishbein learned that the study was deeply flawed, the drug dangerous, and the results had been covered-up. But all of this was an open secret. “The flaws were common knowledge inside the division when I arrived,” Fishbein said. So why hadn’t they been corrected?

Fishbein says that within the Division of AIDS he encountered “a management system guided more by politics than sound science,” and “an atmosphere of intimidation” that made it impossible to properly address and correct the institutional flaws that led to damaged study.

HIVNET 012 focused on finding a use for the troubled AIDS drug Nevirapine. The drug had been around since the early 1990s, and had a bad reputation for toxicity. By 1998 it had earned the FDA’s black-box label, announcing its known toxic potential, including the ability to cause organ failure and bloody skin loss – both of which had resulted in death in patients taking the drug.

So why study a drug for use in poor, rural Africa that is known to be dangerous here? The answers are fairly straightforward: profit, the illusion of progress, and misplaced faith in the purity of big pharma’s humanitarian motives by those who care about poverty and illness in the developing world.

In 1998 in Kampala, Uganda, the Nevirapine study to prevent transmission of HIV from mother to child was underway. The study put 645 expectant mothers on the drug. The problems started immediately. First, the study was carried on without a control group – everyone received one drug or another – AZT or Nevirapine.

A 20 percent rate of "serious adverse events" was reported in newborns in both the Nevirapine and AZT groups, including blood and tissue infection, pneumonia and severe rash. Eighty percent of mothers exhibited laboratory and clinical abnormalities. Twenty-two babies had grade 3 anemia.

Thirty-eight babies died. Sixteen on Nevirapine, twenty-two on AZT.

Nevertheless, Nevirapine found approval, and is being sold and distributed throughout the developing world for use in pregnant women who test reactive on HIV antibody tests.

How did this study get through?

Despite the toxicities, the HIVNET researchers concluded that fewer children registered as HIV positive in the Nevirapine group, at 13.1%, than in the AZT group, at 25.1%. It was decided that this potential benefit outweighed the toxic burden. But, according to Fishbein, the research was so flawed as to make the results meaningless.

"The [Uganda] research was poorly conducted – record keeping was atrocious and good clinical practice was not followed or was severely violated," he explained. "There were irregularities throughout the study – in safety oversight, informed consent, and other human research protection issues."

But the major flaw in the study had to do with the reporting of "serious adverse events" in the trial population.

Kampala, Uganda, where the study took place, is an area with a high level of serious endemic illness, including TB, cholera, sepsis, malaria and the general effects of poverty and lack of access to food, clean water and basic medical supplies.

"In a properly conducted clinical trial, all adverse events, regardless of assumed relationship, are recorded," Fishbein said,

But in the Ugandan study, "an assumption was made that the adverse events were due to local endemic conditions. The people recording data were poorly trained to assess these local conditions. They looked at the patients and said, 'whatever's going on is probably malaria, so I'm not going to write it down.'"

"You can't make determinations about drug safety this way," said Fishbein. "But that's what happened."

According to Fishbein, this lack of careful reporting invalidated any data drawn from the study.

But he wasn't the first at the Division of AIDS to notice the flaws. Dr. Betsy Smith, a researcher in the division, reviewed the data in 2003, and had reached the same

conclusion. But Dr. Smith's concerns about the study had been buried.

In collecting the HIVNET data, Fishbein discovered that Smith's safety report had been rewritten without her knowledge by AIDS Division director, Edmund Tramont. According to Fishbein, Tramont's revisions shielded the investigators, the study and the institute itself from urgent criticism and reform.

"In doing my job – creating clinical research policy – it was essential for me to know the problems that occurred in HIVNET 012 and what had to be addressed to improve oversight, research quality and integrity," said Fishbein. "But during the seven active months in the division, I met considerable resistance from both division and scientific leadership to make reforms."

Fishbein also found himself witness to grave professional misconduct by high-ranking members of the Division of AIDS, including the sexual harassment of female employees and the bullying of researchers who disagreed with department policy.

He voiced his concerns openly – and was quickly faced with a choice – back down, or face an increasingly hostile work environment himself.

Fishbein pursued the issue and filed an official complaint with the division chief, Edmund Tramont. Although he was lauded for his work in the division, even having his name submitted for a cash performance award, On February 20, 2004, two weeks after delivering his written complaint, Fishbein was demoted. Five days later he was told his employment would be terminated.

He immediately filed appeals with Office of Management Assessment, NIAID director Anthony Fauci, AIDS division head Edmund Tramont, NIH chief Elias A Zerhouni, and Department of Health and Human Services (HHS) Secretary Tommy Thompson – but the appeals were ignored.

At that point, he filed an Equal Employment Opportunity Commission (EEOC) complaint and a Whistleblower Complaint with the Office of Special Counsel. Fishbein then brought the HIVNET data to Congressman James Greenwood (R-PA), Chair of the House Energy and Commerce Committee, hoping for a new, independent review.

Meanwhile, the NIH kept him on salary and on probation but with no ability to return work or secure a job reference for over a year. It was understood that at the end of the probation period, Fishbein would be able to file an appeal with the Division. But they fired him a day before the probation was up, dashing his hopes for a fair hearing.

During the same period, another AIDS drug scandal had been brewing involving the use and abuse of orphans in NIH clinical trials in one of the poorest boroughs of New York City.

In 2003, I began my investigation of the NIH trials conducted at the Incarnation Children's Center (ICC) orphanage in Washington Heights, just north of Harlem. Since the early 1990s, abandoned children, mostly of drug-addicted parents, were being used to test dangerous and toxic drugs like Nevirapine and AZT for the AIDS market.

ICC, a Catholic orphanage, is operated by Columbia University's Presbyterian Medical

center, which also runs extensive drug trials in conjunction with the NIH.

I published my first report, “The House That AIDS Built” at altheal.org in January 2004. The story was picked up by other investigators, and has appeared in multiple outlets – *The New York Post*, *NY Press*, *UK Observer*, and as a BBC documentary for which I provided research – but there has been no corrective action from the city or state.

In May 2005, an Associated Press investigation revealed that the problem was widespread – orphans and wards of the state were being used in clinical trials with dangerous drugs nationwide – with little to no oversight.

Following the AP story, Dr. Fishbein wrote Daniel Levinson, the Inspector General for the Department of Health and Human Services (HHS), asking that a medical review and audit of study records be performed by the Inspector General’s office and that awarding of further research funds be withheld from the site until completion of an investigation.

In June 2005, the HHS held a subcommittee meeting on the scandal. The committee concluded that the protected rights of foster children had been violated in some of the AIDS drug trials. The HHS cited Columbia Presbyterian, noting that the hospital’s “records demonstrate a failure … to obtain sufficient information regarding such safeguards with respect to the enrollment of wards of the state or foster children.”

The verdict looked good on paper, but nothing has changed at the ICC orphanage. The drug regimen remains the same and is strictly enforced, despite negative consequences in the children. Children in ICC who refuse to take the drugs by mouth have them pumped through nasal or surgically-inserted gastric tubes. Several children have died in recent years – one on Thalidomide, and one after a stroke that left her blind, which occurred within three months of starting the drugs.

Fishbein says that he is unaware of any investigation into these matters.

“I went to the House Ways and Means human resources subcommittee hearing and it appears that there is some interest in legislating better protections for children in research,” he said. Fishbein cited a pointed comment from the hearing, issued by Congressman Pete Stark (D-CA), “in drug trials, children should at least be elevated to the level of protections we provide prisoners.”

In July 2005, *The New York Times* put out a front-page piece on the ICC orphanage drug trial scandal, but painted my investigation as so much internet hyperbole, excluding mention of the AP investigation or the forced-drugging. The *Times* even colored AZT, one of the drugs tested on the children, as a benign wonder-drug, but omitted any reference to it’s well-documented and often fatal toxicity.

Fishbein rebuffed the story; “*The New York Times* piece was not investigative journalism at all,” he said. “The _Times_’ big problem with the story was that they didn’t break it first! So they tried to make believe there was no story. No surprise there.”

Back in the summer of 2004, Fishbein was still in the fight over HIVNET. He had been looking for help in Congress and had already given the HIVNET data to Congressmen Greenwood, “But when Greenwood suddenly announced his retirement

that summer to go work as the chief of the biotech lobby, I knew he had no intent to hold NIH accountable," Fishbein explained.

He again rebounded, and brought the evidence to Senator Charles Grassley [R-Iowa], who as Chairman of the Senate Finance Committee was just launching his investigation into the arthritis drug Vioxx, which was pulled from the market after being linked to thousands of deaths.

"Grassley looked at it, and commenced his own investigation into HIVNET 012 – and requested that the Inspector General of HHS do the same." Fishbein said. "That investigation is in progress."

In January 2005, Fishbein testified before the Institute of Medicine Committee (a division of the National Academy of Sciences) that "gross violations of Good Clinical Practice in the conduct of the HIVNET 012 study rendered the data invalid."

He spent the rest of the year fighting for his case before the EEOC. "I had irrefutable evidence in my hands that substantiated the allegations I made," Fishbein said.

On December 12, 2005, after two years of battle over HIVNET 012, Dr. Jonathan Fishbein was reinstated to the NIH.

Senator Grassely said: "Dr. Fishbein brought to light serious allegations of systemic problems at the National Institutes of Health…As is typical, Dr. Fishbein suffered mightily for being a whistleblower and for exposing the truth, until now."

But it's not a total victory; Fishbein's reinstatement is not to the Department of AIDS. He is being given time to find another job within the NIH – begging the question – how committed is the Department of AIDS to cleaning up its act?

But, Fishbein says, this is the very reason he looks forward to returning to work.

"I hope to help the Agency achieve its mission and become a better environment in which to work. I will, of course, continue to promote scientific integrity, research safety, and protection of human research subjects," he explained.

"I have never strayed from my desire to contribute to finding an end to the epidemic and I still care a great deal about the NIH. I believe in its mission and I believe in scientific integrity," said the doctor. "That's really what this fight was all about: scientific integrity."

At the end of our conversation, Dr. Fishbein referred me to an apparently unrelated story – the December 29, 2005 *Wall Street Journal* story on Perchlorate – a chemical used in solid-rocket fuel that is at the center of an ongoing battle between the Department of Defense (DOD) and the Environmental Protection Agency (EPA).

The EPA says perchlorate causes neurological damage in fetuses in anything over one part per billion; the DOD says that it's safe at much higher levels than the EPA is allowing for – as much as 200 parts per billion.

Following the EPA guidelines could necessitate clean up of water sources in 35 states, including the massive Colorado River.

“The cleanup would bankrupt the DOD,” said Fishbein.

To settle the fight, the DOD took its case to the White House, who told the EPA to halt any further action in the case. The White House then appointed its own committee to come up with a ruling.

The result? Based on their committee’s review, the allowable level of perchlorate in drinking water is 24 parts per billion – 24 times that of the EPA safety recommendation.

“That’s how political considerations get in the way of science,” said Dr. Fishbein, the good man at the NIH.

Resources:
Dr. Jonathan Fishbein’s official website and documents
Nevirapine (Viramune) Warning Label – 2005
The Trouble with Nevirapine by Anthony Brink, Treatment Information Group 2001

AIDS drugs in Mothers and Children and AZT studies Alberta Reappraising AIDS Society

The Fight to Limit Regulation of a Military Pollutant (Perchlorate) Peter Waldman, Wall Street Journal, Dec 29, 2005

1 Inside Incarnation by Liam Scheff, NY Press, July/Aug 2005