**THE POLITICS OF MEDICINE PART III**

**SCIENTIFIC STUDIES: CLINICAL EVIDENCE OR A LICENSE TO KILL?**

**By Gary Null, PhD and Nancy Ashley, VMD**

**March 30, 2012**

For decades now there have been parents who believe their children were harmed by vaccines – everything from autism to loss of motor function to seizures to autoimmune disorders to death has occurred directly following vaccination. Although the government has a voluntary system to report these adverse events -- the Vaccine Adverse Events Reporting System (VAERS) -- and keeps the information in an accessible database, no one investigates any VAERS reports, even those of death. What could be their rationale for ignoring all of this information? The CDC on its website states that because these reported adverse events did not occur in a controlled study, they are considered simply anecdotaland do not prove they were caused by the vaccine1.  Likewise, illness or death from a prescription medication is largely dismissed or ignored because again, this is anecdotal information that did not occur during the clinical trials. The Adverse Event Reporting System (AERS) is a voluntary system to report adverse drug reactions, and it too is ignored, just like VAERS. We have the right to decline prescription medication, but we can’t always say no to vaccines. In either case we should at least have the right to know what the risks are. So is there something about designing and carrying out a study of people receiving a vaccine or a medication that makes the results more reliable than the reaction of someone subjected to the very same vaccine or medication in real life? Can we depend on the results of these studies to be completely accurate? Let’s take a look.

**The Gold Standard Study**

What is a randomized, placebo-controlled double blinded study, anyway? It is a formally designed research project in which a number of people who meet certain defined criteria are recruited to participate in a program for a specific amount of time in which roughly half of the participants take the drug or vaccine in question and the other half get either a placebo, a different drug, or a different vaccine, and neither the researchers nor the participants know who received what. Why is this type of study good? The random selection of participants to either the drug or placebo group and the lack of knowledge what is being administered are supposed to prevent bias, which in theory makes the results more reliable. Mostly, these studies are done as part of clinical trials which are necessary to get approval for a drug or vaccine, or to expand indications for which a drug or vaccine can be given. The FDA, the CDC, the pharmaceutical companies, the professional journals, and the medical associations praise controlled trials as objective, scientific, and evidence-based, and all assert that only in a controlled trial can safety and efficacy be proven. Once a drug or vaccine has been approved by the FDA, the controlled studies are treated like gospel. Here’s why they shouldn’t be.

**Who Pays the Piper?**

We assume that scientific studies are done in an objective and professional manner and that published reports accurately and honestly present their findings. But is the case? There is significant evidence that the majority of published research claims may be false and the problem starts with funding.2 At one time in this country most research was done by universities. Drug companies gave general grants to medical centers for independent research and hoped their products ended up doing well. Researchers then had the freedom to design a study to answer a scientific question and evaluate the data objectively. This all changed in the 1980s, however, when the Bayh-Dole Act created a money-making relationship between universities and the pharmaceutical industry by requiring that discoveries from NIH-funded (i.e. taxpayer funded) research be patented by the universities doing the research. The universities now make a fortune charging royalties and small biotech firms get to produce a product for huge profit based on free research. These firms surround academic research institutions and carry out initial phases of drug development in the hopes that the large pharmaceutical corporations will market the new drugs.3 And other firms – called Contract Research Organizations (CROs) -- have sprung up to conduct clinical trials, which increasingly take place overseas in poverty-stricken countries with lax regulations.4 So everyone wins financially, except the taxpayer who foots the research expense and then gets to pay again for the high priced patented drugs once they come on the market. While many pharmaceutical companies still have their own researchers and scientists, the trend, as recently seen with Sanofi, is to fire the in-house staff and rely completely on R&D from the small biotech firms5 – a new type of outsourcing.

**Is Information Unbiased?**

Aspiring doctors in medical school are taught that good medical care is based upon scientific evidence, and the latest articles from respected journals are considered the undisputed authority in defining the standard of care for the profession. These studies provide the foundation for evidence-based medicine, and doctors depend on the major journals to stay abreast of information vital to high-quality care of patients. But as the pharmaceutical companies have taken over the funding of clinical trials, medical schools, medical journals, and continuing education for doctors and other health care professionals, research is no longer independent. This fact heavily influences what information reaches the light of day. Instead of providing unbiased scientific data, journal articles are actually marketing tools rather than evidence-based science – a form of direct-to-consumer advertising to the doctor. The published studies no longer have to present any data that is not favorable to the product, and don’t even have to honestly report the findings at all. Find this hard to believe? Let’s look at a couple of examples.

**Pravachol**

Dr. John Abramson, a family practitioner, was interested in a *New England Journal of Medicine* article published in August 2000, about a study of the cholesterol-lowering statin drug, Pravachol, and its effect on the risk of stroke. The article stated that participants in the study who had taken Pravachol reduced their risk of stroke by 19% versus patients who had taken a placebo, Most physicians would have stopped right there, persuaded that Pravachol offered more than its competitors. But Dr. Abramson pulled out his calculator to check the facts – which virtually no doctor does on any regular basis – and discovered something interesting: the true risk of stroke was hidden by a statistical device known as relative risk. In fact, when taken apart, the numbers showed that over a 6 year period, subjects taking Pravachol had only 0.8 fewer strokes. Further, most stroke victims occur in women age 79 and older, and in men age 71 or older, yet the subjects of this study had been chosen from a younger pool, with the average age of only 62. And while most stroke victims are women, this study consisted of 83% men. It is easy to improve results by selecting a group of people for a study that don’t actually represent the target audience. When Dr. Abramson examined the results in this light, he found that:

* The patients in the study age 70 or older who had taken Pravachol had 21% more strokes than those receiving placebo
* The women in the study who received Pravachol had 26% more strokes than women receiving placebo
* Five out of six patients in the study were taking aspirin to reduce the risk of strokes and heart attacks. The people in the study who were not taking aspirin and who received Pravachol had 20% more strokes than those receiving placebo.6

So by selecting patients not likely to experience stroke, and by manipulating the numbers, this study was able to hide the fact that for patients most at risk for stroke, taking Pravachol was **more likely to cause a stroke than prevent one**! At least this article gave enough of the actual data to allow an intrepid investigator to ferret out the truth, which is not always the case.

**Paxil**

The story of Paxil as a treatment for adolescent depression is a chilling example of how bad the situation really is. Paxil, (paroxetine) a selective serotonin reuptake inhibitor (SSRI) made by SmithKline Beecham (SKB) was approved for adult depression in 1992. Shortly thereafter, SKB started a multi-site study of Paxil for use in adolescent major depression. Study 392, which ended in 1997, had a protocol which specified two primary outcome measures and six secondary outcome measures. The results of the study showed that there was no significant difference between Paxil and placebo on ANY of the eight pre-specified outcome measures.7 A company interested in the health of patients would have ended the attempt to use Paxil for adolescent depression then and there. But Paxil was a blockbuster drug, earning $3 billion annually, and SKB was concerned that news of this study might make have a negative impact on sales. Instead of putting patient welfare first, SKB decided to forge ahead to “effectively manage the dissemination of these data in order to minimize any potential negative commercial impact,”8 according to an internal document. They planned to publish “positive data” and not reveal the negative findings. The resulting article, **Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial**, was offered to the *Journal of the American Medical Association*, which turned it down. It was reworked, and submitted to the prestigious *Journal of the American Academy of Child and Adolescent Psychiatry* (JAACAP), which accepted it after much questioning by the editor.9 The author of the article blatantly manipulated the data: four of the eight negative outcome measures specified in the protocol were replaced with positive ones, disclosures of overdose and mania were edited out, and serious adverse events were attributed to other causes. The article did not reveal that Paxil demonstrated no improvement over placebo in treating adolescent depression. Only 15% of adolescents in the study taking Paxil had positive outcomes but, worst of all, the drug caused a **significant increase in suicidal acts**. Fortunately no one died during the study, but 6 out of 93 adolescents (6.5%) receiving Paxil had to be hospitalized for self-harming incidents. Instead of being categorized as suicidal thought or attempts, however, these incidents were categorized as “emotional lability”10 a term which is rather vague and meaningless. Two additional adolescents experienced suicidal ideas or self-harm which were not even categorized as adverse events. Internal memos at the time of the study reported that Patient 70 ingested 82 Tylenol, was hospitalized, and was discontinued from the study. But instead of being coded as suicidal, Patient 70 was coded as non-compliant. Patient 106 was hospitalized after becoming combative and suicidal, but was also labeled non-compliant instead of suicidal.11 None of this negative information appeared in the JAACAP article. Completely ignoring the actual results, the final version of the article, published in July 2001, concluded that, **“**Paroxetine is generally well tolerated and effective for major depression in adolescents**.”**12

On the strength of selectively reporting the evidence of study 329 in the JAACAP article, doctors began prescribing Paxil widely for adolescents, even though the FDA had never approved the drug for this purpose. It wasn’t long, however, before the drastic increase in suicides among adolescents taking Paxil became obvious. On June 10, 2003, the British medical authorities took decisive action and banned the use of Paxil in adolescents.13 Our own FDA, however, was less concerned, and added a black box warning advising of the risk of suicide in adolescents taking Paxil without banning the drug.14

**Ghostwriting**

Numerous lawsuits were filed against GlaxoSmith Kline, formerly SmithKline Beecham, as the death toll mounted. Documents made available as a result of trial revealed that on top of all the chicanery of the Paxil article, it wasn’t even written by the listed authors!15 SmithKline Beecham had contracted with a medical communications agency – **Scientific Therapeutics Information (STI)** – in 1998 to create the draft article for submission to a medical journal. The actual author was Sally Laden, a Masters level medical writer, who interpreted the data from the final study report and created the first draft. She sent the draft to SKB for review prior to showing it to the lead author, Dr. Martin Keller, Chairman of the Department of Psychiatry and Human Behavior at Brown University. Laden also coordinated the publication process, responded to the journal editor, and provided the entire package to Keller for submission to JAACAP.16 So between Laden, SmithKline Beecham, the Journal of the American Academy of Child and Adolescent Psychiatry and Dr. Keller, who do we feel should take the responsibility for altering data results and putting countless adolescents in harm’s way? This article is still cited as justification for using Paxil in adolescents – but why wasn’t it retracted?

We make the logical assumption that studies are written by the scientists whose names appear at the top of the article. But more and more, standard practice has become the opposite: the pharmaceutical company hires professional writers to create a research article and then shops around for appropriate authors who lend the use of their names for money, prestige, and the chance to earn even more money on the lecture circuit promoting research they had nothing to do with. It has been estimated that somewhere between **50 – 100%** of studies are ghostwritten by medical writers17 instead of the key opinion leaders who contribute their names as lead authors. There is no requirement other than one’s innate sense of right and wrong compelling listed authors of articles or pharmaceutical companies to reveal the use of medical writing companies. It isn’t stopped by peer review, and in fact, many articles are published in spite of negative peer review because of pressure put on the journal by the pharmaceutical companies. Journals make huge amounts of money by accepting advertising from pharmaceutical companies, and even more money by providing thousands of reprints of favorable articles to pharmaceutical companies for a fee, which drug reps then make available to the physicians they visit.18 Universities, despite having policies prohibiting ghostwriting, benefit from the huge sums of money given to them by drug companies, and turn a blind eye to the practice. Brown University took no action against Dr. Martin Keller after he was shown to have used his name as lead author on the fraudulent Paxil article. They also never bothered to disclose to the NIH the hundreds of thousands of dollars in personal consulting and speaking fees that Keller was receiving from drug companies each year, despite the fact that he was also receiving millions of dollars in federal research funds from the National Institute of Mental Health.19 Just recently, the University of Pennsylvania refused to punish two prominent faculty members whose names appeared as lead authors for a 2001 article which later turned out to have been ghostwritten, despite the fact that Penn has a policy against ghostwriting.20 To add to the irony, University of Pennsylvania President, Amy Gutmann, is Chairwoman of the new Presidential Commission for the Study of Bioethical Issues.21

**Collateral Damage:**

Dr. David Healy, British psychiatrist, was called as an expert witness in many of the trials involving antidepressant related suicide. In 2000, an article of Healy’s critical of Prozac was published in the Hastings Center Report. Eli Lilly, makers of Prozac, promptly withdrew their financial support of the Hastings Center. Dr. Healy describes what happened next:

In July that year, at the British Association for Psychopharmacology’s (BAP) annual meeting in Cambridge, I presented data on a healthy volunteer study conducted in which two volunteers who had been blindly randomized to Zoloft (sertraline), one of the Prozac group of SSRI drugs, had become suicidal. Professor Charles Nemeroff from Emory University was the guest lecturer at the meeting. Quite extraordinarily in the course of his lecture, he indicated there was research at the meeting which he felt did not have a place at an academic meeting. It appeared clear that he was referring to my work and it seemed likely that when the study was presented in poster format later that day he would be present.

He appeared at the poster, and in the course of a brief encounter he made it clear to me that he had been approached to get involved in legal action against me. He also made it clear that he thought presenting research of this kind was unlikely to be helpful to my career, as pharmaceutical companies roll over people who are awkward to them.

Finally, at the end of November 2000, the University of Toronto and the Centre for Addiction and Mental Health hosted a meeting to celebrate the 75th anniversary of the university department and the 150th anniversary of the mental health services in Ontario. I was one of the guest speakers at the meeting. At the time I was scheduled to move to the University of Toronto, having been interviewed for and offered a post as Professor of Psychiatry earlier that year. The distinguished collection of speakers for the meeting included Dr. Nemeroff. The audience was invited to evaluate both the content and presentation of talks afterwards. My talk was rated the highest on the combined scores.

During the course of that day, I gather Dr. Nemeroff made it clear to members of the university that it would be a mistake to hire Healy. Later that evening I had the first intimations that my appointment was in jeopardy. The following morning, as I understand it, Dr. Nemeroff told colleagues at meetings in New York that Healy had lost his job. A week later I had an email confirming that my contract with the university was terminated.22

**Who Owns the Data?**

The worst problem with the current paradigm isn’t necessarily ghostwriting – unethical though it may be -- rather it is the lack of access to raw data to check against the conclusions. Allowing pharmaceutical companies to own the data from research studies makes it impossible to assess the efficacy and safety of a drug. Since research isn’t independent of drug companies anymore, and since the researchers are no longer the authors of the studies, a medical writer, who doesn’t have all the data and isn’t a scientist or a researcher, is charged with presenting findings. Formerly, an interested party could call up a lead author of a study for clarification of certain points. Now, however, that author has no access to the raw data and cannot answer the question. As recently as 2009, respected academician Dr. Thomas Jefferson of the Cochrane Collaboration was frustrated by unsuccessful attempts to get data for studies on Tamiflu for a second review of the product. Jefferson wanted to examine all of the pertinent clinical trials and approached the authors for their studies, but what he got instead was obfuscation and excuses why the authors could not supply the actual data. Two employees of a communications company ultimately came forward and confessed that they had been paid to ghostwrite the Tamiflu studies, which explained the listed authors’ lack of familiarity with the details. Jefferson was never able to get the actual data or complete studies that led to Tamiflu’s approval, and so excluded them in his second meta-analysis.23 Meanwhile, both the CDC and its British counterpart continue to recommend Tamiflu and quote statistics from studies they know were ghostwritten. And this drug is being stockpiled at taxpayer’s expense.

**Impact of Deception on the Medical Field**

What about the effect of these key opinion leaders on the profession of medicine itself? Academics become opinion leaders because they appear to have their names on a larger amount of the literature in prestigious journals than others. Unfortunately, we have seen the manner by which their names become so prominent – by participating in large scale fraud on behalf of the drug companies. Dr. Martin Keller is still respected and sought-after despite having been involved in this controversial issue in which thousands of adolescents who took Paxil based on the JAACAP article were adversely affected. Many of these key opinion leaders are in prestigious university positions, setting the nefarious standards for upcoming generations of doctors receiving their medical training, and calling into question whether it is even possible to have medical care that is not primarily determined by marketing. The end result is that our current practice of medicine is based on prescribing heavily advertised, expensive drugs or vaccines which the prescriber cannot possibly have adequate information about – drugs which may be unnecessary, may not help, and may ultimately harm or even kill you. And if you criticize the drug companies you may be out of a job.

**Where Do We Go From Here?**

The published results of clinical studies are so far removed from the actual data that it is a crapshoot whether or not the conclusions have any purpose other than marketing. It is a forgone conclusion that the published results will be favorable to the drug because the company wouldn’t go to all the expense for an article that would not translate into sales. And while the FDA usually has all the data available to them, their policy is to make no comment to the public if results show a negative outcome in order to protect their customer – the drug company.24

The issue of funding bias in research results has been addressed by many epidemiologists as well as the venerable independent research group, The Cochrane Collaboration, and the consensus is always the same: the more financial conflict of interest, the more likely the findings will support the product being studied. Dr. John Ioannidis, an epidemiologist based both in Greece and at Tufts University Medical School, has stated that not only do most findings simply repeat the prevailing bias without objectively examining the issue, but, in fact, most research findings are false.25

After so many approved drugs and vaccines have later been shown to cause harm, somehow we miraculously wipe the slate clean after every incident and our faith in the pharmaceutical companies and the entire medical profession is restored to 100%. We forget about all the previous stories of disability and death, and can’t wait to ask our doctor for the latest miracle drug we’ve seen on television -- but we do this at our peril! Don’t forget that the stories on your local TV news, as well as the articles, opinion pieces, and letters to the editor in your local paper, have also been bought and paid for by the drug companies and placed through media firms. So the next time you hear the latest news about a new drug or a new use for an old drug, remember: it is very likely that the study was industry-sponsored, manipulated, and less than honest about the real outcome. If your health care professional tries to convince you that you need to take a medication, don’t assume that he is even minimally informed about the possible consequences to you of that decision. We each have to learn to educate ourselves as best we can. Start by looking up the package inserts of every drug or over the counter medication you take and read the entire document – they are all available on the internet. You will be shocked at the possible side effects, contraindications, and interactions with other drugs. It is time to throw out the antiquated notion that the government, the medical profession, or the schools are looking out for our welfare. The best defense is to avoid any new drug – either prescription or over the counter – until enough years have elapsed to allow news of adverse events and lawsuits time to reach the public, and to reject vaccines completely.

1. Vaccine Adverse Event Reporting System (VAERS), CDC, February 8, 2011, <http://www.cdc.gov/vaccinesafety/Activities/vaers.html>, accessed 3/1/12.
2. Angell M, The Truth About the Drug Companies, *The New York Review of Books*, July 15, 2004.
3. Gardner A, Many Clinical Trials Moving Overseas, *US News & World Report*, February 18, 2009, accessed 3/12/12.
4. Silverman E, [Sanofi CEO: Who Needs Big Pharma Scientists?](http://www.pharmalot.com/2012/03/sanofi-ceo-who-needs-big-pharma-scientists/), March 1, 2012, PHARMALOT, <http://www.pharmalot.com/2012/03/sanofi-ceo-who-needs-big-pharma-scientists/>, accessed 3/5/12.
5. Abramson J, Overdosed America, Harper Collins, New York, 2008.
6. Keller MB, Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial, *Journal of the American Academy of Child and Adolescent Psychiatry*[.](file:///E:\aaaa%20Working%20Articles\Politics%20of%20Medicine\) 2001 Jul;40(7):762-72, http://www.ncbi.nlm.nih.gov/pubmed/11437014, accessed 3/1/12.
7. McHenry LB and Jureidini JN, Industry-Sponsored Ghostwriting in Clinical Trial Reporting: A Case Study, *Accountability in Research: Policies and Quality Assurance*, 15:3, 152-167, July 8, 2008, http://www.tandfonline.com/doi/pdf/10.1080/08989620802194384, accessed 2/15/12.
8. Ibid.
9. Jureidini JN and McHenry LB, “Clinical Trials and Drug Promotion: Selective Reporting of Study 329, International Journal of Risk & Safety in Medicine 20 (2008) 73-81, <http://www.pharmalot.com/wp-content/uploads/2008/04/329-study-paxil.pdf>, accessed 3/1/12.
10. Bass A, Internal documents reveal extent of Paxil drug study chicanery, Alison Bass Blogspot, <http://alison-bass.blogspot.com/2008/09/internal-documents-reveal-extent-of.html>, accessed 3/16/12.
11. Keller MA et al, Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial, *Journal of the American Academy of Child and Adolescent Psychiatry,*
12. GlaxoSmithKline, PAXIL Warning letter to Healthcare Professionals, July 19, 2003, Association of Health Care Professionals, <http://www.ahrp.org/risks/PaxilRisks0603.php#letter2>, accessed 3/22/12.
13. GlaxoSmithKline, Paxil Warning Letter to Health Care Professionals, May 2004, <http://www.fda.gov/downloads/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/UCM166499.pdf>, accessed 3/20/12.
14. McHenry LB and Jureidini JN, Industry-Sponsored Ghostwriting in Clinical Trial Reporting: A Case Study, *Accountability in Research: Policies and Quality Assurance*, 15:3, 152-167, July 8, 2008, http://www.tandfonline.com/doi/pdf/10.1080/08989620802194384, accessed 2/15/12.
15. Ibid.
16. Editorial, Prevalence of Ghostwriting Spurs Calls for Transparency, CMAJ, October 13, 2009, 181 (8) <http://www.cmaj.ca/content/181/8/E161.full.pdf+html>, accessed 3/20/12.
17. Sharp K, Blood Feud, *Dutton Adult*, Boston, September 2011.
18. Bass A, New NIH Rules About Conflicts Of Interest Are A Swiss Cheese Of Loopholes, *Alison Bass Blogspot*, August 24, 2011, <http://alison-bass.blogspot.com/2011/08/new-nih-rules-about-conflicts-of.html>, accessed 3/20/12.
19. Final Statement from the Perelman School of Medicine, University of Pennsylvania, March 1, 2012, <http://www.uphs.upenn.edu/news/News_Releases/2012/03/statement/>, accessed 3/15/12.
20. Kumar P, Critics Respond to Dismissal of Ghostwriting Accusations, University Daily Pennsylvanian, March 11, 2012, <http://thedp.com/index.php/article/2012/03/after_dismissing_of_ghostwriting_accusations_critics_respond>, accessed 3/27/12.
21. Thacker P, Chair of Obama's Bioethics Commission Ignores Ghostwriting on Her Own Campus, Project on Government Oversight, July 12, 2011, <http://pogoblog.typepad.com/pogo/2011/07/amy-gutmann-do-the-right-thing-by-president-obama-be-a-leaderand-resign.html>, accessed 3/24/12.
22. Healy D, Academic Stalking and Brand Fascism, pp. 108-137, Turk J (ed), Universities at Risk. How Politics, Special Interests and Corporatization Threaten Academic Integrity. *Lorimer Press*, Toronto 2008.
23. Epstein H, Flu Warning: Beware the Drug Companies! *New York Review of Books*, May 12, 2011.
24. Transcript, Joint Meeting Of The CDER Psychopharmacologic Drugs Advisory Committee And The FDA Pediatric Advisory Committee, *Department of Health and Human Services, FDA, CDER*, September 14, 2004, <http://www.fda.gov/ohrms/dockets/ac/04/transcripts/2004-4065T2.pdf>, accessed 3/24/12.
25. Ioannidis JPA, Why Most Published Research Findings Are False, PLOS Medicine, August 2005, Volume 2, Issue 8, <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0020124>, accessed 3/5/12.