

# Health Letter

SIDNEY M. WOLFE, M.D., EDITOR

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## Drug Research: To Test or to Tout?

*The following article, which originally appeared in the April 12, 2008, edition of the St. Petersburg Times, has been reprinted with permission.*

By: Robert Farley

In the mental institution in One Flew Over the Cuckoo's Nest, Nurse Ratched is obsessed with keeping order on the ward. She dispenses pills that sedate the residents into near zombies.

The novel was published in the 1960s, when Haldol and Thorazine were the drugs of choice to fight schizophrenia. They calm patients but also can cause uncontrollable shakes.

In the 1990s, drug companies trumpeted a new class of drugs, atypical antipsychotics, that they billed as a dream solution: better treatment, fewer shakes.

They wanted the Food and Drug Administration to let them say their drugs were safer and more effective than Haldol. But the FDA said no, because the drug companies had submitted biased studies, according to documents obtained by the St. Petersburg Times.

It happened when Eli Lilly and Co. asked for approval of Zyprexa, and again when Janssen asked for approval for Risperdal.

The FDA said Risperdal could come to market. But there was a caveat: "We would consider any advertisement or promotion labeling for Risperdal false, misleading or lacking fair balance ... if there is a presentation of data that conveys the

impression that (Risperdal) is superior to haloperidol (generic for Haldol) or any other marketed antipsychotic drug product with regard to safety or effectiveness."

Believing they had invented better drugs, not to mention the opportunity for outsized profits, the drug companies were undaunted by the FDA's red light.

Prohibited from touting their drugs as better? No problem. They paid academics and doctors who said it for them.

The companies funded study after study that found — little surprise — the new drugs were better and safer. State by state, the companies funded committees that set treatment guidelines that decreed atypicals should be the drugs of choice.

Despite the FDA ostensibly reining them in, the drug companies remade

the marketplace.

Atypicals have become the overwhelming drug of choice, and not just for schizophrenia and bipolar disorder, the crippling illnesses they were approved for. Doctors commonly prescribe them to treat anxiety, depression and ADHD in children. They're even given as sleep aids.

The new drugs can cost 20 times as much as the old, so taxpayers pay a small fortune in Medicaid expenses. In Florida alone in the past five years, taxpayers spent more than \$1.1-billion on the new antipsychotic drugs.

The drug companies, meantime, enjoy billions in profits.



Allen Jones knew the instant he was destined to be a whistle-blower. He says it was when his boss told

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him: “Quit being a salmon. Quit swimming against the stream with the pharmaceutical case.”

It was a fluke that the case landed on his desk, and it was a fluke that he was even working in the office of the Inspector General in Pennsylvania.

Twice divorced, a single dad with custody of his kids, he had been swinging a hammer, doing rehab work on houses and flipping them. He figured signing on with the state would give him financial security and early retirement.

But life has a way of veering from script, and in 2002, he happened to draw a case where the state’s chief pharmacist reportedly was earning money on the side — from a pharmaceutical company.

Jones learned that the chief pharmacist headed a government panel that would decide which drugs doctors should reach for first to treat severe mental illnesses in Pennsylvania. All of the drugs being touted as front-line were brand new, patented, and therefore exceptionally expensive. Yet some experts that Jones talked to said the new drugs were no better than the old ones.

“It didn’t pass the smell test,” he said. “There was too much opportunity for fraud.”

He suspected that pharmaceutical companies promoting their new drugs were “buying off” state officials in positions to influence the prescription practices of doctors across Pennsylvania. Taxpayers were paying the freight for these high-priced drugs.

That’s when Jones says his boss told him not to play the part of the salmon. Drop it, the politicians will never stand for a real investigation: “I was told point-blank, ‘These pharmaceutical companies write checks on both sides of the aisle.’”

Jones ended up taking his concerns to the press. It wasn’t long before a security guard escorted him from the building and into the ranks of the unemployed.



The idea of establishing state guidelines for prescription practices originated in Texas in 1996, under an ungainly name:

The Texas Medications Algorithm Project. TMAP for short.

The goal was to bring together some of the best minds in the field to reach consensus on how best to treat schizophrenia and bipolar disorder. TMAP would tell Texas doctors: Start with this drug, and if it doesn’t work, try this one. If a drug made the top of the list, the manufacturer stood to make millions.

The atypical drug companies stacked the deck: TMAP was seeded with a \$1.6-million grant from the charitable arm of the company that owns Janssen, which makes Risperdal. The panel was packed with doctors and academics who were paid on the side from the companies that make atypicals.

Proponents of guideline committees say they discourage unproven practices, such as prescribing combinations of several antipsychotics.

Spearheading TMAP was Steven Shon, the Texas Health Department’s medical director for behavioral health. A state employee, he was not allowed to accept money from the pharmaceutical companies.

He resigned amid an investigation that revealed he was taking money from Janssen. By then, with Shon’s help, the Texas guidelines model had been exported to more than a dozen states, including Florida.

The Florida Behavioral Health Collaborative was the brainchild of Eli Lilly and Co., which proposed it in 2004 and, with other drug companies, gave the state \$10-million to create it.

According to Lilly spokeswoman Janice Chavers, the goal was not to help the company’s profit margin, it was to give patients the best care: “Patients always must be the top priority. It can’t always be about the bottom line.”

The Florida collaborative convened an expert panel to recommend state standards for treating mental illness. National scholars were invited

— all with financial ties to drug companies.



To treat schizophrenia, the panel decided, doctors should try an atypical first. If that didn’t work, they should try a different atypical. If that still didn’t work, they should try a third atypical or, if they would rather, one of the older generation drugs.

Running Allen Jones out of his job only spurred him on. He tracked the medications guidelines in Pennsylvania — Penn-MAP — back to its birthplace in Texas.

In 2004, he filed a whistle-blower lawsuit in Texas against Johnson & Johnson, parent company of Janssen. He said that to boost sales of Risperdal, Janssen misled Texas health officials, overstating the drug’s effectiveness and underplaying the risks.

“They got expert opinion to be the deciding factor,” Jones said in an interview. “Essentially, the drug companies could pay people to say what the drug companies could not claim themselves,” namely that they were superior to the older generation of antipsychotics.

“It was a concentrated, deliberate attempt to substitute illusion for science.”

A company spokesman denied it. “Janssen has always been committed to the highest ethical standards and responsible behavior ... and this includes clear, FDA-approved information about the product’s efficacy and safety profile.”

Jones was not a lone wolf. The Texas attorney general joined his lawsuit in 2006 and demanded the return of tens of millions of taxpayer dollars.

The still-pending lawsuit has reverberated around the country. Nine states sued Eli Lilly, four sued Janssen, two sued AstraZeneca. Dozens more states have teamed in a joint investigation, seeking billions of dollars in restitution for money they say they overpaid for atypicals through Medicaid.

Jones, the single dad just looking for a steady job, has morphed into a full-time megathorn in the side of

pharmaceutical companies. He does investigative work for law firms making cases against drug companies. Senators and congressmen call him to talk about big pharma influence.

And Pennsylvania's chief pharmacist, the man Jones was fired for speaking out about? He was indicted. The charges say that as head of Pennsylvania's mental health guidelines committee, the pharmacist took money and other perks from Pfizer and Janssen, drug companies that make atypicals.

Looking back now, Jones is astonished by how few people it took — academics, psychiatrists, state officials — for the drug companies to influence state guidelines and bump up their sales by billions of dollars.

"The marketing was complex, but not complicated," he said. "Divert attention from the science. Divert attention to the scientists who are in your pocket."



For years, the studies paid for by the drug companies concluded that atypical antipsychotics are more effective and safer than the older class.

But when governments conducted independent studies, the findings were altogether different.

In 2005, the U.S. government funded a \$60-million study called CATIE, short for Clinical Antipsychotic Trials of Intervention Effectiveness. It tracked a big sample (nearly 1,500 schizophrenics) for a long time (18 months).

CATIE analyzed the performance of all the atypicals and one of the typicals, perphenazine.

The two key conclusions: First, the atypicals generally were no more effective than the older drug. Second, slightly fewer people on atypicals dropped out of the study due to tremors, but the new drugs had their own troubling side effects, chiefly weight gain and diabetes.

What CATIE documented also was showing up in courthouses across the country: Tens of thousands of people sued Eli Lilly and AstraZeneca, saying that their drugs, Zyprexa and

Seroquel, gave them diabetes and elevated blood sugar levels. Eli Lilly reports having paid \$1.2-billion to settle nearly 30,000 lawsuits.

In October 2006, a British government-funded study mirrored the CATIE findings. Its results, the study said, "refute the hypothesis that the use of (atypicals) is superior to the use of (typicals) in terms of quality of life at one year."

How to jibe these independent, government findings against the earlier studies that said atypicals were safer and more effective?

In a written commentary, the CATIE study's lead author said "the claims of superiority for the (atypicals) were greatly exaggerated.

"This may have been encouraged by an overly expectant community of clinicians and patients eager to believe in the power of new medications," wrote Dr. Jeffrey Lieberman. "At the same time, the aggressive marketing of these drugs may have contributed to this enhanced perception of their effectiveness in the absence of empirical evidence."

The marketing has been a rousing success: Of the prescribed antipsychotics in Florida last year, 86 percent were atypicals. Nationally, atypical sales have risen every year, nearly double since 2000.

Dr. Robert Rosenheck, a Yale professor who participated in the CATIE study, said the science doesn't justify that.

"There was never any evidence that warranted the amount of money we spend on atypicals," he said. "If you look at it independently, it is very clear the results say there is no benefit" to atypicals over typicals.

Yet the pharmaceutical companies get states to make them the drugs of choice, he said.

"They leverage every single angle they can to persuade every person to secure the opinion that their products are superior," Rosenheck said. "Every possible source of opinion, they use money to establish a relationship with them.

"The issue is not, 'Were these people influenced?' There is nobody

who is not influenced."

In Minnesota, one of the few states with a law that requires disclosure of pharmaceutical company payments to doctors, one report showed that more than one-third of the state's psychiatrists took money from drugmakers.

Last year, a nonprofit group funded by 13 states analyzed the academic studies on atypicals. The Drug Effectiveness Review Project found that an alarming number of study authors were employed by pharmaceutical companies.

While academics and doctors often bristle at the suggestion their opinions could be influenced by pharmaceutical money, another study confirmed a not-unexpected conclusion: In trials of antipsychotic medications, the outcome usually favored the drug of the company that paid for the study.

Rosenheck believes that CATIE and other new studies are starting to shift the tide in academia — slowly.

"Obviously, there's a certain amount of resistance to admitting, one, I was wrong, and two, I was misled by companies who paid me a lot of money. That's a hard thing for a scientist to acknowledge."

He says states should change their medication guidelines so that the older class of drugs are used, unless there is a clear reason to use the newer ones. For many patients newer may be better, he says, but to continue the rampant use of atypicals despite the study findings is bad science.

"The idea that we could spend \$60-million on a study and pay no attention to it, it's like, let's not pay attention to science and just go with marketing."



The landscape had changed in the two years since the Florida Behavioral Health Collaborative set treatment guidelines favoring atypicals.

The CATIE study had been published. Tens of thousands of patients had sued drug companies that made atypicals. The academic

*continued on page 4*

community was more divided about what was best.

Last July, the collaborative convened another group of experts to revisit whether Florida should rely so heavily on atypicals. Two dozen mental health professionals met at the Renaissance Hotel at Tampa's International Plaza.

They gathered in the Kalamata Room, done up in the milquetoast style of a classic hotel meeting room: long tables arranged in a square, at each seat a glass of water and a name tag.

The bland setting belied the grand stakes: The vote could swing hundreds of millions of dollars in pharmaceutical company profits. Cost to taxpayers, however, had no place in the conversation.

The meeting's two main hosts were Rajiv Tandon, chief of psychiatry for the state Department of Children and Families, and Robert Constantine, head of the Florida Behavioral Health Collaborative.

Both believe in atypicals. In two papers they co-wrote in late 2006 and early 2007, they said the CATIE study missed the point: The goal is to create a good antipsychotic effect without the tremors, making atypicals the better choice.

Constantine, a research associate professor at USF's mental health institute, is partly paid through a grant from Bristol-Myers Squibb, which markets the atypical Abilify.

Tandon, a state employee, is not allowed to accept money from drug companies. But three years ago, before coming to Florida from the University of Michigan, he was a paid consultant and on the speaker's bureau for several drug companies that make atypicals.

It was Tandon who invited the four national experts to be voting members on the Florida panel. All are consultants, serve on speakers bureaus or get research support from the drug companies that profit from atypicals.

- William Glazer, who was brought

in as the schizophrenia expert, is president of Glazer Medical Solutions, a national consortium of mental health care consultants. He is a consultant to Eli Lilly and AstraZeneca.

His company Web site makes clear his bias: "Are you interested in building a case for the value of new atypical antipsychotic medications? This section offers a step-wise approach to help providers, family members, consumers and others advocate for access to these agents."

- Madhukar Trivedi, a professor of psychiatry at the University of Texas Southwestern Medical Center, is a consultant, serves on speakers bureaus or receives research money from 24 pharmaceutical companies, including all the atypical makers.
- Terence Ketter, a professor of psychiatry and behavioral sciences and chief of the bipolar clinic at Stanford University, is a paid consultant or a lecturer for all the drug companies that make atypicals.
- John Greden, chairman of the psychiatry department at the University of Michigan Medical Center, serves on scientific advisory boards for five pharmaceutical companies, including two that make atypicals.

Tandon said he selected experts who are knowledgeable, respected leaders in their field, with a working knowledge of the medication guidelines process. Because most experts have ties to the pharmaceutical companies, Tandon said, conflicts of interest are inevitable.

"There are clear conflicts of interest," he said. "Everyone is biased. For someone to say, 'I'm not biased,' they are not truthful or they are not introspective."

Given that there is a divide in the academic world about atypicals, why not bring in someone from the other camp, maybe somebody from the CATIE study, someone who would challenge the existing medications model?

"You could go with extremes,"

Tandon said. "I didn't think that was the way to go," because the point of the process is to reach a consensus.

Atypicals are usually better, he said. "Were the benefits of atypical medications exaggerated? Absolutely. And was it the pharmaceutical companies doing that? Absolutely."

Still ... "By no means are the newer medications astoundingly better, but they are better. If I have a child, I'm not going to start them on a typical."

More than a dozen Florida mental health officials sat on the committee, many of them adamant that the newer drugs generally offer a better alternative to the older ones. They said they feared that if they put the older drugs alongside the newer ones as front-line options, HMOs might require them to go with the cheaper option.

To treat schizophrenia, the previous expert panel had made atypicals the first and second options. For the third option, doctors were left to decide whether to try a third atypical.

This time around, the group kept atypicals the first option. As a small nod to CATIE, the group voted on a recommendation that if that first atypical failed, a doctor should try either a second atypical or an older-class, typical drug.

Asked for a show of hands, all were raised in favor. ♦

*Times researcher Caryn Baird contributed to this report. Robert Farley can be reached at farley@sptimes.com or (727) 893-8603. Copyright St. Petersburg Times. Reprinted with permission.*

# Backsliding on Childhood Immunization

Vaccines are the ultimate public health weapon: they prevent disease, target specific conditions and demographic groups, are highly cost-effective, and lend themselves to campaigns reaching broad populations. Not surprisingly, vaccines against HIV and malaria, which to date have defied scientific and technological know-how, are among the “holy grails” of current medical research.

Effective vaccination against measles, which has been available since 1963, has controlled this disease in many countries, transforming it from a threat that ravaged entire populations to a minor risk very seldom resulting in death. Measles was declared eliminated in the U.S. in 2000. Recently, however, the country has witnessed a resurgence of the disease. Outbreaks have been reported in nine states, with 64 reports of confirmed measles cases during the first four months of 2008, the highest number for the same period since 2001. Ten of these cases acquired measles abroad; the remaining cases are linked to the imported cases.

Of the 64 persons infected by the measles virus, only one had been vaccinated. Of the remaining 63 cases, 14 were infants too young to be vaccinated. Another 16 were children whose parents claimed exemption

from mandatory vaccination because of religious or personal beliefs.

The distrust of vaccines has been the result of a controversial issue which has been debated for fully a decade: whether or not there is an association between vaccines and autism. This was largely prompted by a 1998 article published in *The Lancet* which suggested that the combined MMR (measles, mumps, rubella) vaccine might be linked to increases in autism. The aftermath of this finding was more important than its initial publication. Ten of the 12 of the article’s original authors disavowed the connection and signed a retraction of the study’s conclusions in 2004. In addition, the study’s lead author, who defended the original conclusion, has since been accused of accepting money from people claiming harm from the MMR vaccine. He has therefore been undergoing a disciplinary hearing by the body that licenses physicians in Britain. Nevertheless, he has devoted followers who accuse the General Medical Council of conducting a witch-hunt against one of their own.

In the U.S., any association between vaccines and autism has been repeatedly refuted by many studies and scholars. Because the presumed culprit in any adverse effect was thimerosal, a mercury-containing

preservative used in some vaccines, a number of studies have focused on this ingredient. But several studies examining trends in vaccine use and changes in the prevalence of autism do not support such an association. In addition, a scientific review by the Institute of Medicine (IOM) in 2004 concluded that “the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism.” The CDC supported the conclusion. While the evidence was being gathered, in July 1999 the agencies of the U.S. Public Health Service, the American Academy of Pediatrics, and vaccine manufacturers agreed that thimerosal should be reduced or eliminated as a precautionary measure. Recent data from California show that autism rates have continued to rise even after thimerosal was eliminated from childhood vaccines, thereby reinforcing the IOM’s conclusions.

Still, many parents are not reassured, and many are not immunizing their children with the MMR vaccine, with predictable consequences. Resurgence in measles is thus part of the price that has been paid as a result of faulty science leading to the wrong prescriptions. ♦

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THE PUBLIC CITIZEN HEALTH RESEARCH GROUP

## Health Letter

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The Health Research Group was co-founded in 1971 by Ralph Nader and Sidney Wolfe in Washington, D.C. to fight for the public’s health, and to give consumers more control over decisions that affect their health.

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# Public Citizen Urges Removal of ORTHO-EVRA Patch From Market

The contraceptive patch ORTHO-EVRA (norelgestromin with ethinyl estradiol) exposes women to dangerous levels of the hormone estrogen, posing a possible two-fold increase in the risk of blood clots, and should be removed from the market within six months, Public Citizen told the Food and Drug Administration (FDA) in a petition filed on May 8. Ongoing litigation has recently released unpublished studies that confirm the increased estrogen content of the patch.



Evidence compiled by Public Citizen's Health Research Group in its petition reveals that, compared to standard oral contraceptives, ORTHO-EVRA exposes women to:

- More estrogen and a greater range of estrogen levels;
- A possible two-fold increase in the risk of blood clots;
- Increased painful side effects such as breast discomfort, severe menstrual pain, nausea, and vomiting;
- An increased likelihood of discontinued contraceptive use; and
- No improvement in contraceptive outcomes.

Because the patch is still superior to no contraception at all, withdrawal of any contraceptive from the market carries the risk that some users will not immediately replace their contraception with a method that is as effective as the banned product. A six-month transition period in which ORTHO-EVRA will be available for refill prescriptions is requested to allow women time to meet with their healthcare provider and seek a safer, alternative contraceptive method.

ORTHO-EVRA patches are designed to be worn on the skin for seven consecutive days before removal. Three consecutive patches are worn followed by a patch-free week. When Johnson & Johnson received FDA approval in November 2001 for marketing the patch, the company claimed that its product would have two key advantages over existing oral contraceptives: 1) A constant delivery of hormones instead of the ups and downs associated with pill use, and 2) improvements in compliance compared to the daily dosing regimen of oral contraceptives.

However, evidence soon emerged that these theoretical benefits are outweighed by side effects from receiving high and variable levels of hormone exposure.

A post-market study was the basis for a 2005 label change explaining that overall exposure to estrogen from the ORTHO-EVRA patch was 55 to 60 percent higher from the patch than a standard, 35 microgram (mcg) estrogen oral contraceptive. Comparison studies have also shown that the amount of absorbed estrogen varied 1.2-3.5 times as much for women who used the patch than women who used oral contraceptives.

"Had ORTHO-EVRA been designed as a pill, it is unlikely to have been approved because of its increased estrogen content," said Dr. Sidney Wolfe, director of the Health Research Group at Public Citizen. In 1988, the FDA requested the withdrawal of all oral contraceptives with estrogen levels greater than 50 mcg because of the risk of blood clots and lack of additional contraceptive efficacy.

The ORTHO-EVRA patch contains estrogen equivalent on average to a 56 mcg pill.

The ORTHO-EVRA label was changed again in 2006 and 2008 to include findings from studies that revealed an up to two-fold increase in the risk of blood clots in women using the patch compared to standard oral contraceptives. Further, side effects (such as breast discomfort, painful periods, nausea and vomiting) and discontinuation (stopping the contraceptive entirely) due to side effects were more common among women who used the patch compared to those who used pills.

Finally, Johnson & Johnson advertises that women who use the patch are more likely to use it correctly than women who use pills. Yet there are no measurable differences in pregnancy outcomes. In other words, the patch does not provide any additional benefit that would outweigh the risks of high estrogen.

Although demand for the patch has dropped dramatically in the past several years, from more than 9.9 million filled prescriptions in 2004 to 2.7 million filled prescriptions in 2007 (a decline of 73 percent), ORTHO-EVRA remains among the top 200 brand-name drugs by sales and prescriptions in the United States and is thus still a danger to large numbers of women in this country..

"Women deserve a level of risk at least comparable to or less than the pill for their hormonal contraceptive," Wolfe said. "The absence of any evidence of a unique benefit combined with the considerable safety problems of high-dose, variable estrogen exposure in ORTHO-EVRA tips the balance of risks and benefits against its availability as a contraceptive. ♦

To read the full petition, go to [www.NotMyPatch.org](http://www.NotMyPatch.org).

# Product Recalls

April 16, 2008 - May 14, 2008

This chart includes recalls from the Food and Drug Administration (FDA) Enforcement Report for drugs and dietary supplements, and Consumer Product Safety Commission (CPSC) recalls of consumer products.

## DRUGS AND DIETARY SUPPLEMENTS

The recalls noted here reflect actions taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative, by FDA request or by FDA order under statutory authority. If you have any of the drugs noted here, label them "Do Not Use" and put them in a secure place until you can return them to the place of purchase for a full refund. You can also contact the manufacturer. If you want to report an adverse drug reaction to the FDA, call (800) FDA-1088. The FDA Web site is [www.fda.gov](http://www.fda.gov). Visit [www.recalls.gov](http://www.recalls.gov) for information about FDA recalls and recalls issued by other government agencies.

## Recalls and Field Corrections: Drugs – CLASS II

*Indicates a problem that may cause temporary or reversible health effects; unlikely to cause serious injury or death*

*Name of Drug or Supplement; Problem; Recall Information*

**Atenolol and Chlorthalidone tablets, USP, 50/25 mg**, bottles of 100, Rx only, 4,778/100-tablet bottles, Mislabeled; bottles labeled as Atenolo/Chlorthalidone Tablets 50mg/25mg actually contain Gabapentin 100 mg. Lot # L-1456, exp. date 08/2009; Legacy Pharmaceutical Packaging LLC.

**BP Balance AF (Enhanced BP Balance), Original Chinese formula**, Herbal supplement, 250 milligram Vegetarian Caplets, 100 count and 200 count bottles, 185 containers of 100 count, Unapproved New Drug; product contains undeclared promethazine. There are no codes or lot numbers assigned to these products; Geromatrix Health Products.

**Carbamazepine Tablets USP (Chewable)**, 100 mg, Rx, in bottles of 100 Tablets, 26,008 bottles, Failed USP Dissolution Test Requirement. Lot #s 078198, 078335, 078336 exp. date 07/2010; Recalling Firm: Taro Pharmaceuticals U.S.A., Inc.

**Red Yeast Rice, Dietary Supplement**, 600 mg potency, 60-capsule bottles, UPC 033674155172 and 120-capsule bottles, 74,859 bottles, Product contains excessive levels of lovastatin. 60-Capsule Bottles: Lot #s 509859, exp. date 10/31/2008; 514596, exp. date 1/31/2009; 522011, exp. date 5/31/2009; 528163, exp. date 10/31/2009; 530491, exp. date 11/30/2009; 120-Capsule Bottles: Lot #s 504570, exp. date 6/30/2008; 507169, exp. date 8/31/2008; 511280, exp. date 10/31/2008; 514341, exp. date 1/31/2009; 518847, exp. date 1/31/2009; 520928, exp. date 4/30/2009; 524941, exp. date 8/31/2009; 525251, exp. date 08/31/2009; 528162, exp. date 10/31/2009; 531608, exp. date 11/30/2009; Nature's Way Products Inc.

**InVite brand Yeast Rice Extract**, Herbal Support For Cholesterol Levels Already Within a Normal Range, 600 mg, Dietary Supplement, 120 capsules, 2247 bottles, Unapproved New Drug; product found to contain Lovastatin, the active pharmaceutical ingredient in Mevacor. Lot #s 0710106 (exp. date 10/2010) and 0704020 (exp. date 04/2010); Bactolac Pharmaceutical, Inc.

**Schwarz Pharma Neupro** (rotigotine transdermal system) 2 mg/24 hours, 4 mg/24 hours, 6 mg/24 hours, Rx, 7 systems; Crystallization; active ingredient is forming crystals, which may result in a lower dose being delivered. All lots; Schwarz Pharma Manufacturing.

**Schwarz Pharma Neupro Titration Kits** (rotigotine transdermal system); Kits contain: 7 patches, 2 mg/24 hours, -7 patches, 4 mg/24 hours, -7 patches, 6 mg/24 hours, Rx only; Crystallization; active ingredient is forming crystals, which may result in a lower dose being delivered. All lots; Schwarz Pharma Manufacturing.

**Sertraline Hydrochloride Oral Concentrate**, 20 mg/mL, 60 mL bottle, RX only, 21,822 Units, Product does not meet degradation specifications over shelf life. Lot #s: 657694A, exp. date 09/2008; 657695A, exp. date 09/2008; 658085A exp. date 01/2009; Boehringer Ingelheim Roxane Incorporated.

**Zomig (zolmitriptan) tablets**, 2.5 mg, unit-dose blister package containing 6 tablets per carton, Rx only, 44,028 blister packs, Some blister cells may not contain product. Lot # 106033, exp. date 09/2010; Astra Zeneca.

## CONSUMER PRODUCTS

Contact the Consumer Product Safety Commission (CPSC) for specific instructions or return the item to the place of purchase for a refund. For additional information from the Consumer Product Safety Commission, call their hotline at (800) 638-2772. The CPSC web site is [www.cpsc.gov](http://www.cpsc.gov). Visit [www.recalls.gov](http://www.recalls.gov) for information about FDA recalls and recalls issued by other government agencies.

### *Name of Product; Problem; Recall Information*

**Air Pistols.** The Air Pistols can accidentally discharge, posing a risk of serious injury if the air pistol is loaded and pointed at the user or another person when it discharges. Umarex USA Inc., (866) 633-2910 or [www.umarexusa.com](http://www.umarexusa.com).

**ATVs.** The electric power steering shaft of the Model Year 2008 Honda TRX500 ATVs could break unexpectedly, resulting in the rider s losing steering control. This poses a risk of injury or death to riders. American Honda Motor Co. Inc., (866) 784-1870 or [www.powersports.honda.com](http://www.powersports.honda.com).

**Basketball and Flower Tables.** Surface paint on the Basketball and Flower Tables contains excessive levels of lead, violating the federal lead paint standard. Avon Products Inc., (888) 993-9903 or [www.avon.com](http://www.avon.com).

**Battery Chargers.** The Lithium-polymer battery chargers and lithium-polymer batteries can ignite while charging, posing a fire hazard to consumers. Hobby-Lobby International Inc., (866) 933-5972 or [www.hobby-lobby.com](http://www.hobby-lobby.com).

**Beach Chairs.** The rear leg of the Rio Beach High-Boy Folding Beach Chairs can break, posing a fall hazard to consumers. Rio Brands, (800) 866-8520 or [www.riobrands.com](http://www.riobrands.com).

**Bicycle Resistance Trainers.** The springs in the 2007 and 2008 Performance Travel Trac Trainers can unhook and become a projectile, posing a puncture hazard to users or bystanders. Performance Inc., (800) 727-2433 or [www.performanceinc.com](http://www.performanceinc.com).

**Bicycle Resistance Trainers.** The springs in the 2008 Travel Trac Gravity Inertial Trainers can unhook and become a projectile, posing a puncture hazard to users or bystanders. Nashbar Direct Inc., (877) 688-8600 or [www.nashbar.com](http://www.nashbar.com).

**Charm Key Chains.** The "Hip Charm" Key Chains can contain high levels of lead, which is toxic if ingested and can cause adverse health effects. Wal-Mart Stores Inc., (800) 925-6278 or [www.walmartstores.com](http://www.walmartstores.com).

**Children's Rain Ponchos.** The Children's Rain Ponchos have a drawstring through the hood, posing a strangulation hazard to children. In February 1996, CPSC issued guidelines to help prevent children from strangling or getting entangled on the neck and waist drawstrings in upper garments. Daiso LLC, (866) 768-4620 or [www.daisollc.com](http://www.daisollc.com).

**Children's Storage Bins.** Surface paint on the Children's Storage Bins could contain excessive levels of lead, violating the federal lead paint standard. L G Sourcing, Inc., (866) 493-6563 or [www.lowes.com](http://www.lowes.com).

**Dune Buggies.** The seat belt adjustment for the shoulder buckle of Twister Hammerhead Dune Buggies can break during impact or stress, posing an ejection and injury hazard to driver and passenger. TJ Power Sports LLC, (877) 857-7678 or [www.tjpowersports.com](http://www.tjpowersports.com).

**Electric Simmer Pots.** The Electric Simmer Pots have wire connections that can become loose, posing a risk of fire and electric shock to consumers. Waxcessories Inc., (800) 899-5884 or [www.simmerpotrecall.com](http://www.simmerpotrecall.com).

**Food Warmers.** The Deluxe Bottle and Food Warmers can overheat, posing a fire hazard. Munchkin Inc., (866) 619-8673 or [www.munchkin.com](http://www.munchkin.com).

**Gas Boilers.** If there is a leak in the vent piping, the Weil-McLain CGs and CGi Gas Boilers can leak carbon monoxide (CO) into the buildings in which they are installed, posing a risk of CO poisoning. Weil-McLain, (866) 783-9276 or [www.weil-mclain.com](http://www.weil-mclain.com).



## CONSUMER PRODUCTS

**Gas Boilers.** If there is a leak in the vent piping, the Williamson-Thermoflo GWS and GWI Gas Boilers can leak carbon monoxide (CO) into the buildings in which they are installed, posing a risk of CO poisoning. Weil-McLain, (866) 783-9516 or [www.williamson-thermoflo.com](http://www.williamson-thermoflo.com).

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**Gas Grills.** The bottom of the cook box that contains the burners of Broil King Gas Grills can melt or crack as a result of a grease fire. This poses a fire and burn hazard to consumers. Onward Manufacturing Co., (866) 434-7455 or [www.broilkingbbq.com](http://www.broilkingbbq.com).

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**Hammocks.** The metal frame for the Multi Texteline Hammocks and Striped Quilted Hammocks can crack and break, causing a consumer to fall to the ground. CMRG Apparel, LLC, (800) 535-7639 ext. 7777 or [www.LivingXL.com](http://www.LivingXL.com).

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**Infant Carriers.** The buckles on the carrier shoulder straps of Beco Baby Butterfly Carriers can unexpectedly release tension, causing the strap to slip through, posing a fall hazard to the baby. Beco Baby Carrier Inc., (888) 943-8232/9-GET-BECO or [www.becobabycarrier.com](http://www.becobabycarrier.com).

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**Infant Santa Outfits.** The pom poms on the 2006 and 2007 Infant Santa Outfits and the snaps on the 2007 Infant Santa Outfits can detach, posing a choking hazard to young children. Avon Products Inc., (888) 993-9903 or [www.avon.com](http://www.avon.com).

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**LawnBott Lawnmowers.** The cutting blades continue to rotate when the LawnBott Lawn Mowers are lifted from the ground and the spacing on the side of the lawn mower could allow room for a consumer's foot to go beyond the shield and be struck by the blade. Both instances pose a serious laceration hazard to consumers. Kyodo America Industries Co. LTD., (877) 465-9636 or [www.lawnbott.com](http://www.lawnbott.com).

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**Nintendo Lapel Pins.** The Character-themed lapel pins contain high levels of lead. Lead is toxic if ingested by young children and can cause adverse health effects. Nintendo of America Inc., (800) 431-0971 or [www.nintendo.com](http://www.nintendo.com).

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**Power Strips.** The power strip located inside the Charge-It-All Valets has undersized wires, which can pose fire and shock hazards to consumers. HSN LP, (888) 540-7052 or [www.hsn.com](http://www.hsn.com).

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**Pressure Washers.** The motor on the Master Craft® Pressure Washers can overheat, posing a fire hazard. Fingerhut Direct Marketing, (866) 931-5417 or [www.fingerhut.com](http://www.fingerhut.com).

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**Push Toys.** Surface paint on the glove, shirt, and pants of Western Rider Push Toys contains excessive levels of lead, violating the federal lead paint standard. Santa's Toy Corp., (888) 726-8208 or [info@santastoycorp.com](mailto:info@santastoycorp.com).

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**Space Heaters.** The SoleusAir Space Heaters can overheat, posing a fire hazard to consumers. QVC, (800) 367-9444 or [www.qvc.com](http://www.qvc.com).

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**Swing Sets.** The clevis bearing on the Playground Swing Sets can wear, causing the swing to detach and the user to fall. Playworld Systems Inc., (800) 233-8404 or [www.playworldsystems.com](http://www.playworldsystems.com).

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**Table Saws.** The pivot bracket on the DEWALT DW744 Jobsite Table Saws can separate which can misalign the blade and the fence and cause kick back. This poses a laceration hazard to consumers. DEWALT Industrial Tool Co., (888) 742-9178 or [www.dewalt.com](http://www.dewalt.com).

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### *from page 12*

because of Coast IRB's failure to follow FDA regulations regarding the use of expedited review procedures.

This violation of FDA procedures by a for-profit ethical review board is not meant to imply that the not-for-profit academic IRBs never do anything wrong. However, gaining more business by ads that guarantee a one-day turnaround may make more

money for for-profit IRBs but may endanger, as FDA pointed out, the protection of the rights or welfare of subjects of human experimentation.

# Study Finds New Blood Substitutes Increase Risk of Death, Heart Attacks; Authors Question FDA's Approval Process, Records Access

Public Citizen is taking action to halt ongoing clinical trials of unsafe blood substitutes in Europe and Africa. According to Jay Epstein, director of the Food and Drug Administration's (FDA) office of blood research and review, "It's because of FDA's safety concerns that there currently are no ongoing studies of HBOCs [hemoglobin-based oxygen carriers] in the United States trials and no approved HBOC products." While there are no clinical trials in the U.S., the manufacturers of these unsafe blood substitutes continue to do research on patients in other countries, despite the knowledge that they have been associated with a 30 percent increased risk of death and 2.7-fold increased risk of myocardial infarction.

According to a recent review of the National Institutes of Health clinical trials registry website [clinicaltrials.gov](http://clinicaltrials.gov), there are active studies in eight countries: Belgium, the Czech Republic, Greece, the Netherlands, Poland, South Africa, Sweden, and the United Kingdom. Public Citizen has contacted the ministers of health in each of these countries to make them aware of the safety issues associated with blood substitutes, and has urged them to halt any ongoing trials.

The following is Public Citizen's press release about a *Journal of the American Medical Association* article about clinical trials of blood substitutes coauthored by Dr. Peter Lurie and Dr. Sidney Wolfe, deputy director and director of the Health Research Group at Public Citizen, respectively.



While the idea of a blood substitute that doesn't need refrigeration or cross-matching and has a long shelf life would be an exciting scientific advance, a new study being released Monday online by the *Journal of the American Medical Association*

(*JAMA*) found that these products significantly increase the risk of heart attacks and death.

The authors from the National Institutes of Health and Public Citizen also raise serious questions about the role of the Food and Drug Administration (FDA) in continuing to allow human trials of these products, despite evidence from past clinical trials that found patients given these hemoglobin-based blood substitutes face a 30 percent greater risk of death and a 171 percent increased risk of heart attack than those treated conventionally.

The authors will present their findings April 29-30 at an FDA public workshop on the "Safety of Hemoglobin-based Oxygen Carriers." The workshop will be held at the Natcher Conference Center, Bldg. 45, National Institutes of Health, 8800 Rockville Pike, Bethesda, Md.

Currently, such blood substitutes are not approved for use in the U.S., although at least one product is approved for use outside the U.S. and new clinical trials are being conducted worldwide.

In the *JAMA* article analysis, the authors identified 16 different trials of five different blood substitutes. The studies were combined by the authors using a statistical technique called meta-analysis.

Of those trials, 13 were published in medical literature, sometimes years after they were completed, while others were never published at all. In some cases, the only information available came from company news releases.

One serious problem the authors encountered is that the FDA does not make much of the research into these blood substitutes available for review even though companies are required by law to report such data to the agency.

"When 'secret science' is allowed,

scientists are unable to build on the successes or failures of other researchers testing similar products, and patients can be repeatedly exposed to increased risks unnecessarily," the authors wrote.

Studies available to the FDA, but not always to the scientific community at-large, would have made it clear by 2000 that these hemoglobin-based blood substitutes posed a significant risk to patients. By that point there was already a 27 percent greater risk of death and a 177 percent greater risk of heart attacks based on trials of four products.

"Had the agency placed a moratorium on trials at that point, product-related deaths and [heart attacks] in subsequent trials most likely would have been prevented," the authors wrote.

The authors recommend that the FDA require new and existing blood substitutes to be tested in animals before any further human trials are allowed. They also called on Congress to make it easier for independent researchers to review information and studies submitted to the FDA during the product development process, either through changing FDA policy or amending the Freedom of Information Act.

The authors of the article, titled "Cell-Free Hemoglobin-Based Blood Substitutes and Risk of Myocardial Infarction and Death," are Peter Lurie, M.D. and Sidney Wolfe, M.D., from the Health Research Group at Public Citizen, and Charles Natanson, M.D., Steve Kern, B.S., and the late Steven Banks, Ph.D, from the National Institutes of Health. ◆

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## Human Experimentation and Speedy For-Profit Ethical Review Boards

Not long ago, most human experiments testing the safety and efficacy of new drugs were done in academic medical centers and, although paid for by the drug industry, they were under some degree of control by the medical school/teaching hospital complex. In order for such experiments to be allowed, an institutional ethical review board (IRB) associated with the medical center had to approve the protocol, informed consent and other aspects of the study.

Over the last 15 years we have witnessed the exponential growth of for-profit human experimentation companies (HECs), most of which are entirely outside academic medical centers. Promising faster results for the drug companies who pay for these studies than the more "cumbersome" academic centers, they are still

required to obtain approval from an ethical review board to conduct the studies. However, since they are not affiliated with a medical center, they use non-academically connected ethical review boards. Most, if not all, of these boards also operate on a for-profit basis.

But in order to deliver the faster clinical trial results drug companies desire, approval by the ethical review process also must occur as quickly as possible so as not to hold up the pace of the HEC. A recent ad by such a for-profit ethics company, Colorado-based Coast Institutional Review Board, on its Web site, exemplifies this ethical race:


Coast IRB is a new breed of IRB. We are committed to the basics: Speed - Next day turn around time (Check out our Next Day Guarantee).

A graphic on their Web site points out that "The time you save using Coast IRB can be easily translated into savings for your company. Even a 2-day delay can cost you as shown in the diagram below [diagram estimates \$6.02 million savings for a one-day turnaround time for IRB approval instead of 2 days]." Hence, the importance of the "Next Day Guarantee."

Unfortunately for Coast IRB, the Food and Drug Administration (FDA) recently investigated this speedy process and found that it was a bit too slick. A warning letter to the company in March of this year stated that:

FDA, in order to protect the rights or welfare of subjects, is suspending Coast IRB's use of expedited review procedures until further notice

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