PRAKTIKOS QuickRead Series

Selections from

FDA

Failure, Deception, Abuse

The Story of an Out-of-Control Government Agency and What It Means For Your Health

From *Life Extension Magazine*

- a non-profit research-based organization est. in 1980

This book documents how the FDA

- denies the introduction of life-saving therapies
- suppresses safe methods of preventing disease
- causes the price of drugs to be beyond the means of most
- intimidates those who develop innovative methods
- fails, by its own admission, to keep pace with science
- criminalizes giving scientific information to consumers
- censors medical information that would educate doctors
- fails to protect the safety of our food
- approves prescription drugs that prove lethal

Active ingredient	***Purpose***
Information	To protect you and your family

PRAKTIKOS *QuickRead Series*

Selections from

FDA: Failure, Deception, Abuse

The Story of an Out-of-Control Government Agency and What it Means for Your Health

from Life Extension Foundation

PRAKTIKOS BOOKS

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Contents

Preface

FOUNDED IN 1980 BY WILLIAM FALOON AND SAUL KENT, THE Life Extension Foundation (LEF) is a nonprofit research-based organization dedicated to finding new scientific methods for eradicating old age, disease, and death. The largest organization of its kind in the world, the Life Extension Foundation has been at the forefront of discovering new scientific breakthroughs to reduce, and ultimately eliminate, such age-related killers as heart disease, stroke, cancer, and Alzheimer's disease.

The Life Extension Foundation is responsible for a long and distinguished list of achievements in promoting optimal health. It was the first to recommend the use of coenzyme Q10 and low-dose aspirin therapy for heart health; the first to offer lycopene as a cancer-preventative; the first to introduce melatonin to support immune function; and the first to introduce S-Adenosyl methionine (SAMe) in the United States.

LEF members are provided with the latest scientific breakthroughs, services, and information about products to empower them to make better health choices and live healthier, longer lives.

They also receive the monthly *Life Extension* magazine, which reports current advances in health research and offers scientifically referenced articles on the use of nutritional supplements.

LEF has been a tireless advocate of health freedom—that is, the right of consumers to choose the treatment protocols which they and their medical practitioners believe will support their health. This might include therapies that are backed by solid scientific research but which, for one reason or another, are outside the mainstream of contemporary allopathic medical practice. And it would certainly include the use of nutritional supplements which are scientifically shown to have significant health benefits.

Unfortunately, this is where the US Food and Drug Administration comes in. According to their mission statement,*

> The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
>
> The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

The essays in *FDA: Failure, Deception, Abuse*, most of which were written by William Faloon, are culled from the past fourteen years of *Life Extension* magazine. As you will read in the following excerpts from the book, the FDA's mission and the FDA's actions are utterly at odds with one another. The Agency has been responsible for injuring—not protecting—the public

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* http://www.fda.gov/AboutFDA/WhatWeDo/default.htm; accessed 8/24/09.

health. It has approved drugs and medical devices that are not safe or efficacious. It has impeded public health by censoring scientific research and preventing the dissemination of information that would help the public make informed decisions. It has interfered with the medical education of doctors, promoting the information which their vested commercial interests prefer doctors to have, and censoring the research that a physician actually needs to make the best decisions for and with their patients. For the FDA to say that it helps the public get "the accurate, science-based information they need to use medicines and foods to improve their health" is, to be perfectly blunt, not just the half-truth or white lie that we have come to expect from Washington. It is an outright falsehood.

In a quiet way, this book is a call to action. It gives readers the ammunition—the hard evidence and the scientific data—to become effective advocates for real healthcare change and reform. We hope these excerpts will whet your appetite and explore the topic in greater depth. (*FDA: Failure, Deception, Abuse* is available at your local bookstore and from PraktikosBooks.com.)

Craig R. Smith
Editorial Director
Praktikos Books

EXCERPT FROM

Victory Over the FDA

On Feb. 26, 1987, I was in California, meeting with anti-aging scientists whose research was being funded by the Foundation. Early in the day, I called Foundation headquarters in Florida and knew immediately that something was wrong when no one answered the phone. After an hour, I reached an employee at home, who told me that the Foundation had been raided by the FDA.

I didn't find out the details of the raid until later that evening when I finally reached [LEF co-founder] Bill Faloon at his home in Florida. I was in shock all that day, assuming that the FDA had seized the Foundation's assets and shut it down. I wondered if Faloon had been arrested and whether he was in jail.

WHAT IT WAS LIKE AT THE FOUNDATION

At the Foundation, Faloon didn't have time to think about such things. He had his hands full dealing with the battalion of troops that had invaded the Foundation. Here's what Faloon had to confront that day, as noted in the April–May 1987 issue of *Life Extension Report*:

> On Feb. 26, 1987, an armed force of about 25 FDA agents and US Marshals smashed down the glass doors

> of our store . . . and stormed into our nearby warehouse with guns drawn.
>
> At 10 AM, Bill Faloon received a phone call telling him that the FDA was breaking into our store with a battering ram. As Bill started to leave the warehouse, he suddenly found himself staring down the barrel of a .45-caliber pistol, which belonged to one of a second group of FDA agents, who were simultaneously attacking our warehouse!

TERRORIZED EMPLOYEES

The reaction of the Foundation's employees to the raid was absolute terror. To get some idea of what is was like for them on that day, let's return to the same issue of *Life Extension Report*:

> When Helen Bishop walked to the back of the warehouse, she heard someone say "hello." She thought it was a delivery man, but the next thing she knew "cops were rushing in from both doors to surround us."
>
> One of them stopped her, showed her his badge, and forced her to line up against the wall with the other employees. A search was then conducted of the personal belongings of every employee.
>
> Al Wood, one of our advisors, was working on the upper level of the warehouse when a marshall came up the stairs with his gun drawn and said "Get up!" Wood immediately threw his arms up and was told to march down the stairs. "Everyone moved slowly," he recalls, "so they wouldn't excite the Marshal waving his gun. When we asked him what this was all about, he said he had a search warrant."

ILLEGAL SEARCH AND SEIZURE

We later discovered that the search warrant had been obtained with perjured testimony by FDA agent Martin Katz before Magistrate Lurana S. Snow. This pattern continued throughout the day as FDA agents engaged in continuous illegal and unconstitutional behavior.

When the authorities didn't find the items they were supposed to search for, they seized products, literature, documents, computers, and personal effects NOT on the search warrant! Evidence presented at a later hearing showed that more than 80% of the items seized by the FDA on the day of the raid was done so illegally . . . in direct violation of the 6th amendment to the Constitution! An FDA official testified at the hearing that the FDA's policy is to instruct its agents to seize anything they want! These agents are told, said the official, that "if it turns out that you've seized the wrong things, you can always return them later."

"PLEAD GUILTY"

Every attorney we consulted said we could expect 5-to-20 years in prison and that our only hope of getting reasonable prison time was to "plead guilty."

Everyone we consulted, including attorneys who were FDA "experts," told us we had to submit to the FDA's authority to have any chance of surviving. They told us we had to stop promoting "unapproved" therapies to extend the human lifespan immediately!

We ignored all this advice and instead decided to wage all-out war against the FDA. We did this knowing that we would not only risk our livelihood, but our personal freedom as well.

This was a war that even our most avid supporters thought we could never win.

We were told again and again that the FDA had the unlimited resources of the federal government at its disposal, and that an

organization with fewer than 5,000 members had no chance of winning an all-out war with them.

ENTERING THE POLITICAL ARENA

We knew our position was scientifically correct, and that the public would support us if we could expose the truth about FDA corruption and incompetence. But this was 1987, when the FDA still had the public's confidence and most people still "trusted" the government.

Our first political victory was in 1991 when we helped defeat a bill that would have expanded the FDA's enforcement powers to the point of possibly destroying the supplement industry. Most people have short memories, or don't realize that we were responsible for initiating the public uprising against the FDA that began in 1991.

At the same time we were developing our political capability, we also began to enter the legal arena by filing lawsuits against the FDA. Some of these lawsuits dealt with the FDA's assault on us, but others were on behalf of the American people as a whole. We stood our ground on the actions that caused the FDA to attack us in the first place. These include making claims (based upon scientific evidence) for therapies that have yet to be approved by the FDA, and telling people how, where, and for how much they can obtain these therapies.

Our decision to continue providing accurate information about therapies for health and longevity was at the core of our struggle with the FDA. By refusing to back down on the principles that the FDA attacked us over, we made it clear that nothing could sway us from the pursuit of health, longevity, and physical immortality.

This stand is at the heart of what, ultimately, turned the tide against the powerful and wealthy forces we were up against.

THE FDA STRIKES BACK

In the summer of 1989, an ex-employee told us she had received a subpoena, which would force her to testify before a Grand Jury in Florida. She had been told that the Grand Jury was investigating Saul Kent, William Faloon and the Life Extension Foundation. We soon found that the FDA had referred our case to the US Attorney's Office, which had convened a Grand Jury to seek a criminal indictment against us!

During the rest of the year, subpoenas were sent far and wide in a massive "fishing expedition" for witnesses who might provide testimony that could be used against us. The search for such witnesses even led to scientists whose research we had funded.

The vast majority of these witnesses had little or nothing to tell the Grand Jury, but the FDA continued to send a parade of witnesses to the stand in the hope that they would, eventually, strike paydirt against us.

THE SECOND GRAND JURY

When the Grand Jury ran its course (18 months) without indicting us, the case was transferred to a second Grand Jury, which began to call witnesses all over again.

Many of these witnesses, which included current Foundation employees, were terrorized by the Grand Jury process, which forced them to testify without counsel, and in some cases, subjected them to verbal abuse and fear that they might be a target of the "investigation."

For example, one of our longtime employees, Ursula Arias, was called a liar repeatedly by US attorney Alan Sullivan because she wouldn't admit that the purpose of her vacation trip to Europe was to further some nefarious mission that we had put her up to. Ursula was not only abused verbally for her entirely truthful testimony, but she also had her passport seized! She has yet to get it back!

The enormity of the tax-dollar waste of these multiple grand jury sessions is hard to imagine. The federal government spent enormous sums of money interrogating everyone we had ever had contact with. There was no limit to what the government would spend to get us indicted on "something."

Then the FDA threatened to indict Kent and Faloon on "criminal charges" and to throw them in jail without bail on Oct. 1, 1991!

Kent and Faloon were told—in no uncertain terms—that on Oct. 1st, they would be hit with a massive, multicount criminal indictment that would be followed by other multicount indictments, which would, in effect, "destroy their lives forever" and that their only hope of avoiding lifelong imprisonment would be to plead guilty to "crimes against the state" and voluntarily go out of business!

THE ARREST AND THE INDICTMENT

On the morning of Nov. 7, 1991, we were arrested and taken into custody at the federal court building in Fort Lauderdale. We were photographed, fingerprinted, and taken to a jail cell to await arraignment. The jail was a fenced-in, 8-by-8-foot cubicle that contained two hard benches, a toilet (without a seat), and a small sink. We shared the cell with several men charged with drug-related offenses who were also facing arraignment that day

At 2:30 p.m., we were brought into court (handcuffed to other prisoners). A few minutes later we stood before magistrate Snow. She told us we had been indicted on 28 criminal counts including engaging in a "conspiracy" to sell "unapproved drugs," "prescription drugs," and "misbranded drugs."

Bail was set at $825,000 each. A bail bondsman who we had secured earlier was present to work with our attorneys to execute a bond that would enable us to go free that day.

Magistrate Snow set the following conditions on our release. We would have to report by phone to Pretrial Services every two

weeks and pay a visit in person once a month. We were permitted to travel in the US, but only if we informed Pretrial Services (at least 24 hours prior to leaving) where we were going and how long we would be away from home. We were not permitted to travel outside the continental United States.

After the arraignment, we were led back to our cell (again in handcuffs chained to other prisoners), where we were kept another two hours until we were finally released from custody at 5 p.m.

WHAT WE WERE UP AGAINST

After we left the building, our attorneys told us that if we were convicted on all 28 counts in the indictment, our maximum penalty would be 84 years in prison and a seven million dollar fine! They also told us the FDA's "investigation" of our activities would continue indefinitely, and that we could expect additional multicount criminal indictments in the future!

MOTIONS TO DISMISS THE INDICTMENT

In the Spring of 1992, we filed a motion asking for dismissal of the indictment on the grounds that the FDA had illegally obtained their search warrant, and had then illegally seized vast numbers of items not on the search warrant.

We then filed another motion to dismiss the indictment on the grounds that we were being prosecuted selectively because the FDA was openly permitting organizations such as AIDS Buyers Clubs to engage in acts far more violative of the Food, Drug and Cosmetic Act than anything we were alleged to have done.

We were granted hearings before Magistrate Snow on both these motions. At these hearings, we presented powerful evidence of illegal and unconstitutional actions on the part of the FDA, and revealed the ignorance and shockingly immoral behavior of one FDA employee after another.

FDA enforcement officer Martin Katz admitted he had com-

mitted perjury in writing up the search warrant, and that he had tried to intimidate a radio talk show producer into keeping us off the air. Katz' partner, Roy Rinc, admitted he had threatened to put our printer out of business if he didn't "cooperate" with the agency, and that he believed he could seize anything at all from us, whether it was on the search warrant or not.

Higher FDA officials testified that the FDA actively encourages its agents to ignore search warrants during raids, and that the FDA deliberately avoids defining any of its "rules," "regulations," or "policies," so that it can interpret them in any way it wishes, or ignore them completely if it suits their purpose.

BEATING UP ON THE FDA

Although Magistrate Snow ultimately ruled against us on both motions, the two hearings helped us immensely in our struggle against the FDA.

They forced us to begin constructing a powerful defense that could be used at trial. They enabled us to obtain hard evidence of the corruption and immorality of the FDA. And they helped us buy precious time to search for key witnesses, while the FDA's case gradually began to wither away.

The most valuable benefit, however, may have been the opportunity to beat up on the FDA. During both hearings, our attorneys hammered away at one FDA witness after another with difficult, spirit-sapping questions that must have been quite demoralizing for the agency. It was exhilarating for us to able to give the "bully boys" a taste of their own medicine!

THE TIDE BEGINS TO TURN

One of the first signs that the tide was beginning to turn came in 1992 when we won our lawsuit to have the items seized illegally by the FDA returned to us. While the nutrient products the FDA had been storing at a warehouse since 1987 (at taxpayer

expense) were spoiled by then, it was very encouraging to win a victory over the FDA in court.

Even more encouraging was the fact that the judge ordered the FDA to pay our attorneys' fees for unreasonably holding on to our property. This made it more than just a symbolic victory. Our spirits were buoyed considerably by this award, which further demoralized the agency.

An even greater sign that things were beginning to turn our way also occurred in 1992, when the FDA offered us a deal to settle our case. We were told that most of the charges against us would be dropped, and that we might avoid going to prison entirely, if we would just plead guilty to one or two of the charges against us and agree to submit totally to FDA authority. Moreover, we were told that—if we refused the deal—we would be prosecuted to the full extent of the law, and that we would have to face waves of new criminal indictments.

Although the proposed deal was a major concession that would have tempted most defendants, we didn't hesitate. We replied that we had no intention of giving in to the FDA, that we were totally innocent of any wrongdoing, and that we would continue to provide Americans with lifesaving information, even at the risk of being thrown into prison for life!

This was the first of several "deals" proposed by the FDA, each one followed by a threat that never materialized. Every new deal was better than the previous one, which told us that the FDA was beginning to crack under the pressure we had been submitting them to.

MORE FDA THREATS

In 1995, the FDA made even more serious threats against us. They said they had new evidence that would enable them to incarcerate us for life, and that they were on the verge of seizing every penny we had!

It is hard to describe the psychological effect of this unrelenting government pressure. Historically, the FDA has destroyed its opponents through this type of illegal intimidation, thereby maintaining a dictatorial grip on the practice of medicine in the United States.

THE TRIAL APPROACHES

In mid-1995, the FDA was pushing to bring the case to trial. We had a trial date that might not be possible to postpone, and the FDA had an 88-year history of never giving up on any enforcement action, especially a criminal indictment against a political opponent!

We were then offered a deal to guarantee that we would not go to prison, and that it might even be possible for us to remain in business in some limited capacity. But, by then, we had come to the conclusion that any admission of guilt would irreparably compromise our principles.

So we dug our in our heels and went after the FDA again by having our attorneys file a battery of new legal motions, by escalating our political attacks on the agency, and by spending more and more of our time preparing for a trial that would require our total concentration for months as well a great deal of our money.

THE FDA CAVES IN

As it turned out, our "dread" at going to trial was mild compared to the FDA's horror at facing us in court! By the end of 1995, the FDA and the US Attorney's Office no longer had the stomach to fight us. In short, they figured they would lose and that the process of losing would be an extremely unpleasant experience!

But they still weren't ready to give up completely. In November 1995, the FDA asked Judge Hurley to drop every charge against us, except one. They still intended to prosecute me for "obstruction of justice"—a charge that had absolutely no merit, but had

the apparent virtue of being easy to prosecute.

We then concentrated our efforts on this charge. We interviewed the witnesses the FDA planned to bring against me, and it turned out that the FDA had no case, but was holding on to this charge in the hope that I might be convicted of "something."

In February 1996—exactly 9 years after the FDA launched its brutal attack on the Life Extension Foundation—the US Attorney's Office filed a motion to dismiss this final count.

It is difficult to calculate the total cost of the FDA's war against the Life Extension Foundation because the costs have been so high and so many of the them have been hidden from view, but millions of dollars were spent by both sides in fighting the war. At various stages of the "investigation," almost every US law enforcement agency was involved, including the Federal Bureau of Investigation (FBI), the Drug Enforcement Agency (DEA), the Justice Department and its prosecutorial arm the US Attorneys Office, and the Internal Revenue Service (IRS).

EXCERPT FROM

The Unscientific Bioidentical Hormone Debate

TODAY'S BATTLEGROUND IS OVER WHO WILL DERIVE THE MOST economic benefit from the sale of female hormone drugs. All sides seem to have spokespersons to emphatically state that their product is the safest and most effective.

We at *Life Extension* are in the unique position of arguing against what is in our economic interests. For the past two decades, we have advised women needing estrogen drugs to use individualized combinations of estriol and estradiol topical creams.

The problem is the FDA has effectively forbidden the sale of estriol. This ban is in direct response to pressure from a pharmaceutical company that wanted the FDA to censor your right to obtain estriol, which we consider a safer form of estrogen.

DANGEROUS ESTROGEN DRUGS STILL SELL BRISKLY

The market for female hormone replacement drugs is gargantuan. The lethal side effects of Premarin® (horse urine-derived estrogens) and Prempro® (horse urine-derived estrogens and a synthetic progestin) were revealed in the Women's Health Study in 2002 and 2004. These drugs, however, continue to be sold to unsuspecting female patients.

The fact that medical doctors continue to prescribe horse urine-derived estrogens and synthetic progestins with proven risks is a testament to mainstream medicine's apathy and ignorance.

That the FDA allows the continued sale of horse urine-derived estrogens and synthetic progestin, under the guise that the agency is not sure if plant-derived estrogens and progesterone are safer reveals how much political influence pharmaceutical companies wield in government.

That the maker of Premarin® and Prempro® doesn't even make the effort to bring out "new and improved" versions of their brand-name drugs (using plant-derived estrogen and natural progesterone) shows how little pharmaceutical companies care about the public's health.

I see innovation in the natural products industry virtually every day, yet the same formulas for Premarin® (horse urine-derived estrogens) and Prempro® (horse urine-derived estrogens and a synthetic progestin) have been used for decades.

Premarin®, in fact, was approved by the FDA way back in 1942. What else do you know that was brought out 67 years ago that still sells briskly today? The only answer is antiquated drugs protected by a federal regulatory agency called the FDA.

PLENTY OF PLANT-DERIVED ESTROGEN DRUGS TO CHOOSE FROM

There is no shortage of drug companies that sell estrogen drugs that cost them virtually nothing to make. For example, pharmaceutical manufacturers will produce tens of millions of tablets at a time containing 1 mg of a potent estrogen called estradiol.

These drug companies (and the Life Extension Pharmacy) make money when women buy these 1 mg estradiol tablets. The scientific literature, however, indicates that it is safer and more effective if aging women are prescribed individualized doses of topical creams that provide about 80% estriol and only 20% estradiol.

To reiterate, while it is in Life Extension's economic interest to sell mass-produced estradiol and/or conjugated estrogen tablets, we instead recommend that women in need of estrogen drugs obtain them from compounding pharmacies that provide the more scientifically substantiated estriol. (Our pharmacy does provide compounding services, but we can't offer estriol because of the FDA's ban.)

WHY DRUG COMPANIES ATTACK ESTRIOL

Pharmaceutical companies make their money in an assembly line style which involves selling you the same drug as everyone else. The problem is that you are not like everyone else as far as your individual hormone needs are concerned.

In order to deceive the public into believing they need to be "protected" against compounded estriol-based creams, drug company shills proclaim that compounding pharmacies are "unregulated" and lack the quality control found in FDA-approved manufacturing facilities. These deceptions frighten most of the public into using toxic mass-produced drugs in lieu of safer compounded versions.

The bottom line is that there are billions of dollars to be made if American women can be deceived into using danger-

ous mass-produced estrogen and synthetic progestin drugs. You can believe pharmaceutical giants will leave no stone unturned to sic regulatory agencies against those who sell natural forms of these hormones. An even more sinister tactic is to pay doctors to attack those who seek to alert the public about the suffering and deaths caused by these unnatural and toxic hormone drugs.

CORRUPT FDA ACTIONS CAUSE CONSUMERS TO BE FINANCIALLY RAPED

There is a financial downside for women seeking compounded estriol-based creams.

Since the FDA was so kind (to Big Pharma) to ban the sale of estriol, its gray market price has sharply increased. The FDA's biased action causes US consumers to now pay grossly inflated prices for estriol.

In order to protect the economic interests of the pharmaceutical industry, the FDA has no qualms about bankrupting the healthcare system of the United States. Life Extension exposed this back in the early 1980s, and little has changed since then—except that the medical system is facing virtual insolvency because of unrelenting corrupt FDA practices.

A study this year in fact revealed that more than 60% of personal bankruptcies are caused not by lavish spending, but by medical bills!

OPRAH WINFREY CRITICIZED FOR AIRING SCIENTIFIC TRUTHS

On January 29, 2009, Oprah Winfrey dedicated an entire one-hour program to the bioidentical hormone debate. Oprah did her research and identified numerous maturing women who suffered horrendous quality-of-life deficits that were reversed by bioidentical hormones.

Oprah assigned one of the most prestigious medical doctors in the United States (Dr. Mehmet Oz) to go inside a compounding pharmacy to show the audience how much quality control goes into making a compounded natural hormone cream.

Suzanne Somers was the featured guest, along with doctors who urged aging women to have their blood tested and their hormones naturally restored.

In her *O* magazine, Oprah Winfrey stated:

> After one day on bioidentical estrogen, I felt the veil lift. After three days, the sky was bluer, my brain was no longer fuzzy, my memory was sharper. I was literally singing and had a skip in my step.

Oprah Winfrey tried to air a "balanced" report on her TV show. She found mainstream doctors who supported the FDA's biased position against bioidentical hormones. These doctors attacked the safety of biodentical hormones and suggested that aging women should do virtually nothing to restore youthful hormone balance, or rely only on FDA-approved hormone drugs.

After the program, some media sources were critical that Oprah favored the bioidentical side of the debate, and claimed that Oprah was "damaging" women's health by suggesting women could benefit from bioidentical hormones.

NEWS MEDIA DISSEMINATES BLATANTLY FALSE INFORMATION

Drug companies appear to be terrified of Oprah Winfrey. Many months after Oprah's bioidentical hormone show aired, the news media was still finding doctors to criticize her. Drug companies spend huge amounts of money on public relations firms for the purpose of influencing the public, as well as the FDA and Congress.

One prominent news magazine quoted a doctor as stating:

> Despite (Suzanne) Somers's claim that her specially made, non-FDA-approved bioidenticals are "natural" and safer, they are actually synthetic, just like conventional hormones and FDA-approved bioidenticals from pharmacies—and there are no conclusive clinical studies showing they are less risky.

Numerous clinical studies substantiate the safety and efficacy of these "natural to the human body" hormones extolled by Oprah Winfrey, Suzanne Somers, and tens of thousands of anti-aging doctors and their patients.

Most appalling are the innuendos that bioidentical hormones are no different than FDA-approved Premarin® and Prempro®. Both Premarin® and Prempro® contain horse estrogen extracted from pregnant mares' urine. Unlike bioidentical estrogen creams that provide the hormones found naturally in the human female body, *horse estrogen contains equilin and other equine estrogens found exclusively in horses!*

The human female body contains enzymes to metabolize the natural proportion of estriol, estradiol, and estrone, but not horse estrogens such as equilin. These horse estrogens produce estrogenic effects that are much more potent and longer-lasting than those produced by natural human estrogens.

As two leading reproductive physiologists point out, when women take Premarin®:

> Levels [of equilin] can remain elevated for 13 weeks or more post-treatment due to storage and slow release from adipose [fat] tissue. In addition metabolism of equilin to equilenin and 17-hydroxyequilenin may contribute to the estrogen stimulatory effect of [conjugated estrogen] therapy.

Another metabolite of equilin, 17-dihydroequilin has been found to be eight times more potent than equilin for inducing

endometrial growth, a possible precursor to cancer.

The drug Prempro® consist of conjugated equine estrogens and medroxyprogesterone acetate, a synthetic progestin that has been implicated in many of the adverse effects uncovered in the Women's Health Initiative study. Medroxyprogesterone acetate is not the same as natural progesterone found in bioidentical hormone creams, yet establishment doctors are telling the news media that there is no difference.

There are other FDA-approved estrogen drugs that provide too much estrone and estradiol (and no estriol). These so-called "natural estrogen" drugs are also not the same as bioidentical hormone creams that can be obtained from compounding pharmacies.

On her January 29, 2009, show, Oprah Winfrey warned the medical establishment:

> We have the right to demand a better quality of life for ourselves, and that's what doctors have got to learn to start respecting.

Profit-driven pharmaceutical companies don't want patients to revolt and seem willing to disseminate egregiously falsified propganda to protect their multibillion dollar assembly line franchise of dangerous estrogen/synthetic progestin drugs.

FOLLOW THE MONEY AND YE SHALL FIND THE TRUTH

The Oprah Winfrey Show strongly supported the anti-aging benefits women could attain from bioidentical hormones. Regrettably, the conventional doctors Oprah used to "balance" the program served their purpose, i.e., they cast doubt on the safety of natural hormones. These sound-bite scare tactics (often used by those running for political office), will cause most aging women to do nothing to restore their hormones based on imaginary fears.

A simple method to discern the truth is to see who economically benefits from the hormone debate.

Pharmaceutical companies lavish conventional doctors with enormous financial rewards in exchange for these doctors' support of FDA-approved drugs. The economic incentive for mainstream doctors is thus to toe the pharmaceutical industry's party line and attack those who offer natural alternatives.

But what are the financial motivations of Oprah Winfrey, Suzanne Somers, and the numerous beneficiaries of bioidentical hormones that appeared on Oprah's show? The fact is that *none* of them sells bioidentical hormones. They represent the uncompensated majority who only seeks out the truth, without money influencing their decision-making process.

When listening to future debates about whether women should use FDA-approved hormone drugs that are proven to kill, as opposed to bioidentical hormones whose safety and efficacy are strongly supported, follow the money and you will see who has your best interests at heart.

EXCERPT FROM

Why American Healthcare Is Headed for Collapse

Very soon, Medicare will start paying out more in hos-pital bills than the premiums (taxes) it will collect. When that time arrives, the federal government will have to tap some other source to cover this gargantuan unfunded liability. One obstacle is that the federal government is over $11 trillion in debt and is projected to run trillion dollar deficits for the next several years. If these numbers sound high, they pale in comparison to Medicare's unfunded liability of $34 trillion.

To put this in perspective, the government collects only about $2 trillion each year in total tax revenue (including Medicare premium taxes). There are virtually no reserve funds left to pay promised Medicare (and Medicaid) benefits. The government is relying on the money it takes in each day to cover its enormous Medicare cost burden.

As the country ages, Medicare will devour huge chunks of US economic output and eventually overwhelm every other item on the federal budget. While politicians stick their heads in the sand and disregard this issue, no one can argue against the math showing a financial disaster of unprecedented magnitude.

MEDICARE SCAMS

The government points to rampant fraud as one reason behind Medicare problems. It is estimated that 20% of every dollar Medicare pays out goes to criminals who submit claims for nonexistent or bogus services. For example, it was recently discovered that Medicare paid out $100 million for wheelchairs, canes, prescription drugs, and other items prescribed by dead doctors. In other words, people working at doctor's offices pretended their doctors never died and falsely billed Medicare for medical treatments that were never rendered.

The government brags when it cracks down on Medicare fraud, but they only catch a fraction of the crimes perpetrated. What the government does not like to admit is that another 20% of Medicare dollars are paid out in the form of overpayments to those with political connections. What companies do is lobby Congress to enact legislation mandating that Medicare pay inflated prices for certain products and services that can be obtained for a fraction of the price on the free market. This enables those who are politically connected to grossly overcharge Medicare because Congress mandates the inflated expenditures.

How inflated are the monies Medicare pays out? Take for example, an oxygen concentrator, a device that delivers oxygen through a tube to patients with respiratory illness. You can buy one new on the open market for $600. By law, Medicare is only allowed to rent these devices at a price that winds up costing $7,142 over a 36-month period. Medicare covers 80%, so it spends $5,714, while the patient has to pay the other 20%, or $1,428. Under this absurd system, Medicare and patients can pay ten times the free market price it would cost to buy the device new! (Think how much money would be saved if the devices were bought used?)

Perhaps the most expensive politically-induced overcharge is for prescription drugs. Under the Medicare Prescription Drug Act that *Life Extension* vehemently battled against, Medicare is required by law to pay full retail drug prices.

The Medicare Prescription Drug Act was largely written by pharmaceutical companies and passed under intense pressure by pharmaceutical lobbyists (refer to the August 2007 issue of *Life Extension* magazine for the sordid details). Medicare will pay out hundreds of billions of dollars for drugs that could be obtained for far less in a competitive-bidding system, something that the Medicare Prescription Drug Act prohibits.

THE GENERIC DRUG RIP OFF

Once a brand drug comes off patent, generic equivalents emerge, but they cost far more than they need to because of FDA overregulation.

Take the drug finasteride (Proscar®), for example. It came off patent in the year 2006, but at the end of 2008 chain pharmacies were charging about $90 for 30 tablets (a one-month supply). All it takes to make this drug is to put 5 mg of finasteride into a tablet that dissolves in the stomach. Vitamin companies do this every day with nutrients, but the FDA does not allow them to freely do the same thing with drugs.

We checked on the cost of buying finasteride and making it into tablets. The free market price for 30 tablets is only $10.25, which includes independent assay of the ingredient quality, potency and tablet dissolution—and a reasonable profit margin. It is against the law, however, for GMP-certified (Good Manufacturing Practices) vitamin manufacturers to be able to offer low-cost generic drugs. This prohibition must be lifted as America can no longer afford to subsidize those who are politically connected while the country is driven into insolvency.

Finasteride is a drug that not only helps relieve benign prostate enlargement, but that may also reduce the risk prostate cancer. Widespread use could save Medicare lots of money in expensive prostate treatments. Those who follow *Life Extension*'s other recommendations would be expected to reduce prostate cancer risk even more.

As evidence mounts about the prostate cancer risk reduction associated with drugs like finasteride, more companies are competing to make it, but its average price at chain pharmacies is around $86 a month—a staggering eight times higher than what its free market price would be!

Please note that generic prices tend to wildly fluctuate. In this case, as more competitors entered the market, chain pharmacies did not substantially lower the price of finasteride. In some cases, the opposite occurred, and by the time you read this, the price could be different.

PARTIAL SOLUTIONS

One problem is that Medicare will only pay for FDA-approved medical devices and drugs. As we know, this means that Medicare recipients are forced into overpriced therapies that are laden with side effects. Treating drug-induced side effects results in the expenditure of even more healthcare dollars. To make matters worse, the efficacy of certain FDA-approved drugs is so medio-

cre that patients sometimes live only a few months longer by taking them. The cost to Medicare for these drugs can easily exceed $50,000 per patient. Complementary physicians who prescribe unapproved cancer therapies that cost a fraction of FDA-approved drugs are subject to criminal prosecution.

So we have a system in place today in which progressive doctors are persecuted, while those who sell dangerous and often ineffective therapies receive protection and payment from the federal government. People without the financial wherewithal have no choice, since Medicare will only pay for what the FDA claims is safe and effective. Conventional medicine's goldmine will end when Medicare exhausts its ability to pay.

A group of FDA scientists recently revolted against their superiors and went directly to Congress. The reason was that they were told by their superiors to certify new medical devices as safe and effective, when the clinical testing data showed the opposite. This is just one example of how the FDA contributes to today's healthcare cost crisis by allowing dangerous products on to the market that Medicare then pays for.

EXCERPT FROM

Ending the Atrocities

KETEK® IS A DRUG THE FDA APPROVED TO TREAT MILD TO MOD-erate pneumonia. Ketek® can also cause sudden and serious liver damage. In some cases complete liver failure develops necessitating the need for a liver transplant. Some patients die before a liver transplant can be performed.

The risks of liver failure (and other toxic side effects) were known *before* the FDA approved Ketek®. In order to convince an outside sci-

entific advisory committee to recommend that Ketek® be approved, the FDA knowingly allowed a *fraudulent* safety study to be presented. Here is what the Senate Investigative Committee uncovered:

- FDA accepted the resubmission of a new drug application that included safety data that was fraudulent, in whole or in part.
- FDA instructed its employees preparing to appear before the advisory committee that they should present this fraudulent safety data.
- FDA employees presented the fraudulent study data to the advisory committee tasked with recommending Ketek's approval or disapproval.
- FDA approved a pediatric clinical trial of Ketek®, involving infants as young as 6 months old, despite concerns about known toxicities affecting the heart, eyes, liver, and vascular system.
- FDA continued to knowingly cite the fraudulent study data in publically released safety information on Ketek®.

How fraudulent was this data? While the FDA was presenting this fake data, a criminal investigation was simultaneously being conducted that found the clinic where the "safety" study allegedly occurred was *closed* during the time the study was supposed to have taken place. It was also determined that documents relating to the safety study had date modifications and signature inconsistencies.

Shortly after the advisory committee meeting where the fake safety data was presented by FDA employees, the person who conducted the study was criminally indicted, pled guilty, and sentenced to almost five years in jail.

It is even more shocking that the FDA continued to cite this safety study long after the principal investigator admitted it was fraudulent. While the perpetrator of this "safety" study was in prison for falsifying the data, the FDA used the very same study to issue a Public Health Announcement stating:

> Based on the pre-marketing clinical data it appeared that the risk of liver injury with telithrmycin (Ketek®) was similar to that of other marketed antibiotics.

The "pre-marketing clinical data" FDA cited to tell the public that Ketek® was safe was the fraudulent study, a study that may never have actually occurred. According to the Senate Investigative Committee report, "it defies explanation why the FDA would continue to cite" this fraudulent study to the American public to imply that Ketek® is safe.

The Senate Committee report concluded by stating that

> Retaliation against these individuals, or any other FDA employees who communicate with the committee with reference to Ketek® will not be tolerated.

Based on the tone of the Senate investigative report, it would appear that the FDA functioned as a continuous criminal enterprise in this instance.

THE REVOLVING DOOR

You may wonder why certain officials in the FDA would go to such extreme lengths to get a lethal drug like Ketek® approved.

Look no further than the gargantuan economic benefits drug companies reap when a patented compound like Ketek® receives the FDA seal of approval.

The harsh reality is that the FDA functions primarily to protect the financial interests of the pharmaceutical industry, not the public's health. If anyone ever questioned this, look no further than the FDA's attempts last year to ban the safest form of estrogen (estriol). The FDA has no qualms about publically stating their ban on estriol was based on a petition filed by Wyeth, the maker of dangerous estrogen drugs like Premarin® and PremPro®.

There are a number of estrogen drugs that have not been shown to increase stroke and breast cancer risk. The FDA, however, has

done nothing to remove Premarin® or PremPro®. Instead, the FDA openly seeks to protect Wyeth's market share by denying American women access to natural estriol.

According to the FDA, "bioidentical hormone products are unsupported by medical evidence and are considered false and misleading by the agency." The truth is that bioidentical hormones are far less expensive and pose a major competitive threat to Wyeth, ergo the FDA's aggressive attempts to disallow them.

In a report issued by the Associated Press just last year, it was revealed that a record number of FDA employees are leaving the agency to go to work for pharmaceutical companies. According to the Associated Press, these FDA staffers are resigning in order to go into "the more lucrative side of the business."

How Many Drug-Induced Suicides?

The same Senate committee investigating the Ketek® scandal uncovered another study with falsified data. This fake data was used to support the approval of a popular antidepressant drug used by millions of human beings.

According to a report authored by a Harvard medical doctor, when the Paxil® application was submitted to an FDA advisory committee in 1991, the drug company improperly counted those taking the real drug as placebo subjects. This was done to make it appear there to be no difference in the risk of suicidal behavior in those taking Paxil® compared to placebo.

It took until year 2006 for the manufacturer to send a letter to doctors admitting the risk of suicidal behavior was 6.7 times higher in study subjects taking Paxil® as compared to placebo.

Suicide is the 11th leading cause of death in the United States. It killed over 34,000 people in year 2004. The number of suicides attributed to drugs like Paxil® (select serotonin reuptake inhibitors) could be in the hundreds of thousands during the 13 years it was fraudulently marketed.

EXCERPT FROM

The FDA Indicts Itself

The FDA, in collusion with pharmaceutical giants and conventional medical orthodoxy, is the leading cause of suffering and death in the United States.

Back in the early days, the FDA would defend its position by proclaiming that it served to protect the public's health. An endless number of well-publicized scandals have caused the FDA itself to admit that it is incapable of carrying out its mission.

If all the FDA did was act so cautiously that it almost never approved a dangerous drug, then at least the agency could point to some consumer value it provides. Instead, we are plagued by an antiquated regulatory agency that stifles the development of novel life-saving medications, while allowing a slew of drugs to be sold that have cumulatively cost millions of lives.

Americans thus suffer the "worst of both worlds" as they are poisoned by FDA-sanctioned prescription drugs, but denied the fruits of novel approaches to disease prevention and treatment.

FDA'S INDICTMENT OF ITSELF

In response to a barrage of criticisms, FDA commissioner Dr. Edward von Eschenbach requested that a special committee assess whether the FDA is capable of doing its job. The premise for the FDA's massive audit of itself was the fear that "the nation is at risk if FDA science is at risk."

Their sixty-page report, entitled "FDA Science and Mission at Risk," states that "the world of drug discovery and development has undergone revolutionary change," but the FDA's "evaluation methods have remained largely unchanged over the last half century. "

The following are exact quotes from the report:

- The FDA cannot fulfill its mission because its scientific base has eroded and its scientific organizational structure is weak.
- The FDA cannot fulfill its mission because its scientific work force does not have sufficient capacity and capability.
- The FDA cannot fulfill its mission because its information technology (IT) infrastructure is inadequate.
- The FDA does not have the capacity to ensure the safety of food for the nation.
- The development of medical products based on "new science" cannot be adequately regulated by the FDA.
- There is insufficient capacity in modeling, risk assessment, and analysis.
- The FDA science agenda lacks a coherent structure and vision, as well as effective coordination and prioritization.
- The FDA has substantial recruitment and retention challenges.
- The FDA has an inadequate and ineffective program for scientist performance.
- The FDA has not taken sufficient advantage of external and internal collaborations.
- The FDA lacks the information science capability and information infrastructure to fulfill its regulatory mandate.
- The FDA cannot provide the information infrastructure support to regulate products based on new science.

Most appalling is the FDA's own finding that it "cannot even keep up with the advances in science." Said differently, this means that the FDA cannot keep up with scientific breakthroughs that could cumulatively save millions of human lives!

RESPONSES TO THE FDA'S DAMNING REPORT OF ITSELF

The *Wall Street Journal* wrote an editorial titled "The Real FDA Scandal" and quoted the following about the FDA's statement:

> Particularly in complex and specialized fields like genomics and biotechnology medicine, the FDA lacks

> the basic competence "to understand the impact of product use, to maintain ongoing currency with their evolution or to evaluate the sophisticated products produced" and "to support innovation in the industries and markets that it regulates."

The *Wall Street Journal* further wrote, "Think about that: We live amid a revolution in biology, but the FDA still thinks like it did when Sputnik launched."

Dr. David Kessler was the most publicly recognized FDA commissioner of all time. He is still sought out by the media as a proponent on FDA issues. In response to this horrific report, however, Dr. Kessler stated, "The problems are way bigger than one commissioner. . . . I'm not sure how anybody could do this job now."

FDA commissioner Eschenbach stated, "I think to do what we need to do requires substantially more dollars than what has been invested in the FDA so far. . . . This is a systemic overhaul that must go on for years."

PROBLEMS ARE WORSE THAN FDA ADMITS

Many recent reports from outside organizations have been harshly critical of the FDA. These reports made national news for a day or two and were then quickly forgotten.

Our greatest impediment to saving human lives is an incompetent and corrupt federal bureaucracy that is strangling medical innovation, especially in the areas of genomics and biotechnology where breakthroughs in anti-aging medicine are most expected.

In discussions with scientists about methods to significantly extend our life spans, the problem with "the FDA" inevitably arises. If the FDA's bureaucratic roadblock is not torn down, we may all succumb to a disease that liberated scientists could readily prevent or cure.

There is not a magic immortality pill that the FDA is directly suppressing. Instead, the FDA is restraining the ability for medical

science to progress. This is no longer just opinion. The FDA itself admits it cannot keep up with advances in science. So discoveries that could save human lives are not getting approved by the FDA and the cost is thousands of American lives being lost each day.

EXCERPT FROM

The Little-Known Dangers of Acetaminophen

WHAT IF A DIETARY SUPPLEMENT WAS PROVEN TO CAUSE LIVER damage, liver failure and death? What if each year, this same supplement caused 100,000 calls to poison control centers, 56,000 emergency room visits, 26,000 hospitalizations, and more than 450 deaths from liver failure alone?

You know the answer. The FDA would immediately shut down the supplement company and seek to incarcerate the principals for life.

What if, on the other hand, a highly profitable drug caused this much disease and death? To no one's surprise, the FDA's response is to do the equivalent of nothing.

As we learned long ago, the FDA too often functions to protect the financial interests of pharmaceutical companies. The FDA's intentional inaction in this instance proves that this agency couldn't care less about how many Americans suffer and die each year.

Many people assume that over-the-counter medications are safe when taken as directed. Yet even at recommended doses, aspirin can cause ulcers, antihistamines can cause sedation, and acetaminophen can cause serious liver damage.

You can read about some of these risks in the product information that accompanies over-the-counter medicines. For example, the acetaminophen package insert warns about taking the drug if you consume three or more alcoholic drinks a day. The link between acetaminophen, alcohol, and an increased risk of liver damage was identified in the 1980s. This research identified another factor that can increase the risks associated with acetaminophen: fasting. This can refer to fasting due to abdominal upset or pain, nausea, vomiting, loss of appetite, anorexia, or malnutrition. Consider this case published in 1992:

> A 25-year-old, healthy Swedish man developed gastroenteritis while on holiday in Turkey. For a day and a half before flying home, the man experienced nausea and vomiting, and he was unable to keep food or liquid down. Noticeably ill during the flight, upon landing he was taken directly to a hospital. As his condition worsened, he was diagnosed with liver failure and transferred to await a liver transplant. Information from his brother, who had been with him in Turkey, indicated that the patient had taken 500 mg to 1,000 mg of acetaminophen two to three times each day, with a maximum total intake of 5,000–6,000 mg over two days. Unexpectedly, the patient's condition began to improve, liver transplantation was canceled, and he was discharged ten days later.

What had the Swedish man done wrong to develop liver failure? Nothing. His use of acetaminophen was within the recommended dosage range. The maximum recommended dosage of acetaminophen is 4,000 mg/day. The man took only 2,000 or 3,000 mg/day. He took acetaminophen merely to ease the pain of acute gastroenteritis, as do thousands of people each day. He followed the rules but nearly died.

The doctors presenting this case concluded that liver toxicity "can occur after low, repeated doses of acetaminophen." They added, "The drug should not be used under conditions of starvation, including acute gastroenteritis with nausea and vomiting." Yet today, despite this report and many others, acetaminophen products do not list a warning against using the drug when unable to eat.

A POWERFUL LIVER TOXIN

Many drugs can cause liver damage, liver failure, and death. Yet, acetaminophen prompts the most calls to poison control centers—more than 100,000 per year. Each year, acetaminophen accounts for about 56,000 emergency room visits, 26,000 hospitalizations, and more than 450 deaths from liver failure.Acetaminophen causes more cases of acute liver failure than all other medications combined.

In comparison to the millions of people who take acetaminophen each day without harm, the occurrence of liver failure and death is relatively rare. Still, many experts believe the numbers are too high and must be reduced. Dr. William Lee, a highly respected expert on acetaminophen, wrote, "It still must be asked: Is this amount of injury and death really acceptable for an over-the-counter pain reliever?"

UNINTENTIONAL OVERDOSES TAKE A HEAVY TOLL

Another daunting statistic about acetaminophen is that nearly half of all overdoses are unintentional. These people do not intentionally take excessive amounts of acetaminophen; instead, they lose track of the amount they are taking and inadvertently take more than recommended.

Other individuals intentionally take 5,000–8,000 mg/day of acetaminophen because their pain is not relieved by the recommended doses. These people are not trying to harm themselves,

but merely seeking relief from pain and are not aware that doses even slightly above the maximum therapeutic dose of 4,000 mg/day can be toxic.

REQUESTS FOR BETTER WARNINGS IGNORED

In addition to its alcohol warning, over-the-counter acetaminophen packaging also warns against use "with any other product containing acetaminophen." Unfortunately, this weak warning does not convey the serious risks of acetaminophen overmedication, even at slightly elevated doses. Overuse can cause liver injury, liver failure, and death, but you would never know it by reading the information provided with acetaminophen products.

Despite calls for better warnings, nothing has changed. Over the years, the FDA has intermittently voiced a desire to reduce the number of cases of acetaminophen toxicity. In 2004, the agency launched an educational campaign on the safe use of over-the-counter medications. This initiative appears to have had no impact on acetaminophen statistics. Since then, a large study has been published demonstrating that therapeutic doses of acetaminophen cause liver injuries in a substantial number of users, and has raised serious questions about the safety of therapeutic doses of acetaminophen.

In 2007, an FDA medical officer revealed that the staff of the FDA's Office of Surveillance and Epidemiology (formerly Office of Drug Safety) had recommended initiating measures similar to those adopted in Great Britain to reduce acetaminophen toxicity. These measures include limiting the number of acetaminophen pills in a package and packing the pills individually in foil packs. This recommendation never reached the FDA's Nonprescription Drugs Advisory Committee, where it could have been considered and approved.

Recently, in response to a scathing report by the Institute of Medicine, the FDA has made a lot of noise about enhancing its

efforts to promote drug safety. Until proven otherwise, the FDA's promises are hollow. The tilt of the FDA will continue to be in favor of the drug industry. For years, the FDA has understaffed and underfunded its safety divisions. It has not been unusual for high-ranking FDA officials to approve new drugs despite serious concerns of FDA medical officers about the drugs' safety. Indeed, just recently another article critical of the FDA was published in the *New England Journal of Medicine* (September 6, 2007), in which Dr. Sheila Weiss Smith concluded that the FDA's actions once again underscored "the low priority it assigns to its responsibility for arbitrating drug safety."

FDA IGNORES ITS OWN GUIDELINES

With acetaminophen, FDA officials have long ignored their own regulations. FDA guidelines require drug companies to list adverse drug events if: 1) they are serious; 2) they occur in close proximity to using the drug; and 3) they are consistent with a drug's known effects. Acetaminophen fits all of these requirements. In addition, animal studies provide ample evidence of a link between fasting, acetaminophen use, and liver failure.

Moreover, a recent report demonstrated the link between acetaminophen, fasting, and liver toxicity. Doctors were at first puzzled why a nine-month-old child had developed liver toxicity after only two days of therapeutic doses of acetaminophen. Laboratory analysis revealed that the child had a genetically determined glutathione deficiency, causing her glutathione activity to be only 5% of normal. Without adequate glutathione, standard doses of acetaminophen were toxic in this child. The case provides human evidence that markedly decreased glutathione activity, which can also be caused by fasting, increases the risk of acetaminophen liver toxicity in humans.

FDA guidelines also state that rare, serious adverse events should be listed in product information "even if there are only

one or two reported events." The first cases linking acetaminophen, fasting, and liver toxicity were reported in the 1980s. More than 20 years have passed, during which time many more cases have been published. Where is the warning? Where are the meaningful measures to improve acetaminophen safety?

Perhaps the FDA's inaction is related to resistance by the largest producer of acetaminophen products (McNeil Consumer Health, Tylenol® products) to implement a fasting warning and other safety measures. Acetaminophen is a widely used drug that generates more than two billion dollars per year in sales in the US. Additional warnings might undo acetaminophen's reputation as the safest over-the-counter pain and fever remedy, and safety packaging might depress sales.

EXCERPT FROM

Life-Saving Cancer Drugs Not Approved by the FDA

For the past 27 years, Life Extension has identified life-saving medications that languished too long in the FDA's archaic approval process.

When effective new drugs are delayed, the inevitable consequence is needless human suffering and death. An equally insidious problem is the chilling effect bureaucratic roadblocks have on the development of better drugs that might actually cure the disease.

Just imagine the difficulty of raising the tens of millions of dollars needed to get a new cancer drug into the approval pipeline when prospective investors see the FDA deny a drug with documented efficacy, as was done recently with Provenge®.

Another problem with the FDA's unpredictable approval pattern is the outrageous cost of the cancer drugs that actually make it to market. Even when classes of cancer drugs are finally approved, the out-of-pocket cost of these new drugs can exceed $12,000 per month. The media has reported on heart-wrenching stories of cancer patients who choose to die rather than send their families into bankruptcy from paying these costs.

It's easy to point fingers at drug companies for charging such extortionist prices, but the harsh reality is that getting these medications approved by the FDA is so costly and risky that the high prices can arguably be justified by the hideously inefficient drug approval process that now exists.

There are many drugs that have been shown to be effective against cancer, but are not yet approved by the FDA. While there are dozens of anti-cancer drugs in various stages of the approval process, the sad truth is that thousands of compounds with anti-cancer activity will never be submitted for FDA approval due to lack of patentability, lack of investor funding, or just plain unwillingness to deal with today's cancer bureaucracy.

HOW THE FDA APPROVAL PROCESS WORKS

The clinical trial procedure depends on the ability of the pharmaceutical company to finance clinical trials and to recruit patients to participate in them. Many promising trials need to be halted due to lack of adequate funding or inability to recruit enough patients to make up an acceptable group of patients to form the study and/or control groups.

Clinical trials on promising anti-cancer drugs are done in three phases, with Phase I trials being conducted to establish dose-limiting toxicity, Phase II trials proceeding to establish effectiveness in a limited number of patients, and Phase III trials advancing to include widespread study populations and to gather data to make comparisons between the effectiveness of the new

treatment versus current protocols. Normally, application to the FDA (a New Drug Application, or NDA) for approval takes place after Phase III clinical trials have demonstrated that the new agent, procedure, or protocol is superior to the current standard of treatment in terms of effectiveness and/or tolerability. Only after FDA approval can the new drug or treatment be marketed and made available to the general public, even if such a treatment is approved in another country considered to have advanced medical care by our standards. Medicine clearly has geographical boundaries—drugs and devices approved in the USA may not be approved 10 feet beyond the US border into Canada, and vice versa. Drugs such as Taxotere®—considered to be the most active agent in breast, prostate, head and neck and lung cancer and an approved drug in Europe—were not made available to cancer patients in the USA until the FDA granted its approval. This "process" took approximately five additional years.

AN INTERIM PROPOSAL FOR FDA REFORM

Cancer patients should have access to drugs and technologies that have shown minimal toxicity, but that have shown efficacy based on peer-reviewed literature and formal presentations at recognized medical conferences. Such drugs and/or technologies could be granted a "semi-approval status" by the FDA with the implication that at some future date they could be granted full FDA approval.

The conditions for availability of such drugs and technologies would involve:

- Patient access to drugs with evidence of significant activity and safety.
- Pharmaceutical company ability to charge for agents without jeopardizing economic solvency, while agreeing to cost reductions of agents resulting from semi-approval status.

- Ongoing collection of complete and accurate data by designated physicians that is submitted for review.
- Physician reimbursement for services in delivering therapies.
- Legal counsel preparing documents to eliminate risk of litigious actions. Patients wanting access to agents must assume risks and waive access to liability.
- Creating task forces consisting of scientists, consumers, and other relevant individuals involved in a quarterly review process of clinical data.

EXCERPT FROM

FDA Drops the Ball on Avandia® Warning

THE FDA CAME UNDER RENEWED CRITICISM RECENTLY, WHEN it was revealed that warnings by its own safety committee regarding a popular diabetes drug were ignored by the regulatory agency.* FDA safety staff had recommended that prescribing information for the type 2 diabetes drug, Avandia® (rosiglitazone), should include a so-called "black box" warning—the FDA's most dire alert—indicating that the drug might put some patients at increased risk of congestive heart failure. But the FDA ignored that recommendation.

Instead, the warning is buried on line 351 of the label, noted Senator Charles Grassley (R–IA), whose staff investigated the FDA's inaction. The investigation was prompted by the publi-

* There are numerous other examples of FDA-approved drugs (like Vioxx® and Rezulin®) which were subsequently discovered to be dangerous or even to cause death. Please refer to the Index under "FDA-approved drugs, dangerous."

cation of an analysis of the drug's cardiovascular risk profile in the prestigious *New England Journal of Medicine* in May. In that analysis, researchers from the Cleveland Clinic concluded, "Rosiglitazone was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes."

EXCERPT FROM

FDA Threatens to Raid Cherry Orchards

As Americans struggle to eat a healthier diet, the FDA has taken draconian steps to suppress information about foods that reduce disease risk.

While various agencies of the federal government encourage us to eat more fruits and vegetables, the FDA has issued an edict that precludes cherry companies from posting scientific data on their websites. This censorship of published peer-reviewed studies denies consumers access to information that could be used to make wiser food choices.

FDA INTIMIDATES CHERRY GROWERS

There is not much profit in selling fresh fruits and vegetables. Growers of such foods cannot afford to advertise their produce in a meaningful way. Fortunately, the advent of the Internet has allowed cherry growers to enlighten the public about scientific studies showing that nutrients contained in cherries have significant health benefits. Until recently, consumers could learn of the health benefits of cherries just by logging on to a cherry company's

website. Some individuals might be impressed enough with this data to actually buy cherries at the grocery store instead of trans fat-laden snacks being advertised every second in the mass media.

On October 17, 2005, the FDA banned information about cherries' health benefits from appearing on websites. The FDA sent warning letters to 29 companies that market cherry products. In these letters, the FDA ordered the companies to stop publicizing scientific data about cherries. According to the FDA, when cherry companies disseminate this information, the cherries become unapproved drugs subject to seizure. The FDA warns that if those involved in cherry trafficking continue to inform consumers about these scientific studies, criminal prosecutions will ensue.

WHY AMERICANS DON'T EAT MORE FRUIT

The processed food industry has earned enormous profits by loading cheap and dangerous foods with sugar, salt, preservatives, trans fats, saturated fats, and other unhealthy byproducts. Processed foods taste good to most people and are quite inexpensive compared to fresh produce. In order to convince the public to switch from toxic foods that damage the arterial wall, mutate DNA, and induce age-related disease, those who sell fresh fruits need to inform the public about the benefits scientists have discovered about plant foods.

Fresh fruit can be expensive and it spoils relatively quickly. Many consumers have developed a taste addiction to processed foods, and find it challenging to switch to a healthier diet that costs more and is not as pleasing to the palate.

By censoring scientific information about cherries, the FDA is in effect shutting down an opportunity for more Americans to learn about the remarkable health benefits that have been discovered about this fruit.

DO CHERRIES PREVENT CANCER?

In a warning letter to Friske Orchards of Ellsworth, MI, the FDA recites the following information contained on this orchard's website: "Tart cherries may reduce the risk of colon cancer because of the anthocyanins and cyanidin contained in the cherry."

The FDA goes on to say in its warning letter:

> These claims cause your product to be a drug as defined in section 201(g). . . . Because this product is not generally recognized as safe and effective when used as labeled, it is also defined as a new drug in section 201(p). . . . Under section 505 of the Act (21 USC 355), a new drug may not be legally marketed in the United States without an approved New Drug Application. . . .

Interestingly, the FDA is not denying the veracity of this information. Instead, it insists that a new drug application has to be approved before the public can be informed about the scientific data supporting cherries. The FDA also asserts, without any basis, that cherries "have not been recognized as safe and effective when used as labeled." According to the FDA's interpretation of the law, cherry growers are engaged in criminal conduct by relaying findings that have been published in peer-reviewed scientific journals. Whether you or other Americans develop cancer does not appear to be a consideration of an agency whose written mission statement includes the following:

> The FDA is responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

It would appear that the FDA is concerned that if too many arthritis sufferers discover that eating cherries could alleviate

inflammation and pain, the multibillion-dollar market for anti-inflammatory drugs would be detrimentally affected. Pharmaceutical industry profits have been spared for the moment by the flagrant acts perpetrated against cherry companies by the FDA.

EXCERPT FROM

Drug Makers Abuse FDA Approval Process

MOST DRUG COMPANIES BENEFITING FROM THE FDA'S "ACCELerated approval" process—a means of expediting approval of drugs intended for patients with life-threatening illness—have not conducted legally required post-marketing studies on their products, according to Rep. Edward J. Markey (D-MA).

Created in 1992, the FDA's accelerated approval process uses preliminary data indicating drug safety and efficacy to help bring drugs to the marketplace more quickly. This process greatly reduces the typical 10-to-15-year time period required to conceive, develop, and thoroughly test new drugs in animals and humans. In return for the enormous marketing advantages realized by drug makers, it was agreed that rigorous studies validating the preliminary data would continue in accordance with normal approval procedures.

Released on June 1, 2005, Rep. Markey's report, *Conspiracy of Silence: How the FDA Allows Drug Companies to Abuse the Accelerated Approval Process*, reveals that at least 17 drug companies have not completed the FDA-required post-marketing studies. Of the 91 post-marketing studies promised since 1992, only 49 have been completed. Of the 42 pending studies, half have not even

been initiated, though some of the approved drugs have been on the market for years; three are in progress but behind schedule; and only 18 are currently meeting scheduled milestones.

Although the FDA has the authority to withdraw drugs from the market in the absence of supporting data, it has not done so in any cases. The need for post-approval studies is well illustrated by AstraZeneca's Iressa®, approved in May 2003 to treat non-small cell lung cancer. While preliminary data suggested that Iressa® would benefit 10% of patients, the FDA's review of the mandated follow-up studies by AstraZeneca concluded that Iressa® provided no survival benefit and that patients taking it should discuss treatment alternatives with their physicians.

The FDA must enforce its requirements for post-marketing studies by drug makers in order to protect public safety.

EXCERPT FROM

Inside the Vioxx® Debacle

On a crisp November day in 2004, Dr. David Graham, a senior FDA scientist, asked members of the US Senate Finance Committee to imagine the unimaginable.

"What would you do if two to four aircraft had crashed, killing all aboard, every week for the past five years?" he asked. "What would you want to know? And what would you do about it?"

Of course, airline safety was not Dr. Graham's concern that day. He was referring to the biggest prescription drug scandal in history: the approval and continued use of the pain drug Vioxx®. And he was talking about the campaign of harassment and intimidation waged against him by senior FDA officials when he tried to alert the public to the dangers associated with Vioxx®.

Before it was removed from the market in late 2004, Vioxx® had been implicated in about 160,000 cases of heart attack and stroke in the US between 1999 and 2004—the equivalent of 100,000 unnecessary deaths.

A CATASTROPHE IN THE MAKING

When Vioxx® gained FDA approval in 1999, it was hailed, along with Pfizer's pain drug Celebrex®, as a miracle drug for people suffering from chronic arthritis. Merck marketed Vioxx® as an effective painkiller that did not cause the gastrointestinal side effects of other common pain drugs such as aspirin or ibuprofen.

Even before Vioxx® was approved, however, there were clear warnings that it was linked to heart attack and stroke. Nevertheless, the drug hit the market in a flurry of consumer advertising and favorable media coverage. Between 1999 and 2004, more than 20 million Americans took Vioxx®.

But the evidence against Vioxx continued to accumulate. Finally, in September 2004, a study was released linking chronic Vioxx® use to increased rates of heart attack and stroke. Merck halted the study early when researchers uncovered the cardiovascular risk associated with Vioxx®.

The public outcry was immediate and enormous. In the days following the announcement, Merck's shares tumbled and the Vioxx® story was front-page news across the country. On September 30, Merck voluntarily withdrew Vioxx® from the market. The company today faces hundreds of lawsuits over Vioxx® and about $2 billion a year in lost revenue.

But the fallout over Vioxx® did not stop with Merck. Attention soon turned to the FDA, who is responsible for ensuring that dangerous drugs like Vioxx® do not make it to the market. Yet somehow, Vioxx® had slipped through the system. Worse, there were indications that the FDA had actively tried to protect Vioxx® despite evidence that it was dangerous.

Even before the drug was approved, an internal Merck study had found a sevenfold increase in heart attack risk associated with low-dose Vioxx®. A year later, another internal Merck study linked high-dose Vioxx® to heart attack and stroke. The company tried to explain away the results, but its argument was unconvincing. Not long afterward, the nonprofit public interest organization Public Citizen recommended that people stop taking Vioxx®.

Given its role as a protector of the public, the FDA should have taken action based on this information alone. Indeed, in 2000, after the second Merck study, a mild warning was added to the Vioxx® label concerning the dangers of high-dose Vioxx®. But the agency implemented no ban, and sales of high-dose Vioxx® were not affected.

FINDINGS PROVOKE FDA INTIMIDATION

Worried about the mounting evidence against the drug, Dr. Graham, associate director for the Office of Drug Safety and a 20-year FDA veteran, launched a study of Vioxx® in 2001. His team included researchers from California-based Kaiser Permanente and the Vanderbilt University School of Medicine in Nashville, TN. They analyzed data from 1.4 million people in California who had taken Vioxx® between 1999 and 2004.

They worked for three years, compiling data. Finally, in early August 2004, almost two months before Vioxx® was removed from the market, Dr. Graham completed the study. The results were explosive—his team found that high-dose Vioxx® increased heart attack risk 3.7-fold, while low-dose Vioxx® increased the risk 1.5-fold.

Dr. Graham prepared his findings for presentation at the International Conference on Pharmacoepidemiology in Bordeaux, France. He concluded that high-dose Vioxx® should not be prescribed or used by patients. As part of normal FDA procedure,

he submitted this conclusion for internal review by the FDA. His superiors did not react favorably.

"These conclusions triggered an explosive response from the Office of New Drugs," Dr. Graham told the Senate committee, referring to the FDA office responsible for granting new drug approvals. "The response from senior management in my office, the Office of Drug Safety, was equally stressful."

Instead of acting to protect the public, FDA officials at the highest levels lashed out at Dr. Graham. He was intimidated, pressured to change his conclusions, and forced to delay publication of his study. One senior FDA official even wrote to the editorial board of the prestigious British medical journal *The Lancet*—which had accepted the study for publication in September 2004—raising questions about the integrity of Dr. Graham's research. As a result, *The Lancet* delayed publication of the study for more than three months.

Internal emails show that FDA officials even wanted Dr. Graham to send his results to Merck before the study's release.

After being repeatedly attacked by senior staff members at the FDA, Dr. Graham finally responded in an email to Dr. Paul Seligman, director of the Office of Pharmacoepidemiology and Statistical Sciences, stating, "I've gone about as far as I can without compromising my deeply held conclusions about these safety questions."

Nevertheless, they had gotten to him. When Dr. Graham presented his findings in France, he had altered his conclusion about high-dose Vioxx®. The FDA later used this as evidence that Dr. Graham had questioned his own research. Agency spokespeople announced that Dr. Graham had "voluntarily" changed his conclusions.

According to Dr. Graham, however, the real story was somewhat different. "There's voluntary and there's voluntary," he explained in an exclusive interview with *Life Extension*. "If some-

one puts a gun to your head and says, 'Sign over your house,' and you sign over your house, that's technically voluntary."

Dr. Graham said he changed his conclusions because the information was so important that it overshadowed his own convictions.

"They weren't going to allow me to go to France with my conclusion the way it was," he said. "I decided it was more important to get this information out into the scientific community than to make my conclusion what I really believed. The FDA can maintain it was voluntary, but the fact is, if it was voluntary, the conclusions would have remained."

By attacking Dr. Graham, the FDA was doing everything within its power to withhold this damaging information from the public for as long as possible. Even after Vioxx® was withdrawn, the FDA was slow to act. On November 2, 2004—the day of the US presidential election—the FDA quietly posted Dr. Graham's study on the Internet. By then, Vioxx® had already been off the market for more than a month.

THE TOLL: 100,000 NEEDLESS DEATHS

In Dr. Graham's view, the FDA is to blame for as many as 100,000 needless deaths due to Vioxx®. Although Merck was responsible for defending its drug in light of the mounting evidence against it, the FDA's job is to guarantee that prescription drugs approved for sale in the US meet the highest safety standards. By any standard, the FDA failed that responsibility.

"The FDA has let the American people down, and sadly, betrayed a public trust," Dr. Graham told members of the Senate Finance Committee. "We are talking about a catastrophe that I strongly believe could have, should have been, largely avoided. But it wasn't, and over 100,000 Americans have paid dearly for this failure."

As of this writing, Dr. Graham is still employed at the FDA, as associate director of the Office of Drug Safety. However, he told

Life Extension that his life has been "surreal" since the Vioxx® scandal broke. His superiors have ostracized him, and every day he has to face the same people who tried to destroy him professionally for simply telling the truth about Vioxx®.

"It's very difficult," he said. "I periodically have to sit down with supervisors who I knew in November were lying to Congress about me, lying to *The Lancet* about me, and who tried to prevent my getting protection as a government whistleblower. They were doing hateful things, and now they pretend nothing happened."

Dr. Graham hopes that his testimony and experience will be the first steps in reforming the FDA—and there are some hopeful signs. Following Dr. Graham's testimony, Senate Finance Committee Chairman Charles Grassley (R–IA) issued a blistering statement:

> Americans rely on scientists at the FDA as frontline defenders to ensure the safety of prescription drugs. . . . A giant pharmaceutical company, which announced a voluntary global recall in September, said studies showed the use of its multibillion-dollar Vioxx® could put cardiovascular health at risk. And now it appears the FDA did nothing about mounting evidence that suggested this risk. . . . My bottom line is this: The FDA must remember its mission. To put the public health and safety first and foremost. The American people must be the FDA's first and only concern.

Other signs, however, are less promising. At various times since the Vioxx® scandal broke, FDA officials have "categorically denied" Dr. Graham's charges or, alternatively, tried to argue that because all prescription drugs pose some degree of risk, the agency was not lax in its oversight of Vioxx®. The road ahead to true FDA reform appears to be long and difficult.

VIOXX®: TIP OF THE ICEBERG?

The situation might not be so bad if Vioxx® were an isolated case. But it is not. In recent years, other FDA scientists have come forward with their own stories. Unfortunately, the treatment they received was no better than the intimidation directed at Dr. Graham.

"I wasn't surprised at the FDA's reaction because the tradition at the FDA has been to react negatively to new information that illustrates how the FDA's policies are inadequate or wrong," Dr. Graham said. "When you illustrate that the FDA's policies are harmful, the reaction is negative and immediate."

In fact, Dr. Graham was the second FDA scientist to appear before the Senate Finance Committee in late 2004. The first was Dr. Andrew Mosholder, an FDA epidemiologist who testified last fall that FDA superiors had asked him to soften recommendations concerning antidepressants.

In 2004, Dr. Mosholder conducted a meta-analysis of 22 studies on the use of antidepressants in children. His research showed that children who took antidepressants, such as Prozac® and Zoloft®, were twice as likely to become suicidal as children who took a placebo.

Once again, however, senior FDA officials intervened before Dr. Mosholder could make his results public. Dr. Mosholder was told to alter his research findings in material that was submitted to Congress, and was threatened with disciplinary action by the FDA's Office of Internal Affairs if he went to the media. On another occasion, he was barred from testifying at a public hearing on antidepressants and children.

And once again, there had been warning signs. According to the Senate investigation, the link between antidepressants and children had been studied since 1996, yet no drug label changes were made and no drugs were taken off the market.

"There is something terribly rotten at the FDA," Rep. Peter Deutsch (D-FL) told the *Los Angeles Times* after Mosholder's testimony. "No agency charged with protecting the public health should have behaved with such indifference."

The only thing unusual about these cases is that they became public, according to Dr. Graham. In fact, without urgent reform at the FDA, it seems almost inevitable that another Vioxx®-sized disaster will occur. Dr. Graham himself has identified several other drugs that demand immediate action:

- Meridia®, used for weight loss, has been associated with high blood pressure and stroke.
- Crestor®, used to lower cholesterol, has been associated with renal failure and other serious side effects.
- Accutane®, used to treat acne, has been linked to birth defects, and Dr. Graham believes its sale should be restricted immediately.
- Serevent®, used to treat asthma, can actually aggravate and cause death due to asthma.

Dr. Graham, along with other consumer groups such as Public Citizen, are calling on the FDA to scrutinize other COX-2 inhibitors, such as Bextra® and Celebrex®. In late January 2005, Public Citizen filed a petition with the FDA, demanding that it remove Bextra® and Celebrex® from the market.

"The Food & Drug Administration should immediately ban the sale of Celebrex® and Bextra®, which put millions of people, many of them elderly, at risk of heart attack," said Dr. Sidney Wolfe, director of Public Citizen's Health Research Group. "These drugs are not only more expensive and more dangerous than older, safer pain relievers, they are no better at protecting the gastrointestinal tract."

Even the FDA's own scientists lack faith in the agency's ability to protect the American people. December 2004 saw the release

of a previously unpublished FDA internal management review, in which 846 FDA scientists were asked to complete an extensive survey. About half answered. The study found that:

- Two-thirds of FDA scientists lack confidence that the agency "adequately monitors the safety of prescription drugs once they are on the market."
- More than a third (36%) were not at all or only somewhat confident that "final decisions adequately assess the safety of a drug."
- Nearly 20% said they "have been pressured to approve or recommend approval [for a drug] despite reservations about the safety, efficacy, or quality of the drug."

With findings like these, it is no wonder the FDA tried to prevent the survey from ever seeing the light of day. In fact, it might never have been made public if not for the efforts of two public interest groups, Public Employees for Environmental Responsibility (PEER) and the Union of Concerned Scientists (UCS).

"Many concerns had been raised about the manipulation of science within the [Bush] administration," said Suzanne Shaw, UCS director of communications. "There had also been concerns raised at the FDA. In thinking about how to design a tool to get more data, we heard about the survey. But when we tried to see the actual results, we were told we couldn't see the report."

Eventually, it took a request under the Freedom of Information of Act to pry the report loose from the FDA.

SERVING DRUG COMPANIES, NOT THE PUBLIC

Dr. Graham is certain that without urgent reform, Vioxx® is only the beginning of the disasters that will flow from FDA incompetence and arrogance. Congress must act, because the FDA's problems are so fundamental that nothing except reform forced on

the agency from the outside can work.

The basic problem, according to Dr. Graham, is that the FDA does not serve the American public, but instead serves the pharmaceutical industry.

Under FDA regulations, pharmaceutical companies submit new drugs to the FDA's Office of New Drugs. These companies are always racing against time because their drugs are protected by a patent for only 17 years, which includes the time it takes to get the drug approved in the first place.

To speed drug approval, the FDA charges fees to pharmaceutical companies during the approval process. The fees help "expedite" the complicated but required evaluation of human and animal studies. This means that the FDA accepts money from the very industry it is supposed to regulate.

"You want to be evidence based, but the FDA would rather suspend its judgment so it can better serve its clients: industry," said Dr. Graham.

This process results in a biased flow of information, dictated almost entirely by pharmaceutical companies. During the approval process and afterward, the drug makers are not required to release studies that reflect poorly on their drugs.

"There's no incentive for the company to do post-marketing studies," said Dr. Graham. "They've already been given a free pass on safety. It's all downside for the company, and the FDA has no incentive to do post-marketing studies because it only cares about getting new drugs on the market. The FDA's main client is industry."

As Dr. Graham's story demonstrates, once questions are raised, the Office of New Drugs is willing to say or do virtually anything—including pressuring its senior scientists to alter their conclusions, and even trying to destroy their careers and reputations—to protect drug company interests.

As long as the FDA remains beholden to the pharmaceutical

companies, financially and otherwise, it will be unable to protect the American public. Considering the FDA's recent history, there is no reason to believe the agency can reform itself. The only real hope is that Congress will act to dismantle and rebuild the FDA from the ground up.

"Right now, it's the FDA's fault, but if it happens again, Congress will be partly responsible," said Dr. Graham. "I'm an idealist. I hope people can rise above their political philosophy and unite to create a system of drug safety. If they don't unite, another disaster will come, and it might be a family member of someone in Congress. Then they will become believers. The men and women in Congress need to understand that these are people's lives."

EXCERPT FROM

FDA Permits New Fish Oil Health Claim

IT WAS LONG AGO ESTABLISHED THAT CONSUMPTION OF COLD-water fish reduces the risk of heart attack. In fact, just two to three servings of fish a week may protect against many diseases, including arthritis, stroke, certain cancers, and a host of inflammation-related disorders.

When scientists sought to discover which components of fish are responsible for preventing heart attacks, they found that the oil plays a critical role. Coldwater fish oil is high in omega-3 fatty acids that function in multiple ways to reduce cardiovascular disease risk.

Based on the published scientific evidence about fish oil, a lawsuit was filed against the FDA in 1994 by Durk Pearson and Sandy

Shaw, seeking to force the agency to allow the following health claim on fish oil supplement labels: "Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease." The FDA rejected this one-sentence claim and a multiyear litigation battle ensued.

In their lawsuit, Durk and Sandy pointed out that consumers would benefit by learning of the value of fish oil in protecting against heart disease. They also argued that the FDA lacked the constitutional authority to ban this truthful health claim.

The FDA contended that this health claim was not adequately backed by scientific studies and that the agency had the legal authority to ban these kinds of health claims.

Seven years of extensive litigation ensued as the FDA asserted that it had the sole authority to dictate what Americans could read on the label of fish oil supplements. After an onslaught of irrefutable scientific evidence was presented, including articles published in the most prestigious scientific journals in the world, the FDA capitulated and said it would permit the following claim:

> Consumption of omega-3 fatty acids may reduce the risk of coronary heart disease. FDA evaluated the data and determined that although there is scientific evidence supporting the claim, the evidence is not conclusive.

LIFE EXTENSION CHALLENGES FDA ON FISH OIL HEALTH CLAIM

The FDA's compromise health claim that the evidence was "not conclusive" did not satisfy the Life Extension Foundation. The scientific literature provided overwhelming validation that consuming coldwater fish or fish oils dramatically lowers heart attack risk. To substantiate this position, a massive document enumerating the scientific studies backing the benefits of omega-3 fatty

acids was filed, along with legal arguments supporting the constitutional right to disseminate this truthful information.

On September 8, 2004, the FDA announced that it would allow an expanded health claim on products containing the omega-3 fatty acids eiscosopentaenoic acid (EPA) and docosahexaenoic acid (DHA).

According to Acting FDA Commissioner Dr. Lester M. Crawford, "Coronary heart disease is a significant health problem that causes 500,000 deaths annually in the United States. This new qualified health claim for omega-3 fatty acids should help consumers as they work to improve their health by identifying foods that contain these important compounds (EPA and DHA)."

The FDA now permits the following statement to be printed on the label of fish oil supplements: "Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids may reduce the risk of coronary heart disease."

The FDA went on to recommend that consumers not exceed more than 3 grams per day of EPA and DHA omega-3 fatty acids, with no more than 2 grams per day derived from a dietary supplement. Life Extension argues that many scientific studies show that higher amounts of EPA and DHA are often needed to obtain optimal benefits, such as reduction of triglycerides and prevention of restenosis (re-occlusion of a blocked artery).

This battle over what can be stated about fish oil began back in 1994. While the FDA's announcement of a broader health claim represents a significant legal victory, Life Extension is still not satisfied with the FDA's latest health claim on fish oil supplements. We reiterate our position that evidence from peer-reviewed scientific publications supporting the benefit of EPA and DHA supplements in reducing heart attack risk is conclusive and not merely "supportive" as the FDA contends.

EXCERPT FROM

Medications Side Effects

PRESCRIPTION DRUGS HELP MILLIONS OF PEOPLE. STILL, MOST people don't like taking drugs, although many of us ultimately need to. So how can you get the treatment you need while minimizing the risks?

Mainstream medicine's record on preventing medication side effects is poor. A 1998 article in the *Journal of the American Medical Association (JAMA)* defined the scope of the problem: 106,000 deaths and 2,000,000 severe reactions from medications annually in US hospitals, making side effects the fourth leading cause of death in America. These numbers aren't new. The side effect problem has continued for decades and persists unrecognized by many doctors and authorities.

But patients understand. Patients' first concern about medications is safety. They know intuitively that, as a leading drug reference states, "Any drug, no matter how trivial its therapeutic actions, has the potential to do harm."

How can you maximize safety while getting the treatment you need? There are ways, ways in accordance with scientific principles and proven by medical studies, yet routinely ignored by drug companies, the FDA and doctors.

THE FIRST KEY TO AVOIDING SIDE EFFECTS

Side effects occur because most drugs aren't specific in their actions. We may call a drug an "anti-inflammatory" or "antidepressant," but medications don't just go to the cells involved in these problems. They go to most of the cells of our bodies, which can provoke undesirable effects. Thus, an anti-inflammatory may

reduce your joint pain, but it may also cause stomach bleeding, kidney failure or anxiety. An antidepressant can improve mood but can also cause insomnia, nausea, weight gain or diminished sex drive.

Most of these unintended effects—side effects—are dose-related. In the 1998 *JAMA* study cited above, 76.2% of all side effects were dose-related. *Melmon and Morrelli's Clinical Pharmacology* places the number at 75% to 85%. The number may be higher, because many drug interactions are also dose-related. When people take multiple drugs, higher doses cause more adverse interactions than lower doses. Whatever the actual number, the first key to avoiding side effects is this: The best way to avoid side effects is to use the lowest dose that works. Excessive dosing merely increases risks.

THE SECOND KEY: INDIVIDUAL VARIATION

Why do side effects occur in some people but not in others? Because people vary tremendously in their sensitivities to medications.

The American Medical Association states that the difference in people's response to a specific drug can vary "4-to 40-fold." So it isn't surprising that some people need 80 mg of the antidepressant Prozac® or the cholesterol-lowering drug Lipitor®, while others need just 2.5 mg.

INDIVIDUAL VARIATION WITH MEDICATIONS ISN'T THE EXCEPTION; IT'S THE RULE

The basis of individual variation is well known. People differ greatly in how they absorb, metabolize and eliminate drugs. The new science of pharmacogenetics has revealed wide variations in the efficiency of people's liver enzymes in processing drugs. People also differ in the sensitivity of their tissues to medication effects. These factors change with age, and many people become more sensitive as they get older.

Because of the great variability between people, it is essential for drug doses to be tailored to each person's needs. I call this precision prescribing. Doctors already practice this with a few drugs—digoxin, insulin, thyroid drugs—but not with most drugs. Many drugs are prescribed one-size-fits-all or at doses that are identical for young and old, big and small, healthy or taking six other drugs at the same time. The failure to match drug doses to individual needs underlies the high incidence of side effects.

CREATING A SIDE EFFECT EPIDEMIC

Drug companies and the FDA routinely ignore the wide differences in people's drug tolerances and the fact that most side effects are dose-related. Doctors, accepting uncritically drug company dosage guidelines, don't think twice about prescribing the same doses of powerful drugs to young and old, big and small, healthy and frail. They ignore patients with long histories of medication reactions. Cookbook dosing is the rule, and an epidemic of side effects is the result.

Even when studies show that half and quarter doses are effective, the data is ignored and dosing is one-size-fits-all. Even when studies show that women or the elderly respond to lower doses, they get the same higher doses as younger, larger men. Something is very wrong when Shaquille O'Neal, Ally McBeal and Grandma Moses are getting the exact same doses of potent drugs, yet this is exactly how many drugs are prescribed.

"To think that the same dose will do the same thing to all patients is absurd," says Dr. Raymond Woosley, Vice President of Health Services at the University of Arizona. "Patients need to be titrated, starting with the lowest possible dose that could have the desired effect."

Experts everywhere agree with him, but that's not how it's done today. The side effect epidemic isn't caused by a few bad drugs, but by bad dosing methods with many drugs.

DOSAGE PROBLEMS WITH ANTIDEPRESSANTS

Doctors follow the guidelines in the drug company-written *PDR*. The *PDR* still advises 75 mg initially for Elavil® (amitriptyline), yet 10 mg or 25 mg is frequently enough for mild depressions or pain syndromes. Effexor® is recommended at 75 mg, but 37.5 mg or 50 mg often is enough initially. Zoloft® is recommended at 50 mg, but 25 mg works well for many mild depressions. Serzone is recommended at 100 mg twice daily, but 50 mg once or twice daily is usually plenty initially.

Similar strategies apply to Paxil®, Wellbutrin®, Celexa®, Norpramin®, Pamelor®, imipramine, doxepin and just about every other antidepressant. "The sales representatives for most antidepressants are now giving out sample packs starting with half-strength doses," Dr. Anthony Weisenberger, a top psychopharmacologist, recently told me. "They lose so many sales because patients get side effects and quit treatment, the drug companies have finally caught on that the dose makes a big difference."

Why is this happening with drug after drug? One reason is that the standard doses of antidepressants are based on studies of major depression—a severe disorder that requires strong treatment. In contrast, the great majority of office patients with depression have mild disorders. Yet, no distinction is made about treating mild and severe disorders in the dosage guidelines of most antidepressants, so doctors prescribe the same doses to everyone.

DRUGS FOR ELEVATED CHOLESTEROL AND C-REACTIVE PROTEIN

The statins—Lipitor®, Zocor®, Pravachol®, Mevacor®, Lescol®—were the best-selling group of drugs in America in 2001. There's no doubt that statins help millions by reducing heart attacks, strokes and overall cardiac mortality. But statins harm thousands, perhaps millions more, often unnecessarily.

Duane Graveline's first dose of Lipitor® caused amnesia "so severe that I landed in the emergency room of a hospital near my Vermont home. I didn't remember any of it." Dr. Graveline, a retired family doctor, flight surgeon and astronaut, was perplexed. After all, he wasn't usually sensitive to medications, and he'd taken only 10 mg, the lowest dose recommended and marketed by the manufacturer.

Yet, 10 mg of Lipitor® is very strong, much stronger than many people need. It was much stronger than Dr. Graveline needed, because he needed only 2.5 mg of Lipitor®—75% less medication than he got. Experts advise doctors to select statin doses based on the reduction in LDL-C (the bad, low density lipoprotein-cholesterol) that each person needs. 10 mg of Lipitor® reduces LDL-C 39%, a strong response needed by cardiac patients and people with severely elevated cholesterol.

But most people with high cholesterol have mild-to-moderate elevations and no cardiac history, and they require only 20% to 30% reductions in LDL-C. This can be attained with only 2.5 mg or 5 mg of Lipitor®. Dr. Graveline required a 25% reduction in LDL-C and should have been started at 2.5 mg mg. Yet, there's no information about 2.5 or 5 mg of Lipitor® in the package insert or *PDR* and no pills in these doses, so doctors start everyone at 10 mg, or even 20 mg or 40 mg.

EXCESSIVE STATIN DOSES, UNNECESSARY SIDE EFFECTS

Dr. Graveline received 400% more medication than he needed and got a major dose-related side effect because of it. This is a common story. Cognitive and memory problems, sometimes severe and long lasting, occur far more often with statins than doctors recognize. Muscle pain and abdominal discomfort occur frequently. All of these are dose-related.

Liver disorders occur in 1% of patients taking statins. With statins now recommended for 35 million Americans, that's

350,000 people with liver problems, which include liver toxicity and, rarely, death. Dr. W. C. Roberts, the editor-in-chief of the *American Journal of Cardiology*, states, "With each doubling of the dose, the frequency of liver enzyme elevations also doubles." Liver enzyme elevations signify liver injury. So if you get 10 mg of Lipitor® when you only need 2.5 mg, your risk of liver injury is also quadrupled.

Lipitor® is the best-selling drug in America. In 2001, patients filled more than 57 million prescriptions for Lipitor®, and sales are skyrocketing. Zocor®, the third best-selling drug, presents the same dose problems as Lipitor®. Zocor's® standard starting dose, 20 mg, reduces LDL-C 38%. Many people need only 10 mg or even 5 mg, which reduce LDL-C 30% and 26%, respectively.If the standard doses of such widely advertised, top-selling drugs, are so strong, how can we rely on the standard doses of any drug?

DRUGS FOR HIGH BLOOD PRESSURE

Fifty million Americans have high blood pressure (hypertension), and 90% of us will ultimately develop this potentially deadly disease as we age. Hypertension is a particularly vicious disease, a silent destroyer of blood vessels that causes heart attacks, strokes, kidney disease, peripheral vascular diseases and erectile dysfunctions in men. Much of this is preventable with treatment. Yet half of the people starting treatment for hypertension quit within a year. Most do not last 90 days. Why? Medication side effects.

Experts acknowledge the problem: "Often, the cure is perceived as being worse than the disease, and when this is the case, the patient is unlikely to remain [in] treatment."

People get worn down by side effects such as dizziness, weakness, drowsiness, fatigue, diarrhea, muscle cramps and sexual impairments, and give up. Doctors often dismiss so-called "minor" side effects, but minor reactions drive millions from needed treatment—with dire consequences. There's a better solution.

LOWER DOSES RECOMMENDED BY EXPERTS

Because most side effects with antihypertensive drugs are dose-related, experts recommend starting with the very lowest effective doses. But what are they? Most doctors turn to the *PDR*, but the *PDR*'s doses often aren't the lowest. In an analysis I published in the *Archives of Internal Medicine* in 2001, I found that for 23 of 40 top-selling antihypertensive drugs, the initial doses recommended by the drug companies in the *PDR* were much higher than recommended by the Joint National Committee-the national board of medical experts on hypertension.

For example, the manufacturer's initial dose for Norvasc®, the fifth most prescribed drug in the US in 2001, is 5 mg. The experts recommend 2.5 mg, 50% less medication. The manufacturer of Capoten® (captopril) recommends 50 mg to 75 mg/day initially, 100% to 600% more than the 12.5 mg to 25 mg recommended by experts.

When Tenormin® (atenolol) was introduced in 1976, the one-size-fits-all dose was 100 mg. It wasn't until 1980 that a 50 mg dose was available and until 1989 that 25 mg was produced. The manufacturer still recommends 50 mg initially, 100% higher than the 25 mg recommended by the national board.

Similar over-dosing is seen with top-sellers Zestril®, Prinivil®, Altace®, Inderal® (propanolol), Cardura®, Cozaar®, and many others. Is it any wonder why so many people quit treatment?

Some savvy doctors recognize that starting with the lowest dose not only reduces risks, but allows people time to improve their diets, lose weight, start exercising and learn stress reduction or meditation. These methods not only lower blood pressure, but can reduce the amount of medication you need. As one specialist put it, "With blood pressure, it's easy to overshoot the mark. That's why I always start low and give people time to make other changes. Very often, their blood vessels relax over a

period of time and you wind up ultimately needing less medication. When I start with standard doses, we spend the rest of our lives combating side effects."

EXCEPTIONS

There are some drugs for which the low-dose approach does not apply. For example, antibiotics, antifungal and anticancer drugs should be used at full doses. These drugs are not targeting you, but invaders that can be made stronger if inadequate doses are used.

THE ELDERLY

"The overall incidence of adverse drugs reactions in the elderly is two to three times that found in young adults," states the *New England Journal of Medicine*. Although people over age 60 comprise 19% of the population, they account for 39% of all hospitalizations and 51% of all deaths related to medication reactions. Seniors metabolize drugs more slowly than younger people, so they are frequently more sensitive to their effects. That's why gerontologists recommend extra caution in treating seniors and starting with low doses. Yet, for scores of top-selling drugs, drug company guidelines tell doctors to use the same strong doses for young and old. Even when we know that blood levels of drugs rise much higher in seniors, doctors are told to ignore this fact and prescribe the same doses.

For example, Allegra® blood levels rise 99% higher in seniors versus younger adults. Claritin® rises 50% higher. Blood levels of top-selling antihypertensives Zestril® and Prinivil® rise 100% higher. Blood levels of Prilosec® and Nexium® are higher in the elderly. Yet, the recommended doses of all these drugs are the same for young and old.

The FDA itself states, "There is evidence that older adults tend to be more sensitive to drugs than younger adults, due to their generally slower metabolisms and organ functions. The old adage, 'Start

low and go slow,' applies especially to the elderly."Yet the FDA keeps approving drugs at identical doses for young and old. Perhaps this explains why 9% of all hospital admissions for seniors are related to side effects from standard doses of prescription drugs.

WOMEN

In summer 2002, two studies caused alarm by revealing increased risks of cancer and heart disease with Premarin® and Prempro®, the top-selling hormone replacement therapies (HRT) for menopausal women. The dose of estrogens in these drugs: 0.625 mg. But we've known for years that lower doses of Premarin® (0.3 mg) and other estrogens are often effective and cause fewer risks. Might these doses be safe enough today? Quite possibly, but the studies ignored this obvious question, leaving women in the lurch.

The studies also didn't mention that from 1964 through 1999, the recommended dose of Premarin® for hot flashes was 1.25 mg. How much cancer did this double dose cause? Why was such a strong dose approved in the first place? These questions weren't answered.

A similar pattern was seen with birth control pills. The hormone doses in the first pills were 300% to 1000% higher than in today's pills, yet it took decades—and hundreds of women's lives—before high-dose pills were withdrawn and replaced with today's lower doses.

Similar problems are seen with other medications. A study of ibuprofen for menstrual pain showed that 44% of women did just fine with the 200 mg over-the-counter dose, but the researchers still recommended 400 mg for all women. Studies of cholesterol-lowering drugs show that many women respond to lower doses, but they are routinely prescribed the same doses as men.

Side effects with antihypertensive drugs occur more often in women, which, according to the *American Journal of the Medical Sciences*, "could be due to the fact that women are treated with

antihypertensives using the dosage and schedule established with men, even though it is well known that body size, fat distribution and coronary artery size differ in women and men."Not all women require lower doses, but many do, especially small women. Why aren't doses developed for them? A 2001 report of the US General Accounting Office found not only that women are underrepresented in the dose studies, but even when dose differences are identified, they usually aren't reflected in the final dosage guidelines. A 2001 report by the National Academy of Sciences recommended additional attention to differences between men and women in diseases and treatments. The panel's report added that medical researchers often view men as the norm while underreporting rather than highlighting sex differences. Commenting on this report, Dr. Woosley added that many drug studies he sees "don't consider sex differences at all."

Is this important? In the US, 55% of women versus 37% of men take a prescription drug daily. And of the 11 drugs withdrawn in recent years, eight (maybe nine) affected women more than men.

ENTRENCHED PROBLEMS WITH THE MEDICAL–PHARMACEUTICAL COMPLEX

"It's long been known that for individual subjects the dosage listed on a drug label is not necessarily the right one," Dr. Carl Peck, the highly respected director of Georgetown's Center of Drug Development Science and a former division director at the FDA, stated in September 2002. This is a chilling, and accurate, comment. Yet, the medical—pharmaceutical complex-drug companies, FDA and mainstream doctors—maintain that our medications are as safe as possible. Clearly, this isn't the case.

PROBLEMS IN DRUG INDUSTRY RESEARCH

Why aren't drug doses designed to fit individuals and to prevent side effects? Strong doses produce higher efficacy numbers, which

are essential for introducing a new drug into a competitive market. Dr. Thomas Bodenheimer of the University of California, San Francisco, reported:

> Drug company studies are often done in younger, healthier populations—providing better rates of effectiveness and fewer adverse reactions—than those who will actually receive the drug.

Dr. Alexander Herxheimer, Professor Emeritus at the Cochrane Center in Britain, concurred in *Lancet*. "For quick market penetration, a drug must be simple to use and effective in the greatest number of people. Drugs are often introduced at a dose that will be effective in around 90% of the target population, because this helps market penetration. The 25% of patients who are most sensitive to the drug get much more than they need." With nearly 100 million Americans taking a prescription drug daily, that's 25 million people.

CONSEQUENCES OF A FLAWED SYSTEM

The failure of the system is revealed by disaster after disaster. "Discovery of new dangers of drugs after marketing is common," a 1998 study in *JAMA* declared. "Overall, 51% of approved drugs have serious adverse effects not detected prior to approval."

Another study disclosed that 20% of all new drugs ultimately require a new "black box" warning, indicating serious or fatal reactions. The study noted: "Serious adverse drug reactions commonly emerge after FDA approval. The safety of new agents cannot be known with certainty until a drug has been on the market for many years."

How can long-term side effects be minimized? By using the lowest, safest doses. For example, the jury is still out on the long-term safety of statin drugs, but already serious nerve injuries are being reported. A 2002 study found that "people who had taken

statins were 4 to 14 times more likely to develop" peripheral nerve injuries (tingling, numbness, shooting or electrical pain, muscle weakness). These reactions occur in one in 2,000 users of statin drugs per year. With 35 million Americans projected to take statins, that's 17,500 cases of peripheral neuropathies each year. Discontinuation doesn't always bring reversal. Most important, the risk is cumulative: the higher the dose, the greater the risk.

DOCTORS AND THE DRUG INDUSTRY

Some doctors are terrific. Some aren't. But even good doctors often don't have all of the information you'd like in order to make good dose decisions.

Doctors ultimately decide which drugs are successful, so doctors are in a position to demand better drug information, a wider range of drug doses to fit patients and better information about non-drug alternatives. Doctors can play a pivotal role, but so far they haven't demanded anything. Many doctors aren't even aware that a problem exists.

"There is an informational void about pharmaceuticals in the training of most doctors, despite the importance of the prescription in medical care," stated Harvard physician Jerry Avorn. "Most of those who have looked thoughtfully at this process have been appalled at its inadequacy."

The result is that doctor's knowledge of medications is less than ideal, which is directly linked to the high rate of side effects. "Much of the morbidity and mortality currently associated with drug therapy is due to well-recognized adverse effects and reflects our inability as health professionals to implement current knowledge fully," Dr. Alastair Wood, Vice Chancellor of Medical Affairs at Vanderbilt, wrote in 1998.

"If a medication doesn't work or causes side effects," a pharmacist told me years ago, "most physicians just switch from one to another, then another, then another, until they either find a drug

that works, or they or the patient give up. Very few physicians go to the trouble of adjusting drug dosages to fit their patients. Most don't deviate from the drug companies' recommendations."

"Doctors don't like to be challenged," a pharmacist wrote to me. "One doctor was prescribing Paxil® well above the highest recommended dosage. When I asked him about it, he said, "Are you a doctor? Who are you to be telling me what to do!"

Indeed, some doctors have difficulty admitting even common side effects listed in the *PDR*. Being defensive doesn't strengthen doctor-patient relationships. More and more, doctors are perceived as pill pushers and as defenders of the medical-pharmaceutical machine instead of their own patients.

EXCERPT FROM

Cancer-Causing Drug Tamoxifen Approved for Healthy Women

DESPITE WHAT YOU MIGHT HAVE HEARD, THE USE OF TAMOXI-fen for breast cancer prevention is highly controversial. Its long term effects on healthy women are unknown, while tamoxifen's cancer-causing properties raise considerable concern.

In a stunning move, the Food and Drug Administration approved the use of tamoxifen (Nolvadex®) chemotherapy for healthy women with no evidence of breast cancer. The approval came after almost two decades of wrangling over research that cost American taxpayers hundreds of millions of dollars, created fraud, prompted a congressional hearing, and spanned great controversy. The FDA's decision—announced on October 30, 1998—

allows Zeneca Pharmaceuticals to tap into a market potentially worth 36 billion dollars annually. The decision allowing the drug to be sold for breast cancer prevention was made despite objections from women's health organizations and researchers around the world. When the advisory committee recommending approval was asked whether the tamoxifen prevention study demonstrated that the drug had "a favorable benefit-risk ratio for the prevention of breast cancer in women at increased risk as defined by the study population," it said "no" unanimously. Yet, the FDA approved tamoxifen for healthy women anyway.

Tamoxifen is a synthetic estrogen blocker—one of many that have been around since the early '70s that once had potential as birth control pills. Like diethylstilbestrol (DES) tamoxifen blocks estradiol, but also like DES, it has estrogenic properties that cause cells to grow. Despite its dual personality, tamoxifen has been successfully used to prevent recurrence of breast cancer in women who are estrogen-receptor positive.

Using tamoxifen in cancer patients is one thing; using it in healthy women is another. Tamoxifen is a well-known carcinogen which causes DNA strand breaks. This is an accepted feature of standard chemotherapy where the overriding concern is to keep cancer cells from growing. Carcinogens have not traditionally been an accepted part of preventive medicine, however. The FDA's decisions to allow the sale of tamoxifen and certain cholesterol-lowering drugs (notably the peroxisome inhibitors clofibrate and gemfibrozil) to healthy people marks the first time that drugs with cancer-causing potential have been approved as health enhancements. This marks a dangerous new trend in drug approval.

The paucity of data makes the approval of tamoxifen for prevention particularly questionable. Approval was based on a single study run at various hospitals around the United States under the auspices of the National Cancer Institute (NCI). An outgrowth

of the "National Surgical Adjuvant Breast and Bowel Project" (NSABP) begun in the '80s, the study was about 10 years shy of producing any meaningful information, according to one expert. Two similar European studies reported no preventive effect of tamoxifen. The FDA rejected these studies as irrelevant because they were too small (3500 people combined).

THE HYPE

There was no statistical difference in survival for the women taking tamoxifen versus women taking placebo in the NCI study. The justification for Zeneca's claim of a 50% reduction in breast cancer lies in the difference between a 1.4% incidence of cancer in women taking tamoxifen versus a 2.7% incidence in those taking placebo. The price of that 1.3% difference was very dear. Tamoxifen doubled the risk of endometrial cancer for women under 50. It quadrupled it in women over 50.

In short, what a healthy woman over 50 got when she took tamoxifen was a proven four times higher risk of endometrial cancer in return for an unknown amount of risk reduction for breast cancer in the short term. And that's not all. Thirty-five tamoxifen-takers developed blood clots in the lung, and three of them died. The risk of cataracts was doubled, and almost half the women participating rated the side effects as "quite a bit or extremely bothersome." Technically, tamoxifen also doubled the risk of suicide (two on tamoxifen versus one on placebo). Worth it? Well, there was a 0.4% reduced risk of a certain type of bone fracture.

OTHER STUDIES FIND NO BENEFIT

Two European studies reported interim findings about the same time as the NCI study, which wrapped up early. Both found no preventive effect of tamoxifen in healthy women. The authors of the NCI study devoted considerable space to discrediting these two European trials. One of the studies was conducted at the

Royal Marsden Hospital in England; the other at the European Institute of Oncology in Italy. Together, these two studies had more women on tamoxifen much longer than the American study where only 25% of the participants took the drug five years or longer. Unlike the American study which was halted before long-term effects could be discovered, these studies are ongoing so as to get a picture of what tamoxifen does in the long run. Although both the advisory committee and the FDA dismissed them as unimportant, the studies have in fact produced new information about tamoxifen.

It appears that women who take hormone replacement therapy plus tamoxifen may have some benefit. However, some of the data indicate that if a woman took hormone replacement therapy before she entered the study, she is at higher risk for breast cancer. This hints at the yet unexplored interaction between tamoxifen and synthetic estrogens in the environment, including synthetic hormone replacement therapy. At present, no one knows what happens when a synthetic estrogen blocker with estrogenic potential is given to women exposed to synthetic estrogens.

TAMOXIFEN-INDUCED CANCER

While no conclusions can be drawn from the study on whether tamoxifen can prevent breast cancer, conclusions can be drawn about tamoxifen's ability to cause endometrial cancer. About a thousand published studies deal with tamoxifen and endometrial (or uterine) cancer. An analysis of several large studies shows that tamoxifen approximately doubles a woman's risk for uterine cancer when used for one to two years, and quadruples it at five years. While this may be an acceptable risk for women diagnosed with breast cancer (or a woman without a uterus), it is an unacceptable risk for healthy women with no evidence of cancer.

Tamoxifen is also associated with stomach and colorectal cancer. Some data indicates that prior treatment with hormones

adds to this risk. What is especially chilling is the likelihood that the risk of cancer with tamoxifen may be a function of total lifetime dose. In other words, the longer you take it, the higher the risk. Women taking tamoxifen longer than five years are reported to have a high incidence of various cancers. Despite the statistics Dr. Norman Wolmark, head of the study, advises women to start taking tamoxifen as soon as they discover they are at high risk for breast cancer. Don't wait, he urges. Age thirty-five has been designated as the age to start worrying.

PUTTING A FACE ON APPROVAL

One might ask why tamoxifen was approved when so many serious questions remain. The FDA didn't approve tamoxifen by itself. It had help from a group known as an "advisory committee." By law, advisory committee members are not supposed to have financial interests in the company that manufactures the drug they're advising on. In addition, advisory committees are supposed to be made up of people with "diverse professional education, training and experience." This is so that they bring different points of view to the table. In recent years, advisory committees have recommended approval for a number of dangerous drugs. The public should be aware that participants in the approval process are frequently paid consultants to drug companies.

The committee that endorsed tamoxifen was composed of 11 people, eight of whom are doctors who routinely test emotherapies. Some, including Richard L. Schilsky, Derek Raghavan and Robert F. Ozols, accept grants from drug companies. Others such as Kim A. Margolin, Kathy S. Albain and Janice P. Dutcher test chemotherapeutic drugs with taxpayer money through the National Cancer Institute (NCI).

The tamoxifen committee represented very little diversity. Its role as an independent body was also questionable. Ozols and Schilsky have both collaborated on studies with doctors who con-

ducted the tamoxifen study. One of the committee members, Richard Simon, works at the National Cancer Institute, which conducted the study. A statistician by training, Simon's forte is number crunching—not breast cancer.

The public expects committee members to be impartial. Yet before he ever sat on the tamoxifen committee, Simon had attacked data showing tamoxifen causes increased risk of colorectal and stomach cancer. The motivation for the attack is not known. He failed to respond to a request to clarify his position.

FRAUDULENT STUDIES

The study on which tamoxifen was approved for healthy women has a lurid history. A surgeon named Bernard Fisher was the driving force behind tamoxifen's approval as a preventative agent. Fisher began conducting studies on tamoxifen in the early '80s under the taxpayer-funded NSABP. The project, which he headed, was receiving about $18M a year in federal money when NCI decided to spend $68M to see whether tamoxifen would prevent breast cancer. Fisher was to coordinate the massive project which began in 1992.

In 1990, it was discovered that a doctor participating in NSABP trials had falsified data for 99 people enrolled in 14 breast cancer studies that preceded the prevention trials. Fisher was accused of not reporting the falsification, then using the data in an article published in the *New England Journal of Medicine*. In 1993, it was discovered that secretaries in charge of enrolling women at a hospital participating in the breast cancer prevention trial had manufactured data. One of them was receiving $250 a head for each woman she enrolled. The fraud was discovered during a routine audit, and Fisher's office was notified. Apparently Fisher buried the report and never told NCI. A few months later, a woman named Hazel Cunningham, who wanted to enroll in the tamoxifen prevention trial, discovered that the consent form being used

by Fisher didn't inform women about the true number of uterine cancer deaths occurring in the cancer trials. She filed a petition to stop the trials.

Representative John Dingell began congressional hearings into the NSABP, and Fisher was stripped of his position. The trials were halted. Although Fisher refused to appear at hearing—citing medical problems—he had enough fortitude to file lawsuits against five federal agencies, their directors, and the University of Pittsburgh. A federal judge threw out the case against the agencies in 1996. After much wrangling Fisher, who admitted knowing about the fraudulent data but felt the study would have been hurt if he eliminated it, was exonerated by an investigative arm of the Department of Health and Human Services which has been accused of favoring bigwig researchers. His case against the University of Pittsburgh was settled, and he was ultimately paid money and reinstated on the study. A judge also ordered the NCI to quit flagging his research as unreliable.

FDA REVIEW FALLS SHORT

In light of all that had occurred, the FDA had valid reasons to carefully review all the data from the prevention trial. It did not. In fact, the agency may have set a record for fast review. According to Dr. Susan Honig who was in charge, the FDA received the final data on tamoxifen on August 4th, four weeks before the advisory committee hearing on September 2nd. Originally, the FDA was sent submissions missing crucial data. According to the transcript of the advisory committee hearing, the agency reviewed 625 of the 6681 case report forms of the women who got tamoxifen. (Case report forms are the actual record of what occurred to the patient, as filled out by healthcare workers who actually interacted with her. This is distinct from data summaries created by the drug manufacturer). Reviewing case forms is important, as numerous investigators on drug trials have

been caught falsifying data. Given that it was already known that data had been falsified in tamoxifen trials, it would seem crucial for the FDA to review a substantial number of the case report forms. Instead, it held a committee meeting four weeks after receiving data from the trial, and announced its approval four weeks later.

COMMITTEE REJECTS MONITORING OF WOMEN ON TAMOXIFEN

One might wonder how a committee that refused to endorse the statement that tamoxifen has a favorable risk/benefit ratio for the prevention of breast cancer would ultimately approve tamoxifen for the prevention of breast cancer. The answer lies in semantics. A review of the record shows that the committee refused to use the word "prevention" but reframed the issues until they could recommend approval. The actual recommendation of the committee is that tamoxifen be approved for the "risk reduction of the short-term incidence of breast cancer in women at increased risk as defined by the study population." Despite the refusal of the committee to recommend tamoxifen for prevention, the American Cancer Society and the media immediately hailed tamoxifen as a breast cancer prevention drug.

And despite evidence that tamoxifen causes endometrial cancer, the committee rejected advising women to undergo endometrial testing while on tamoxifen. During the discussion among committee members, George W. Sledge Jr., a drug researcher, stated his belief that such testing would be nothing more than an employment act for OB-GYNs. The committee agreed with Sledge and voted not to warn women to have endometrial testing. They also nixed yearly eye examinations for cataracts. The issue of warning women about blood clots never came up, although the committee felt the FDA should ask someone to look into it further.

After the committee finished with tamoxifen, they went on

to another hearing about the drug, Herceptin. Drs. Schilsky and Raghavan's conflicts-of-interest were duly noted for the record.

EXCERPT FROM

The FDA Versus Folic Acid

THE FDA ARGUES AGAINST FOLIC ACID SUPPLEMENTATION because the presence of folic acid in the blood could mask a serious vitamin B12 deficiency. But the *Journal of the American Medical Association* (Dec. 18, 1996) noted that folic acid supplements fortified with vitamin B12 would be a prudent way of gaining the cardiovascular benefits of folic acid without risking a B12 deficiency. In addition, the April 9, 1998, issue of the *New England Journal of Medicine* endorses folic acid as a means of reducing the incidence of heart attack and stroke. Nevertheless, the FDA refuses to accept that folic acid has any benefit other than preventing a certain type of birth defect.

In fact, it took the FDA more than 30 years to even acknowledge that folic acid prevents neural tube birth defects. Tens of thousands of deformed babies have been born because the FDA prohibited claims that pregnant women should take folic acid. When former Commissioner David Kessler was confronted with overwhelming evidence that women of childbearing age should supplement with folic acid, he responded in an NBC interview, "The quandary we're in at the Food and Drug Administration is how to make folic acid available to women of childbearing age, but not put it in excessive amounts in the food supply for other populations such as teenage boys or elderly people."

A newly released study shows just how fatally flawed the FDA's position is. Data from the famous Nurses' Health Study con-

ducted at the Harvard Medical School show that long-term supplementation with folic acid reduces the risk of colon cancer in women by an astounding 75%. The fact that there are 90,000 women participating in the study makes this finding especially significant. The authors explain that folic acid obtained from supplements had a stronger protective effect against colon cancer than folic acid consumed in the diet.

The Nurses' Health Study also demonstrates that the degree of protection against cancer is correlated with how long a dna-protecting substance (such as folic acid) is consumed. The women who took more than 400 micrograms of folic acid a day for 15 years experienced the 75% reduction in colon cancer; short-term supplementation produced only marginal protection.

There now exists a massive body of evidence that supplementation with folic acid can prevent both cardiovascular disease and cancer, yet the FDA has proposed rules that would prohibit the American public from even learning about these benefits. Colon cancer will kill 47,000 Americans this year. Too bad the FDA didn't allow these colon cancer victims to learn of folic acid in time.

EXCERPT FROM

The FDA's Vendetta Against Dr. Burzynski

Stanislaw R. Burzynski is an MD with a PhD in biochemistry. In 1967, while studying blood as a graduate student, he found certain peptides that had never been described before. Comparing the blood of patients with different diseases, Dr. Burzynski found that over 98% of cancer patients were deficient

in the peptides he had found—often with blood levels of only 2% of those of healthy individuals. This led him to suspect that these compounds—or a lack thereof—were implicated in the development of neoplastic (cancerous) disease.

Most cancer experts believe we all develop cancer cells hundreds if not millions of times in our lifetimes. Given the trillions of developing cells, the millions of errors that can occur in the differentiation (maturing) process of each cell, and our constant exposure to carcinogenic substances (smoke, car fumes, radiation, etc.), the laws of probability dictate that mis-developing cells must occur frequently in the life of each individual. It stands to reason that a healthy body has a corrective system to "reprogram" newly-developed cancer cells into normal differentiation pathways before the cancer can take hold.

Dr. Burzynski postulated that healthy organisms have just such a corrective mechanism, which he termed the "Biochemical Defense System." He called the substances produced by this system "antineoplastons." Their purpose is to "reprogram" cancer cells to die like normal cells. Healthy cells are not affected.

Dr. Burzynski continued his research at Baylor University until 1977, when he felt he was ready to begin treating advanced cancer patients with the peptides he had discovered. After getting a written opinion from his lawyer that doing so would not violate any state or federal laws as long as he treated patients only in Texas, Dr. Burzynski began to give antineoplastons to patients with hopeless cancers—often with dramatic results.

THE FDA SEEKS AN INJUNCTION

In 1983 however, the FDA went to court for an injunction to stop Dr. Burzynski from manufacturing or using antineoplastons in his practice. US District Court Judge Gabrielle McDonald turned them down. In an 18-page decision, Judge McDonald made it clear that Dr. Burzynski could continue to "manufacture,

package, sell, and distribute antineoplastons, so long as it occurs wholly intrastate."

Ignoring Judge McDonald's decision, the FDA tried to stop Dr. Burzynski by writing dozens of letters to Senators, Congressmen, insurance companies and pharmaceutical firms. These letters contained lies and distortions so outrageous that on October 23, 1985 Judge McDonald issued a Cease and Desist order, commanding the FDA to stop issuing false and misleading information about Dr. Burzynski.

A SERIES OF RAIDS AND GRAND JURY INVESTIGATIONS

In 1985, FDA agents and armed Federal Marshalls raided Dr. Burzynski's clinic and seized all his patient records—200,000 documents in all. In order to continue treating patients with advanced cancer, Dr. Burzynski had to install a copier—at his expense—at FDA headquarters and hire someone to shuttle back and forth, making copies of his records and bringing them back to the clinic. Dr. Burzynski had to make appointments with the FDA to make copies of his own documents.

Later in 1985, Federal prosecutors representing the FDA presented everything they seized in the raid—plus another 100,000 documents subpoenaed shortly after the raid—to a Federal Grand Jury. Their investigation of Dr. Burzynski lasted nine months, but prosecutors couldn't convince the Grand Jury that there was probable cause to believe a crime had been committed. No indictment was returned.

In 1990, the US Attorney's office in Houston, representing the FDA, convened another grand jury to investigate Dr. Burzynski, again for alleged violations of Judge McDonald's order. To the FDA's dismay, this Grand Jury also refused to indict Dr. Burzynski.

MORE RAIDS AND GRAND JURIES

In 1993, the FDA again raided the Burzynski Research Institute because of alleged bacterial contamination of antineoplastons, but tests proved conclusively that there was no contamination.

In 1994, US Attorneys—again representing the FDA—convened a third Grand Jury to investigate Dr. Burzynski. And for the third time, a skeptical Grand Jury refused to return an indictment. The main casualty this time was the Assistant US Attorney on the case, who was removed for prosecutorial misconduct involving abusive and improper use of subpoenas.

The latest chapter in the FDA's twelve-year campaign to stop Dr. Burzynski from treating patients with antineoplastons kicked off on March 24, 1995 with another raid on the clinic. Seven federal agents herded employees into a room and kept them there until they filled out forms with personal information. They then spent seven hours rifling through file cabinets and drawers, leaving with boxes of patient records and other documents.

Shortly thereafter the FDA began serving clinic employees with subpoenas commanding them to testify before a Federal Grand Jury investigating Dr. Burzynski. To date, federal prosecutors representing the FDA have subpoenaed nine employees including Dr. Burzynski. In addition, they have ordered him to turn over tens of thousands of pages of documents, including more patient records and diagnostic films.

AN ARBITRARY FISHING EXPEDITION

The law prohibits Grand Juries from "arbitrary fishing expeditions." Yet that is exactly what federal prosecutors are engaged in. Besides patient records—many of which have already been presented four times to various government investigators—prosecutors have subpoenaed "any and all agreements, draft agreements, proposals, correspondence, notes, memos, tape recordings, notes of conversations, telephone messages, reports, raw data, studies

or other items to, from, or with any foreign or domestic pharmaceutical company or university, including contact person's name, title and phone number."

While this information is of no use in investigating criminal activity, it gives the FDA the opportunity to write letters to everyone they uncover, letting them know that Dr. Burzynski is the target of a federal investigation and to issue subpoenas to some of these people. This is more than just speculation. It is the exact behavior that sparked a 1985 "Cease and Desist" order against the FDA by US District Court Judge Gabrielle McDonald.

And so, on June 15 1995, prosecutor Amy LeCocq subpoenaed a huge Dutch pharmaceutical conglomerate—which has conducted negotiations with Dr. Burzynski—for all correspondence, memos, documents or other records it had regarding Dr. Burzynski or anyone associated with him. The obvious purpose of this subpoena was to frighten the company—which does a large business in the US—into having no further contact with Dr. Burzynski.

Prosecutors have also subpoenaed all patient billing records, again with no time limitation whatever. Dr. Burzynski has been treating patients since 1977. They have subpoenaed his accountants for every conceivable document an accountant can possess (again with no limitation on time), a classic fishing expedition. Prosecutors have even subpoenaed the names and addresses of every person who has ever received a brochure from Dr. Burzynski! As if that weren't enough, the subpoena went on to demand "Any other lists of persons," an absurdly general and burdensome request.

FDA HARASSMENT, ILLEGAL ACTIONS, AND TERRORISM

Besides throwing the entire clinic into chaos, wasting thousands of hours of employee time, and terrifying advanced cancer patients who don't know whether they will be able to con-

tinue getting the only medicine that has been able to help them, the grand jury's actions have severely threatened Dr. Burzynski's ability to practice medicine. Without patients' previous MRIs and CAT scans, Dr. Burzynski has nothing to which he can compare new scans, and no way of knowing if patients' tumors are growing or shrinking.

Moreover, the FDA has been careful to seize films and medical records of Dr. Burzynski's most successful cases, crippling his ability to defend himself by confiscating his single most valuable asset—proof of the anti-cancer activity of antineoplastons.

In the current case there has been illegal use of subpoenas as well. Dr. Ralph Moss, an award-winning journalist and author of books about cancer, was subpoenaed and ordered to produce every document in his possession—electronic, magnetic, printed or otherwise—relating to Dr. Burzynski. Dr. Moss has written favorably about Dr. Burzynski in the past.

Unfortunately for Amy Lecocq, the prosecutor in charge of this case, her subpoena of Dr. Moss violated at least six federal laws governing subpoenas of journalists. Such violations carry a penalty of administrative reprimand or other disciplinary action. When Dr. Moss pointed this out to Lecocq and gave her the opportunity to withdraw the subpoena, she did so with alacrity.

It's been said that a prosecutor can get a Grand Jury to indict virtually anyone. But despite the avalanche of documents supplied by the government to four Grand Juries, it has yet to convince any of them of probable cause to believe Dr. Burzynski has committed a crime. And so, unable to stop him legally, the FDA seems determined to harass him to death.

THE NCI REPORT ON DR. BURZYNSKI

The FDA's actions are all the more outrageous because their own oncology division has granted Dr. Burzynski permission to conduct Phase II clinical trials! In addition the National Cancer Insti-

tute (NCI)—following a visit by seven NCI experts to Dr. Burzynski's Houston clinic for a review of patient records—confirmed several remissions in patients with "hopeless" brain tumors after treatment with antineoplastons. Their report states that "The site visit team documented anti-cancer activity in this best-case series and determined that Phase II trials are warranted to determine the response rate."

In other words, the question is no longer "Do antineoplastons work?" but rather "How consistently do they work?"

And yet, despite the NCI report, despite the fact that the FDA's own scientists wish to see antineoplastons tested, the FDA's "enforcers" remain obsessed with shutting Dr. Burzynski down.