

Turning Medicine



Into Snake Oil

**HOW PHARMACEUTICAL MARKETERS
PUT PATIENTS AT RISK**

NJPIRG Law & Policy
Center

MAY 2006

A Multi-Headed Hydra

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Alliance for Human Research
Protection

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Baltimore

THE FDA TURNS A BLIND EYE
CORPORATE & ACADEMIC MARKETERS
SKEW SCIENCE / MEDICINE
DECEIVE DOCTORS

RESULT:
TAKING A MEDICINE
INCREASES RISKS OF HARM
INTEGRITY OF SCIENCE UNDERMINED

How does a lethal drug gain FDA approval?

How does it become a blockbuster seller?

How does it remain on the market once the lethal risk is detected?

“Vioxx is a terrible tragedy and a profound regulatory failure. I would argue that the FDA, as currently configured, is incapable of protecting America against another Vioxx. We are virtually defenseless””

Dr. David Graham, Senate Testimony, 2004

“The Truth About Drug Companies”

Dr. Marcia Angell, former editor NEJM

“this industry uses its wealth and power to co-opt every institution that might stand in its way, including the U.S. Congress, the Food and Drug Administration, academic medical centers and the medical profession itself.”

Where was the resistance?

Without the willing collaboration of the medical profession and its academic institutions industry could not have taken control.

Without the collaboration of medicine's leadership and the FDA, children would be off-limits for brain-damaging drugs.

Food Drug & Cosmetics Act 1938

Statutory basis for drug approval is 1962

amended FDC Act [505(d)] requiring:

“substantial evidence of effectiveness” from
“adequate, well-controlled investigations.”

FDA'S post-approval mission

“helping the public get accurate, science-based information they need to use medicines and foods to improve their health.”

FDA Approval

Drug is deemed “safe and effective”
for the conditions listed on the label

Companies are legally prohibited from:

- making unproven claims beyond the
FDA-approved label
- promoting a drug for “off label” uses

Those restrictions are decidedly
unenforced.

Deceptive marketing is pervasive

2001-2005 FDA sent 170 warning letters to 85 companies promoting 150 drugs using false /deceptive adverts

869 deceptive messages

– 535 (62%) targeted doctors

– 334 (38%) targeted consumers

358 deceptive Ads

– NJPIRG Law & Policy Center Report, 2006

Deceptive Marketing to Doctors

FDA letters address only “classic marketing”

detail /sales aids (20%)

journal ads (17%)

brochures (9%)

sales rep oral statements (9%)

convention exhibits (7%)

mailers; case studies; visuals (5%)

posters, conference abstracts, dear

doctor letter; info packs...

Deceptive consumer Ads \$4.5 billion

print ads (32%)

TV ads (26%)

websites (21%)

35% misrepresented risks

22% promoted unproven uses

38% unsupported/ misleading claims.

72% FDA letters cite multiple violations

Industry's most powerful sales tool

Physicians' Rx license overcomes legal limits on a company's marketing license.

Marketers disseminate deceptive information widely

FDA warning letters are seen by few

FDA letters "grossly understate false advertising"

Recidivism is widespread.

FDA Warning Pfizer (2002)

“The Geodon Challenge” brochure distributed at APA conference states:

no arrhythmia

rare incidence of QT interval

well-characterized EC

Geodon (antipsychotic) label warning:

“greater capacity to prolong QT interval compared to other antipsychotic drugs... potential to cause [cardiac] arrhythmia and sudden death.”

Janssen “Dear Doctor” letter 2003

“contradicts Risperdal label warnings”

“misrepresents evidence” lethal effects:
hyperglycemia, diabetes mellitus, death

“minimizes importance of blood monitoring
to detect diabetes mellitus”

“falsely claims that Risperdal is safer than
other atypical antipsychotic drugs”

How many doctors know about the deceptions
& FDA’s warning letters?

Sales Rep Physician interaction

Out of FDA radar

Secret Glaxo memo (2003) instructs sales reps:

“do not discuss with your customers”

evidence from Paxil pediatric study 329:

7.5% suicidal / 0-placebo;

6.5% hostile / 1-placebo

www.ahrp.org/infomail/04/09/30.php

Table 4: General Recidivism**Companies Receiving More Than One Letter in the Study Period**

Companies	# Letters received by each	Total letters
Pfizer, Inc.	15	15
Novartis Pharmaceuticals Corp.	9	9
AstraZeneca, Aventis, GlaxoSmithKline	7	21
Hoffman-LaRoche	6	6
Berlex Laboratories, Boehringer Ingelheim, Bristol-Myers Squibb Company.	5	15
Abbot Laboratories, Alcon Research, Ltd. (including one received by Alcon Laboratories for the same drug at issue in one of Alcon Research, Ltd.'s letters)	4	8
Allergan, Inc., Alza Corporation, Bayer Corporation, Fujisawa Healthcare, Inc., SuperGen, Inc.	3	15
Actelion Pharmaceuticals US, Inc., Connetics Corporation, Elan Pharmaceuticals, Eli Lilly, Fujisawa Healthcare, Inc., Galderma Laboratories, Gilead Sciences, Inc., Janssen Pharmaceutica, Janssen Research Foundation, Pharmacia Corporation, Sanofi-Synthelabo, Inc., Schering Corporation.	2	24
Total number of letters received by general recidivists:		113

Absentee Guardian

FDA fails to ensure that: “the public gets accurate, science-based information.”

Physicians are misinformed by marketing propaganda masquerading as science.

Physician ignorance about hazardous effects of drugs they prescribe poses a serious public health hazard.

Conflict of Interest Derailed FDA

Rx Drug User Fee Act, 1992

FDA financially dependent on industry

FDA Modernization Act, 1997

Fast-track approval overrides safety

Financial incentives to test drugs on kids

FDA Chief Counsel, Daniel Troy argued:

deceptive marketing is protected under

1st amendment

Fast-track approval

Increased approval of lethal drugs

1950-1992: 7 drugs removed

1997-2005: 15 removed

e.g. Fen-Phen, Redux , Posicor, Duract, Rezulin,
Lotronex Propulsid Baycol, Vioxx, Pemoline,
Tysabri

Public Citizen lists 211 currently marketed

“worst drugs”

Worst Drugs are the Most Advertised

Painkillers: Oxycontin, Neurontin

COX-2 pain: Celebrex, Bextra

Statins: Crestor, Lipitor, Zocor, Mevacor

Sleeping pills: Ambien, Sonata, Lunesta

Antidepressants: Prozac-Cymbalta, Paxil,
Zoloft, Lexapro, Celexa, Effexor

Antipsychotics: Zyprexa, Risperdal,
Geodon, Seroquel

Doctors Rx these widely off-label

\$18 billion spent on shaping doctors' Rx

“Doctors are bombarded with false messages in all areas of their professional life, when reading journals, attending conferences, meeting with sales representatives...”

Abigail Caplovitz, NJ PIRG, 2006

FDA fails to use its authority to provide countervailing accurate information.

FDA officials deny the drug-related casualties

“My experience with Vioxx is typical of how CDER responds to serious drug safety issues in general.

This is similar to what Dr. Mosholder went through earlier this year when he reached his conclusion that most SSRIs should not be used by children.”

Dr. David Graham, Senate Testimony, 2004

Vioxx for Children

“In mid-August, despite our study results showing an increased risk of heart attack with Vioxx, and despite the results of other studies published in the literature, FDA announced it had approved Vioxx for use in children with rheumatoid arthritis.”

Dr. David Graham, Senate Testimony, 2004

Where have all the doctors gone?

“On the Take”

“the billion-dollar onslaught of industry money has deflected many physicians' moral compasses and directly impacted the everyday care we receive from the doctors and institutions we trust most.”

Dr. Jerome Kassirer [former] Editor, NEJM

\$18.5 billion Buys Control

All influential professional sources that doctors trust:

sales reps / clinical trials

journal reports, reviews

leading medical authorities (KOLs)

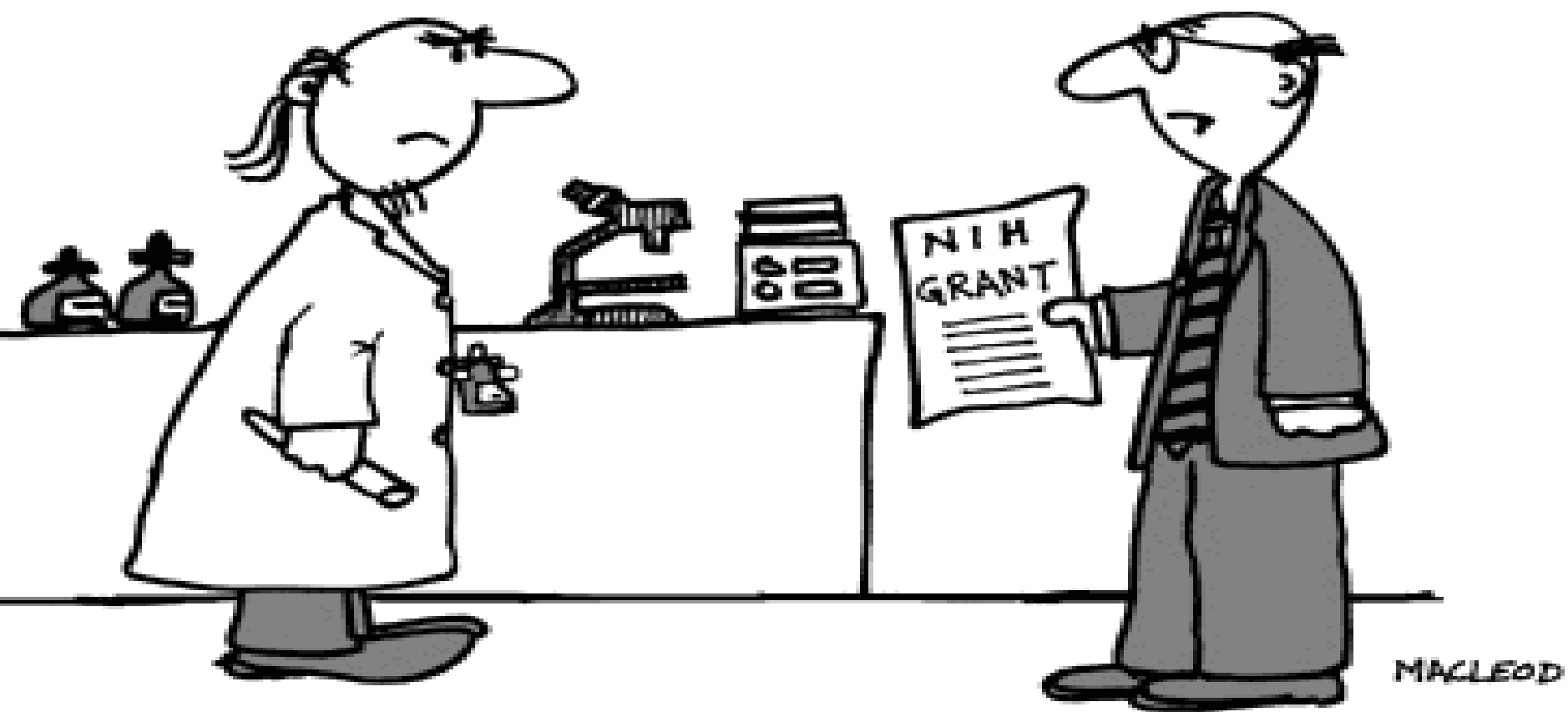
continuing medical education (CME)

practice guidelines.

All these “authoritative” sources provide the appearance of scientific legitimacy.

Industry spends \$14 billion annually on clinical trials that transform science into a marketing tool.

Companies engage in corrupt practices skewing trial results and concealing failed efficacy and lethal drug effects.



"You are completely free to carry out whatever research you want, so long as you come to these conclusions."

Companies get the Results They Want

Analysis of every published trial
comparing 5 new antipsychotics:
9 in 10 favored funding company's drug.

"it appears that whichever company
sponsors the trial produces the better
antipsychotic drug."

John Davis MD, American Journal of Psychiatry 2006

2001-2004: Pharma funded 36,839 trials

No one counts the human subjects

“Big Pharma’s Shameful Secret”

“Across the U.S., the centers that test drugs—and the regulators who watch them—allow scores of human test subjects to be injured or killed.”

Bloomberg News Series, 2005

Ghostly Business

Marketers hire academics to sign off on ghostwritten promotional copy masquerading as science in medical journals.

A Glaxo PR firm ghosted a letter for publication “minimizing Paxil withdrawal symptoms.”

They found three willing psychiatrists to ‘author’ it. Dr. Bruce Pollack (U. Pitts) signed it. The *Journal of Clinical Psychiatry* published it.

They Have No Shame

"Merck designed the trial, paid for the trial, ran the trial. Merck came to me after the study was completed and said, 'We want your help to work on the paper.' The initial paper was written at Merck, and then it was sent to me for editing."

"Basically, I went with the cardiovascular data that was presented to me."

Dr. Jeffrey Lisse, first listed "author" of Vioxx report in the Annals of Internal Medicine, 2003

Berenson, NYT, April 24, 2005

I WRITE WHAT YOU SAY



Thanks Academic Authors
We couldn't control the science without you

KEEP 'EM FLYING • INFORMATION AT YOUR LOCAL POST
OFFICE • AN MHRA PUBLIC SERVICE ANNOUNCEMENT

Integrity of Medicine

Industry funds 80% clinical trials

Retains control of data –denies access to data

Essence of science undermined:

75% of trials published in major journals
are controlled by industry

*The New England Journal of Medicine, The Lancet,
The Journal of the American Medical Association*

Journals: high impact marketing

Journal reports are more valuable than ads
prestige of a journal lends credibility

- doctors trust journal reports
- mass media eagerly relay findings

“The drug industry has even managed to turn peer-reviewed scientific literature into a sophisticated marketing device.”

Carl Elliott,

2003

Science Gatekeepers

“Journals have devolved into information-laundering operations for industry” *Richard Horton, Editor, The Lancet, 2004*

“Medical journals are an extension of the marketing arm of pharmaceutical companies”

Richard

Smith, former editor BMJ, PLoS 2005

New neuroleptics: Worse than Old

Severe adverse drug effects:

acute weight gain

blood lipid changes

Metabolic Syndrome

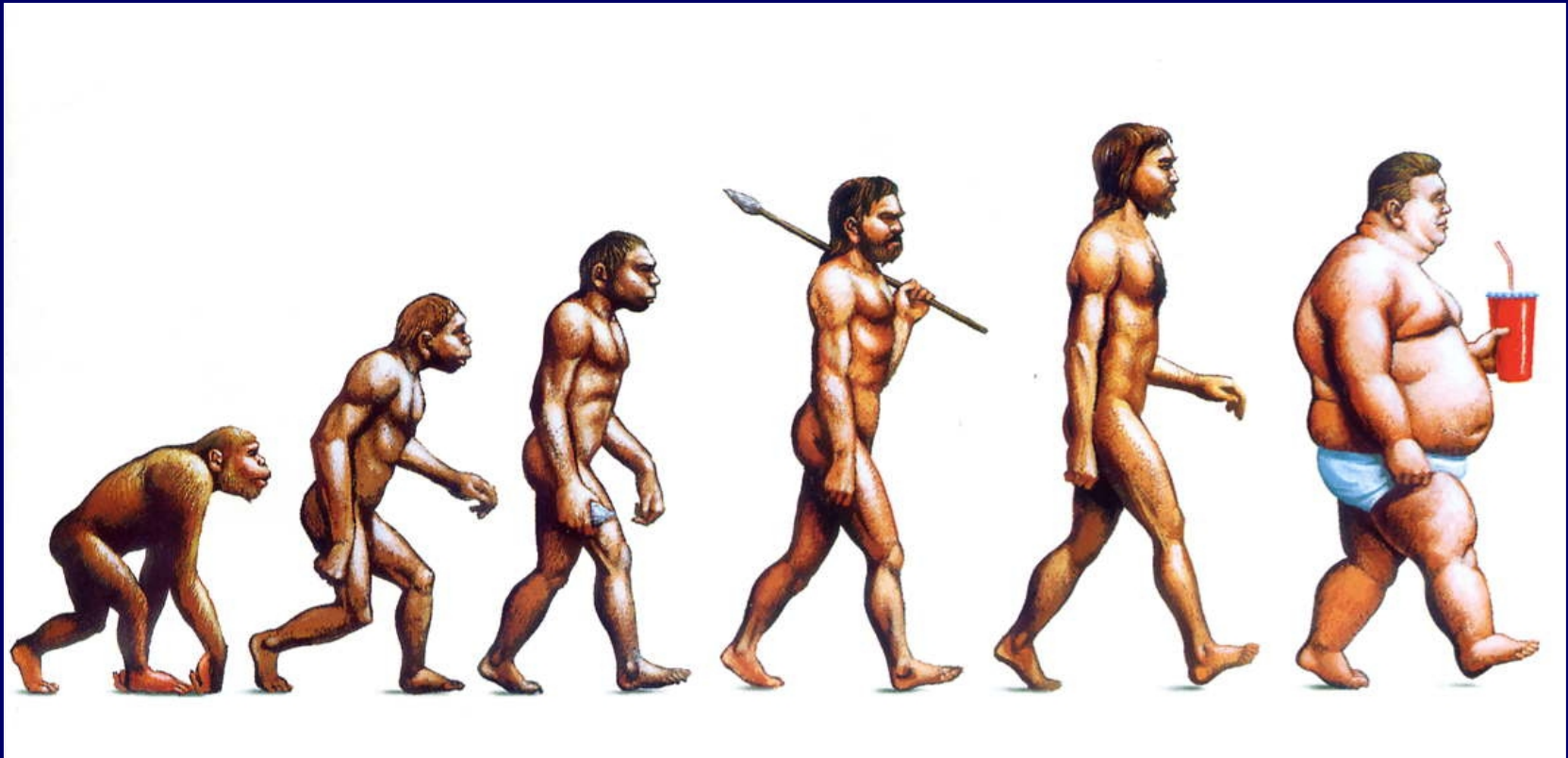
dangerously abnormal: liver function,
cholesterol level, cardio-vascular disease,
hyperglycemia, diabetes mellitus—death

No evidence drugs help patients recover

- Life-span shortened: possibly 25-years

Colton & Manderscheid Mortality Rates, CMHS, CDC, 2006

Evolution of Metabolic Syndrome— a.k.a. Zyprexa Syndrome



The Economist Newspaper Limited (2003), Cover illustration. The Economist; Dec. 13

Zyprexa

2001: FDA safety officer:

MedWatch data 10-fold diabetes risk.

Koller, Doraiswamy, JAMA

2002: Japan, UK add label warning

2002: Duke reported

100 of 289 Zyprexa users who

developed diabetes suffered

ketoacidosis within 6 months—23 died.

Zyprexa Lawsuits Looming

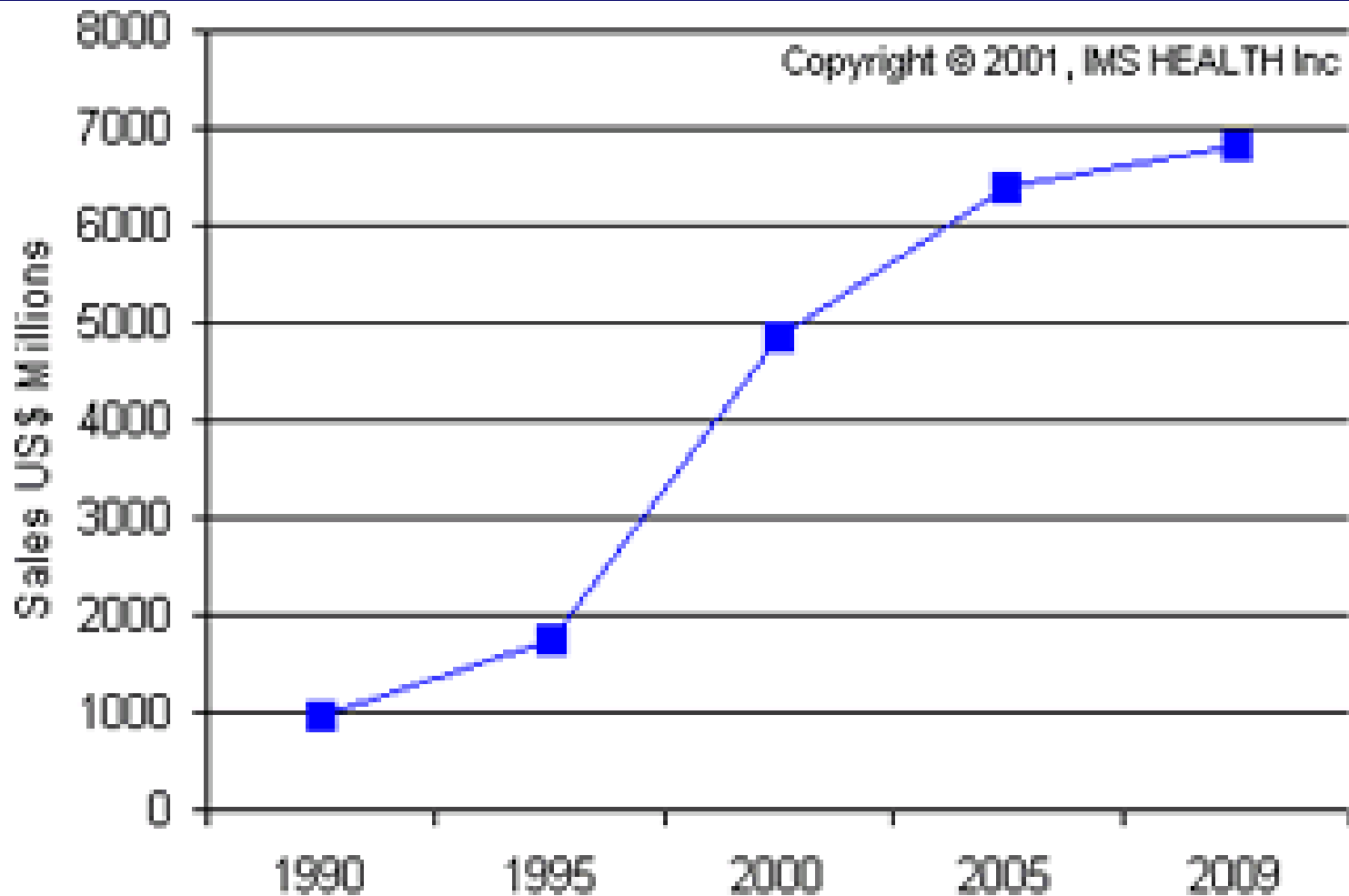
2004: FDA finally issues diabetes warning

2004: diabetes lawsuits filed by 8,000

2006: Lilly settled for \$690 million

Why did FDA wait 1½ years after UK warning?

Antipsychotic Sales: Real & Projected



"the side effect outcomes are staggering in their magnitude and extent and demonstrate the significant medication burden for persons with schizophrenia... Sky-high drug discontinuation rates were seen, suggesting rampant drug dissatisfaction and inefficacy."

Dr. Carol Tamminga. Editorial. AJP. 2006

Despite the “staggering” adverse effects,

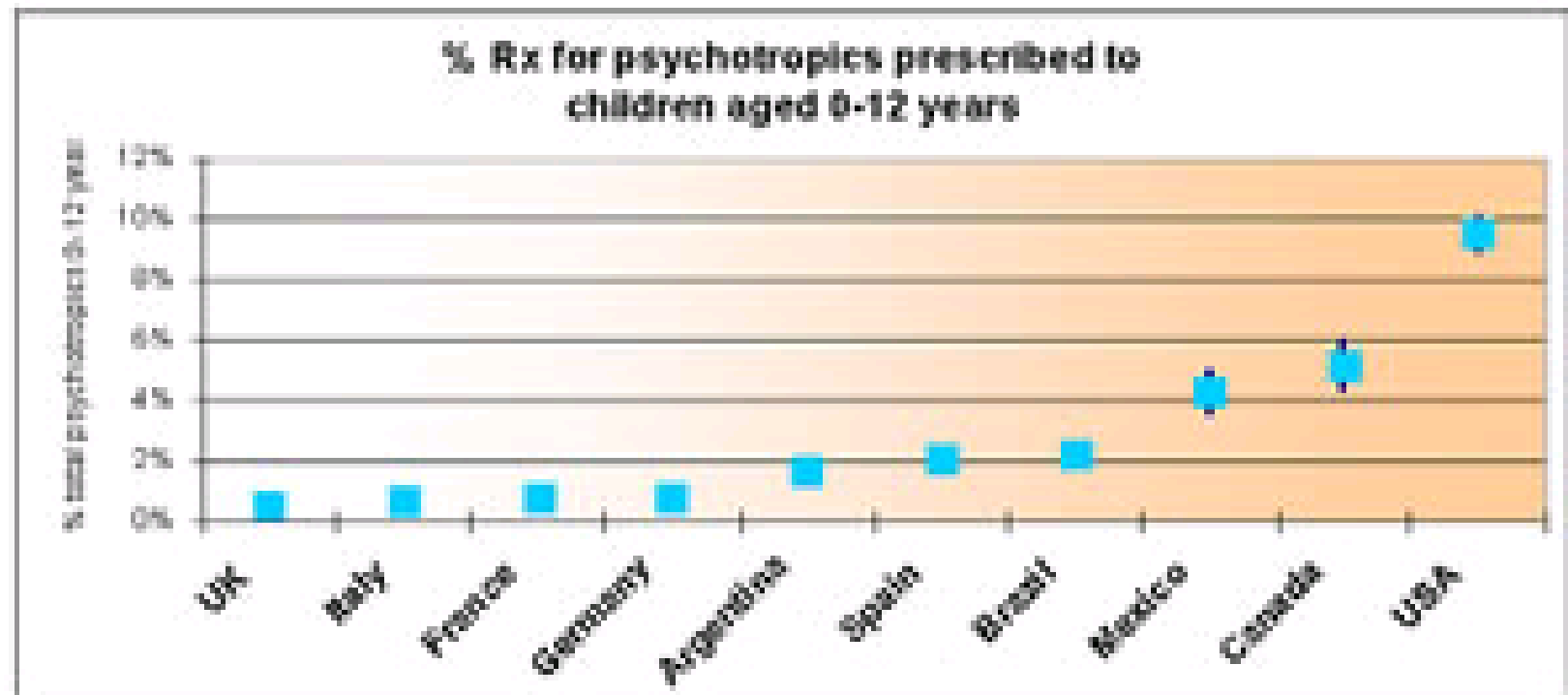
Sales are up: \$10.05 billion

Zyprexa remains top in class at \$2.9 billion

IMS, 2006

Are children 0-12 years so different?

- In North America significantly higher proportion Rx in 0-12 years



Overlapping Diagnoses

Doctors have a hard time diagnosing mental illnesses in children, as they often have symptoms that are indicators of multiple disorders. Here are four illnesses that often cause confusion for physicians and parents.

DISORDER	Attention deficit hyperactivity disorder (A.D.H.D.)	Oppositional defiant disorder (O.D.D.)	Conduct disorder (C.D.)	Bipolar disorder																											
SYMPTOMS INCLUDE	<ul style="list-style-type: none"> • Difficulty sustaining attention • Does not seem to listen when spoken to directly • Easily distracted • Forgetful • Often talks excessively • Often interrupts or intrudes • Cuts in line • Often leaves seat in classroom or when sitting is expected 	<ul style="list-style-type: none"> • Often loses temper • Argues with adults • Often deliberately annoys people • Touchy and easily annoyed by others • Often spiteful or vindictive 	<p><i>More severe form of O.D.D.</i></p> <ul style="list-style-type: none"> • Often bullies, threatens others • Often starts fights • Has been cruel to others, or animals • Skips school • Often stays out at night despite parents' rules • Has destroyed property • Often lies 	<ul style="list-style-type: none"> • Bursts of energy, exuberant or destructive, that last minutes to hours, or longer • Trouble sleeping • Periods of sadness or negative mood, resembling depression • Severe problems regulating emotions, from anger to sadness to excitement 																											
AFFECTED	3-5% of school age children	2-16% of school age children	4-12% of youths under 18, mostly preteens and teens	0-1% of youths																											
PERCENT WHO COULD ALSO BE DIAGNOSED WITH ...	<table border="0"> <tr> <td>O.D.D.</td> <td>C.D.</td> </tr> <tr> <td></td> <td></td> </tr> <tr> <td>60-70%</td> <td>15-30%</td> </tr> </table>	O.D.D.	C.D.			60-70%	15-30%	<table border="0"> <tr> <td>A.D.H.D.</td> <td>C.D.</td> </tr> <tr> <td></td> <td></td> </tr> <tr> <td>50-70%</td> <td>5-10%</td> </tr> </table>	A.D.H.D.	C.D.			50-70%	5-10%	<table border="0"> <tr> <td>A.D.H.D.</td> <td>O.D.D.</td> </tr> <tr> <td></td> <td></td> </tr> <tr> <td>10%</td> <td>100%</td> </tr> </table>	A.D.H.D.	O.D.D.			10%	100%	<table border="0"> <tr> <td>A.D.H.D.</td> <td>O.D.D.</td> <td>C.D.</td> </tr> <tr> <td></td> <td></td> <td></td> </tr> <tr> <td>40-90%</td> <td>30-75%</td> <td>30-75%</td> </tr> </table>	A.D.H.D.	O.D.D.	C.D.				40-90%	30-75%	30-75%
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Sources: Diagnostic and Statistical Manual of Mental Disorders; Dr. Joseph Biedeman and Dr. Stephen Faraone, Harvard Medical School; Dr. Barbara Geller, Washington University in St. Louis; Dr. Gabrielle Carlson, Stony Brook University

Selling pathology—Bipolar Child



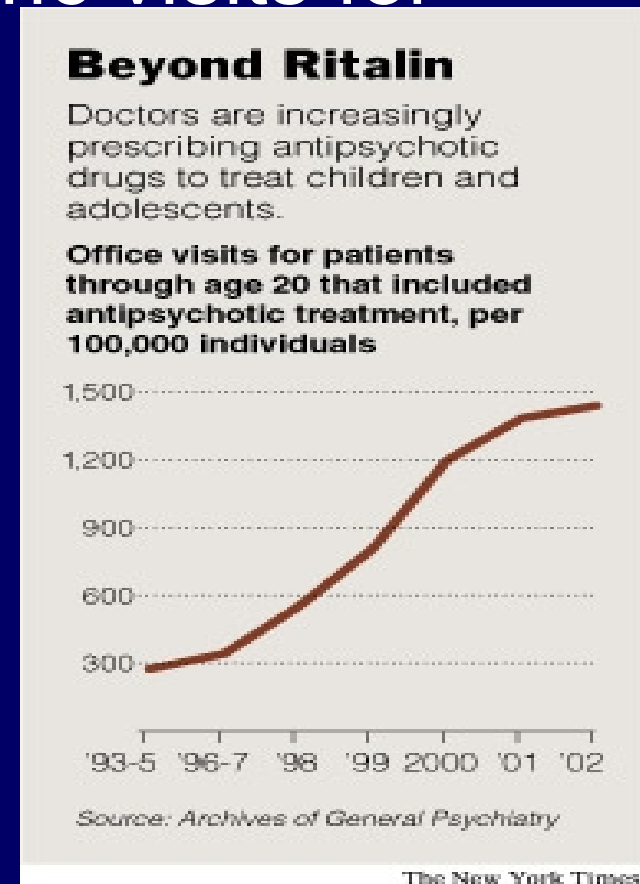
- “During the manic phase of the illness children may experience exceedingly high self-esteem, an inflated sense of power or ability... They may act extremely happy, silly and giddy, but their moods can change rapidly.”
- “An extreme example...a manic preschooler who believed that she made the sun rise and set.”

Dr. Joan Luby Washington University, Dec. 2005

1995-2002: Five fold increase Rx of antipsychotics for children

"to me the most striking thing was that nearly one in five psychiatric visits for young people included a prescription for antipsychotics."

Mark Olfson, MD, Columbia U 2006



Dr. John March, Duke child /adolescent psychiatry

"We are using these medications and don't know how they work, if they work, or at what cost."

"It amounts to a huge experiment with the lives of American kids, and what it tells us is that we've got to do something other than we're doing now..."

—

NYT, 2006

Dr. Adrian Angold, Duke

1 in 10 children aged 2 to 5

“had obvious signs / symptoms of psychiatric illnesses

“It suggests that such conditions begin very early in life, perhaps even in the womb”

“Screening and treating these disorders in babies and infants is the way forward – waiting until childhood or adulthood is too late.”

Newsweek, 11-2005



Surreal Rx for Disaster

- “Even before their first birthday, babies can suffer from clinical depression, traumatic stress disorder, and a variety of other mental health problems.”

Florida Strategic Plan for Infant Mental Health, 2001

- “Psychopharmacology is on the horizon as preventive therapy for children with genetic susceptibility to mental health problems.”

David Willis, M.D., Medical Director, NW Institute

Pediatric News, January, 2004

Psychiatrists say 1 in 40 infants depressed



NYU Doctors say 1 in 40 infants will experience depression.

Would you allow your baby to take antidepressants if doctors determined that he or she was depressed?

- Absolutely not. It's not safe. 5,501
 - No. Babies can't be depressed. 614
 - Yes. If the doctors thought it was safe. 129
- Total Vote: 6,244



Solutions: Transparency, accountability

Deceptive promotion by doctors—including “authorship” of ghost written journal reports should be subject to professional misconduct penalties;

All trials with humans should be registered

***Full data of all clinical trials should be published on the web not in medical journals that advance an incomplete, corporate manipulated “story.”