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NORD ON-LINE
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PEOPLE ARE TALKING ABOUT.....

"I have made this decision with great care, and I pray it is the right one."

President Bush announcing his decision to allow federal funding of research on a limited number of embryonic stem cell lines.

"I don't want people to see us as an 800-pound gorilla."

Carl Gulbrandsen of the Wisconsin Alumni Research Foundation, which holds the patent on embryonic stem cells, talking about concerns of the scientific community that the patent may hinder future research.

"We understand that this was not only a terrible mistake, but that it was wrong. To say it is totally inappropriate is an understatement."

The apology of Phillip Morris Senior Vice President, Steven Parrish, for a study commissioned by his company that showed the early deaths of cigarette smokers saves money for European health systems.

"I am still getting used to it. And the biggest thing is getting used to not having a heartbeat. I have a whirring sound and that makes me realize that I'm alive."

Artificial heart recipient, Robert Tools.

"This is fiscal mismanagement, big time."

Senator Kent Conrad (D-ND) commenting on new government projections showing that the budget surplus has disappeared, and only two-thirds of the money needed for a Medicare prescription drug benefit will be available.

NOTICE: This NORD On-line was written just before the World Trade Center tragedy. In the days since, the entire political landscape has changed. We can safely assume that health legislation, Social Security and Medicare reform, and even debate on the federal budget may be put on the congressional back burner for the remainder of this year, and even beyond. Nevertheless, this NORD On-line presents the federal debate about health policy up to the day before the World Trade Center and the Pentagon were destroyed.



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HERE TODAY, GONE TOMORROW

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Between last spring and the end of August, the federal budget surplus disappeared. Experts suggest that the surplus may have evaporated because of the slowing economy and President Bush's tax rebate. Last Spring, Congress set aside \$300 billion in the FY2002 budget resolution for a Medicare prescription drug benefit, to be spent over the next ten years. However, on August 22nd the Office of Management and Budget (OMB) released an updated budget outlook that showed only \$190 billion will be left for the proposed Medicare prescription drug benefit.

The OMB now estimates that all but \$1 billion of the FY 2002 non-Social Security federal surplus has disappeared, and only \$190 billion will be available for the prescription drug Medicare program that is projected to cost \$300 billion. **This may make the Medicare prescription drug benefit unattainable in the near future.**

ARE HUMAN RESEARCH PROTECTIONS ADEQUATE?

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Just as Johns Hopkins University was recovering from the controversial death of a healthy young woman in an asthma study, the university is again mired in controversy due to a scathing 98-page Maryland Appeals Court decision that accuses the university of conducting an unethical study on children, and purposely misleading parents about the dangers involved in the study.

The study by the Kennedy Krieger Institute of Johns Hopkins, purposely exposed children from poor families in the Baltimore slums to lead paint during the 1990s. Judge Dale Cathell of the Maryland Court of Appeals wrote, "It can be argued that the researchers intended that the children be the canaries in the coal mines, but never told the parents." The judge called the Johns Hopkins Institutional Review Board (IRB) a "non-objective house organ" because the IRB instructed

researchers to rewrite the informed consent documents "to get around federal regulations" requiring disclosure about risks. The seven-judge court suggested that the scientific and medical communities should not have sole authority in overseeing research on children because they do not adequately protect human subjects.

The Law Suit

The case involved lawsuits from two Baltimore families whose children suffered brain damage from lead poisoning. Baltimore landlords said they would abandon houses in low-income neighborhoods because they could not afford to remove the lead paint. The study was designed to determine the effectiveness of cheaper methods of removing lead paint from the old apartment buildings. Landlords who cooperated in the study rented apartments to 108 low-income families who were then split into four groups. One group was housed in apartments that had been completely cleared of lead. The other three groups were put into homes with varying levels of lead paint, and they underwent various cleaning methods while the families continued to live there. Researchers monitored the levels of lead in the children's blood for about two years.

Parents were asked to consent to the children's blood tests, but were not told the purpose of the study, nor that there might be risks to their children's health as they breathed in lead laden dust while the apartments were renovated. Researchers did not tell parents when the blood tests showed high levels of lead, nor did they remove the families from the apartments when the tests indicated lead poisoning. The children with lead poisoning are now neurologically impaired. When the parents of two children realized what happened, they sued, but two Baltimore judges in lower courts dismissed the lawsuits saying that Kennedy Kreiger had no legal obligation to inform parents about risks to their children in the experiment.

At the end of August, a seven-judge panel of the Maryland Court of Appeals overturned the lower court's decision in a scathing 98-page ruling. **The judges compared the lead paint study to the infamous "Tuskegee experiment,"** which purposely withheld treatment from poor southern African-American males

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with syphilis so that scientists could study their deterioration. The Baltimore lead study was sponsored by grants from the federal Environmental Protection Agency, the Maryland Department of Housing and Community Development, the Baltimore City Health Department, and the Maryland Department of Environment. The court accused all of these bodies, the researchers, and the university of "abdicating their responsibility" to protect human research subjects. They point out that the children were healthy when the trial began, and "it is not in the best interests of any healthy child to be intentionally put in a non-therapeutic situation where his or her health may be impaired."

The Hopkins investigator defended the study by saying it was morally defensible to offer some families modest repairs that might help their children somewhat. (Interestingly, this same defense was used to defend the American-sponsored African studies where pregnant women were denied drugs that could have prevented transmission of HIV to their babies. In that case, investigators defended their actions by saying if they didn't do the study, the women would have had no intervention at all.) In the Baltimore study, the investigators insisted it was okay to give some children less lead poisoning than they might have gotten in another apartment in Baltimore, in order to find a cheaper way of preventing lead poisoning!

Some experts suggest that this case proves our human research protection system has failed, and it is desperately in need of a complete overhaul. If you wish to read the entire decision in this appalling case (*Grimes vs Kennedy-Kreiger Institute*, and *Higgins vs. Kennedy-Kreiger*), you will find it at:
<http://www.courts.state.md.us/opinions/coa/2001/128a00.pdf>

Independent Review

In defense of its actions, Johns Hopkins hired an independent panel of experts to review recent ethics controversies at the university. At the end of August, the panel released its findings that Hopkins human research protection system is "**grossly inadequate**," and it encourages a "culture of possible coercion" by making employees feel they must volunteer to participate in studies. The panel also expressed disappointment at the "adversarial relationship" between the university and federal regulators. "Our interviews suggest that many people at Hopkins believe that

oversight and regulatory processes are a barrier to research and are to be reduced to the minimum rather than serving as an important safeguard," the panel wrote in their nine-page report. This report contradicts an earlier report on the asthma study, which found that Hopkins had done nothing wrong. As a result of the death of a young woman in that study, as well as the revelations about the lead study, Hopkins is adding three new Institutional Review Boards, requiring researchers to undergo ethics training; and it is forming a committee to determine if university employees should be volunteers in Hopkins experiments.

HUMAN SUBJECT PROTECTION HEARING CANCELLED

The U.S. Senate Committee on Health, Education, Labor, and Pensions (HELP) cancelled a September 13, 2001 hearing on protection of human subjects in research due to the World Trade Center/Pentagon tragedy. NORD's President, Abbey Meyers, was scheduled to testify at that hearing about the history of human protection rules, and appropriate remedies needing congressional action. You can read the testimony in the "What's New" section of NORD's Web site: www.rarediseases.org.

OTHER HUMAN RESEARCH PROTECTION INITIATIVES

The National Bioethics Advisory Commission (NBAC), created in 1995 by President Clinton, will cease to exist in several months when it is replaced by a Presidential Commission created by President Bush. NBAC leaves a legacy of reports and recommendations that cover a wide variety of serious problems affecting the protection of human subjects in research.

A key recommendation of the Commission is that human protection rules should be applied to all research, regardless of whether it is publicly or privately funded. Additionally, all research should be governed by a single set of rules. Since there are many government agencies and departments that support or conduct human research, the Commission



recommended that **one independent agency** should be created through legislation to regulate all research involving human subjects.

Research on Children

The National Human Research Protection Advisory Committee (NHRPAC), which advises the Department of Health and Human Services (HHS) about the protection of human subjects, is recommending that the FDA allow teenagers, under certain circumstances, to enroll in clinical trials for experimental medications without the consent of their parents. NORD's President, Abbey Meyers, serves on NHRPAC.

HHS already allows teens to participate in some research projects without the consent of their parents, as long as ethics committees approve. This generally involves studies of abused children, pregnant teens, and studies of sexually-transmitted diseases if teens do not want parents to know their diagnosis. However, the Food & Drug Administration (FDA) refuses to adopt the HHS rules and insists that informed consent can only be given by an adult.

NHRPAC says that the FDA's refusal to adopt the broader standard has denied mature teenagers the right to participate in studies of treatments for sexually transmitted diseases, including AIDS. In some cases (e.g., child abuse), informing parents could be dangerous to the child, so each case must be considered independently to determine if a child is mature enough and is capable of giving their informed consent. It is up to the FDA to accept or reject the committee's advice, but the situation illustrates the problem of each government agency having its own human subject protection rules.

Overseas Drug Trials

As a result of last winter's six-part *Washington Post* series, *The Body Hunters*, a House of Representatives committee has tacked an amendment on to an export bill that would require drug companies to obtain an export license on drugs intended for clinical trials overseas. Additionally, the manufacturer would have to show that a U.S. ethics committee has approved the clinical trial before the license would be issued. If enacted, this may stop some companies from performing clinical tests in third-world countries in order to avoid American safety and ethics rules.

Meanwhile, a lawsuit was filed against Pfizer for a bacterial meningitis trial it conducted in 1996 on 200 children in northern Nigeria. The company tested the drug during an epidemic of meningitis, measles, and cholera without obtaining parental consent and without explaining that the treatment was experimental, according to the lawsuit. The children could have obtained a standard treatment that was being distributed at no cost by a charitable medical organization at the time, but parents were not told there was a choice.

Pfizer split the group of 200 children into two groups. One group was given the experimental drug, while the other was given an **especially low dose** of a standard drug that is proven to be safe and effective for meningitis. The suit alleges that there were deaths and injuries in the low dose control group so that Pfizer could claim that its experimental drug was superior to the standard therapy. Pfizer denies the charges.

PHARMACEUTICALS: IS FDA TOO SLOW?

The pharmaceutical industry is complaining that the FDA is too slow. Consumer groups complain that the FDA is approving drugs too fast and that dangerous drugs are reaching the market because the FDA doesn't take enough time to study them. The FDA is perpetually in a no-win situation.

In answer to the industry's criticism, the FDA says that its approval rate has remained normal. Breakthrough medications are speeded through the approval process in six months or less, and "standard" drugs that are only slightly different than other available treatments get through the approval process in one year.

The drug industry says that last year the FDA took four months longer to approve new drugs. The FDA says the statistics were skewed because the agency approved drugs that were languishing for years, such as RU-486, which took four years to approve due to political and manufacturing problems. The agency also says that manufacturers are submitting applications for fewer novel drugs (that are given priority status), and submitting more applications for "me-too" drugs that are only slightly different than existing products. These



types of drugs are given a "standard" review, which takes 12 months.

Reviews of biotechnology drugs, however, increased from 11.5 months in 1998 to 16.5 months in 1999. The FDA says this is because more companies submitted incomplete applications that could not be reviewed. Critics suggest that it is better for companies to blame the FDA for a slow approval process, than to admit to Wall Street that the clinical information a company submitted was not adequate.

The FDA expects to receive applications this year for only 28 new drugs, which are 15 fewer than in 1998. "That's not our slow down," said Dr. Janet Woodcock of the FDA, "We're sitting here with open arms." However, consumers suspect that the agency is rejecting more new drug applications because it has been forced to withdraw many drugs from the market in recent years, after they killed and maimed people.

BAYER WITHDRAWAL

German-based pharmaceutical company, Bayer AG, was forced to withdraw its cholesterol drug, Baycol (cerivastatin), from the market in early August after 52 people died from serious side effects. The drug was prescribed to an estimated 700,000 Americans, and when serious side effects appeared, Bayer twice re-labeled the drug to warn doctors. The warnings did not reduce the incidence of side effects, and Bayer decided to "voluntarily" withdraw it from the market in the USA and Europe. The drug was approved in 1997 and marketed in 1998. Baycol is the 12th prescription drug to be removed from the American market since 1997 due to serious side effects. Sales of Baycol were \$554 million last year.

INHALERS RECALLED

The consumer group, Public Citizen, charges that at least ten asthma patients may have died from albuterol inhalers that were later recalled by Schering-Plough.

The March 2000 recall was because the inhalers were improperly filled, according to the company, and it denies that any of the deaths were caused by its product. Public Citizen cites 17 deaths in which the inhalers were indicated as the probable cause.

DRUG COMPANIES PAY FOR AMA ETHICS CAMPAIGN

The American Medical Association (AMA) has launched a \$1 million campaign to educate doctors about AMA ethics guidelines that prohibit physicians from accepting gifts of more than minimal value from drug companies. Nine large pharmaceutical companies have given contributions totaling \$675,000 to the AMA to underwrite the campaign. The guidelines were first instituted in 1990, and updated in 1998. The AMA says that most doctors are unaware that the guidelines exist.

COX-2 INHIBITORS

Cox-2 inhibitors have been touted as a "major breakthrough" in the treatment of arthritis, especially because they are believed to be easier on the stomach than other anti-inflammatory drugs such as aspirin. Now studies are indicating that these drugs, sold as **Celebrex** and **Vioxx**, may carry an increased risk for cardiovascular events such as heart attack and stroke (*JAMA*, August 22, 2001, Mukherjee et al.) The manufacturers of these drugs deny any link to cardiovascular events, but authors of the *JAMA* article say until a better assessment of risks is known, they "urge caution in prescribing these agents to patients at risk for cardiovascular morbidity." Both products have sales over \$1 billion annually.

FAILURE OF EMPHYSEMA SURGERY

Since 1994, lung reduction surgery has been touted as the only effective treatment for emphysema. The surgery was supposed to give the lungs more elastic properties, allowing patients to breathe easier. The operation costs \$25,000 to \$60,000, but because insurance will not usually pay, most people had to pay



cash. In 1995, Medicare refused to pay for the surgery, and it was intensely criticized by consumers for denying care to dying patients with no other treatment options. Doctors who have performed the surgery over the past several years claimed that the procedure offers emphysema patients a 70 percent improvement in their condition. Ultimately, Medicare joined with the NIH to sponsor a large clinical study that would decide if the surgery was actually effective.

NIH has had great difficulty enrolling patients in the 1,800-patient, five-year randomized, controlled study because many people did not want to be "randomly assigned" to the non-surgical group. They were convinced that the surgery would be effective. However, the study was stopped early because researchers found that people who had the surgery were more likely to die early than those who did not have lung reduction. Eleven of 69 patients who had the surgery died, and none had improvement in their quality of life. The study will be published during October in the *New England Journal of Medicine*, but results were released early because it was "of immediate importance to doctors and patients."

THE STEM CELL CONTROVERSY

On August 9, 2001 President Bush announced his decision about embryonic stem cell research. The President decided that he would allow the research to go forward with federal funding, but it would be restricted to 60 cell lines that already existed before the date and hour of his speech. That means that no more fertilized eggs can be destroyed by federally-funded scientists who are trying to obtain new stem cells.

The announcement met with extreme criticism from both the left and the right. Anti-abortion advocates did not want any stem cell research to go forward even if the eggs have already been destroyed, while scientists complained that 60 cell lines were not enough. The scientific community became very vocal about the number of cell lines that NIH projected because they were convinced there were only about ten existing lines.

The fertilized eggs are created in fertility clinics, and if they are not needed for implantation into a mother's womb, they are frozen until the parents decide they do not want them anymore. At that time, they are discarded. Only a small number of frozen embryos have been used in the U.S.A. to start new lines of stem

cells that are grown in laboratories with mouse cells. These mouse cells are known as "feeder" cells because they excrete a substance that enables the human stem cells to stay alive. Unfortunately, the FDA categorizes any human cells that are mixed with animal cells as "xenotransplantation" because it is possible that the animal cells could carry unknown viruses that may cause disease in humans. Therefore, scientists say, the existing cell lines may never be used in humans because they were grown with mouse cells.

Where are the Cells?

On August 27, the NIH finally announced the location of the 64 stem cell lines, temporarily calming the scientific community. Most of them exist outside the United States. Almost 40 percent of the cell lines are in Sweden. In the United States there are only four sources that will be allowed to distribute their cell lines: a private company in San Diego, CyThera, has nine lines; the Wisconsin Alumni Research Foundation, in Madison, Wisconsin holds five lines; BresaGen, an Australian company with offices in Georgia has several lines; and the University of California in San Francisco owns two lines. However, the UCSF scientist who created the lines is so frustrated with the Bush administration's policy that he is moving to Great Britain and taking his cells with him.

The remaining cell lines are from India, Australia, and Israel. NIH points out that this research is just in its initial stages, and many years of basic research on stem cells is needed before any conclusions can be made about their therapeutic value in humans. Additionally, the President's restrictions do not apply to privately-funded research so companies can continue to destroy frozen embryos if federal funds are not involved.

The NIH is creating a *Human Embryonic Stem Cell Registry* to maintain information on all the stem cell lines that meet the President's research criteria. The source of each stem cell line will have to prove the cells were derived from embryos before 9:00 p.m. on August 9, 2001; that the parents gave their informed consent to allow the cells to be used for research; and that the cells were derived from an excess embryo that was created only for reproductive purposes.

More Questions

In 1998, the Wisconsin Alumni Research Foundation (WARF) patented the stem cell isolation discovery that



made stem cell research possible. Therefore, anyone who has isolated stem cells would probably have to pay the Foundation a royalty. This may be why the existence of cell lines outside of Wisconsin has been kept secret until now. After President Bush's announcement, academic scientists who wanted to pursue this research were not certain they would be able to afford the prices that cell line holders would charge for access to their stem cells. However, at a September congressional hearing, HHS Secretary Tommy Thompson announced that WARF agreed not to block government-funded scientists with its stem cell patent, and would supply the cells at a nominal cost.

However, the Swedish cell lines are now in question. A Swedish researcher from Goteborg University was quite surprised that the Bush administration claimed the university has 19 stem cell lines. According to the researcher, the university has three defined cell lines; they are trying to develop four more lines; and they have about 12 others "that could possibly be developed in the future." He went on to say, "Maybe they wanted to come up to the number that the White House had already used so they have to stretch things, I don't know. It could have been a deliberately over-optimistic interpretation of what we said."

At the September 5th Senate hearing, Secretary Thompson admitted that **fewer than half of the 64 cell lines are fully established and ready for research.** However, he noted that government grants for this research will not be awarded for eight or nine months, and he assured the Senators that the growing cells should be ready by that time.

NEW BIOETHICS PANEL

In the wake of the stem cell debate, President Bush announced that the existing **National Bioethics Advisory Commission** will be dissolved in October and replaced by a new **Presidential Bioethics Council**. The Council will be chaired by Leon Kass, M.D., Ph.D. of the University of Chicago. Kass was a major advisor to Bush in the stem cell debate. He opposes cloning human embryos for stem cell research.

Besides stem cell research issues, the Council will examine the ethics of assisted reproduction (in vitro

fertilization), genetic screening, human cloning, gene therapy, euthanasia, brain implants, and psychoactive drugs. Kass is a well respected and conservative bioethicist who is 62 years old.

POSSIBLE MAD COW THERAPY

Scientists are studying a combination of Quinacrine (an anti-malaria drug), and Chlorpromazine (an anti-psychotic drug), to treat the human variant of mad cow disease. A University of California-San Francisco study published in the *Proceedings of the National Academy of Science* during August indicated that mouse cells infected by "prions" (which cause mad cow disease) responded to the combination of the two drugs. Researchers do not know if the drugs will affect humans, but there is no current treatment available for prion diseases. Creutzfeldt-Jakob disease is caused by infectious "prions."

EQUAL PROTECTION VOTING RIGHTS ACT (S.565 AND H.R. 1170)

The American Association of People with Disabilities is urging organizations to endorse this bill, which mandates access to polling places and voting machines (by November 2004) for blind and disabled voters. It would also allow a disabled person to bring a person of their choice into the voting booth. For more information, you can contact AAPD at: www.aapd-dc.org or 800-840-8844.

MEDICAID CHILDHOOD SCREENING

Medicaid law requires children to receive *Early and Periodic Screening, Diagnostic and Treatment* services (EPSDT). In recent years, states have been allowed to contract with managed care insurers to provide Medicaid services to low-income families. EPSDT services include health and developmental history, physical exams, immunizations, laboratory tests, vision, dental, and hearing services.



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The General Accounting Office (GAO) recently found that more than 56 percent of Medicaid beneficiaries are now in managed care, and because these insurance companies are not paid for each service they provide, no one is keeping tabs on whether children are receiving the mandated EPSDT services. Data on each service are not collected because the state gives each managed care insurer a capitated amount for each patient each year (no matter how many services are or are not provided).

PHARMACIST DILUTES DRUGS

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A Kansas City pharmacist was arrested for allegedly diluting cancer chemotherapy drugs and keeping the profit for himself. Tests by the FBI and FDA on the drugs showed that he was selling intravenous drugs to doctors that were diluted between 17 percent and 39 percent of their prescribed strength. Some samples showed they contained only one percent of the intravenous drug. Investigators are trying to locate all of the patients who may have been victimized by the pharmacist, but some are dead. The scheme was discovered when a salesman from Eli Lilly discovered that the pharmacy was ordering less of the drugs than it was selling to local doctors.

NOT WORKING AS PREDICTED: MEDICARE+CHOICE

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In 1997, Congress created the Medicare+Choice program to entice seniors in managed care. Congress predicted that 30 percent of Medicare beneficiaries would soon switch to the managed care program. But a few years later many managed care insurers dropped out of the program claiming they could not earn enough profit. In the past two years, the number of Medicare beneficiaries in Medicare+Choice insurance dropped from 6.4 million to 5.7 million, mostly because the insurers withdrew from the market. These people returned to the standard Medicare fee-for-service program. Congress is studying new incentives to attract managed care insurers back into the Medicare+Choice program.

MEDICARE RX DISCOUNT CARD BLOCKED

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Several months ago President Bush proposed to make prescription drug discount cards available to Medicare beneficiaries, which would enable them to purchase drugs at discount prices. Private companies would be able to charge up to \$25 for the annual discount card. The Department of Health and Human Services would decide which companies would be permitted to sell the cards to 39 million Medicare beneficiaries by the beginning of 2002. Twenty-eight pharmacy benefit companies applied to HHS for permission to sell the cards.

Five days after the President announced the program, HHS was sued by the National Association of Chain Drug Stores and the National Community Pharmacy Association. They argued that the program was illegal, it was created by government officials in "secret meetings," and it failed to allow public participation in drafting the program's regulations. The pharmacy trade groups also feared that any discounts the program provides would come at the expense of pharmacists.

On September 6, 2001, the federal judge agreed that the White House has no legal authority to create the new program, and that the government is required to invite public input when drafting federal regulations. The judge issued an injunction on an emergency basis to stop the program before it is launched because he said harm would be done if HHS is allowed to choose which companies could participate.

Meanwhile, this saga continues for 39 million Medicare beneficiaries who have no prescription drug benefits.

CHIP ENROLLS ADULTS, NOT KIDS

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In October, 2000, the New Jersey Child Health Insurance Program (CHIP) opened enrollment to parents as well as children from low and middle-income families. To date, the program has enrolled 121,000 adults, and only 5,000 new children. The new "Family Care" program has enrolled only 48 percent of the estimated eligible children in New Jersey, but 97 percent of eligible adults.



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**PATIENTS' BILL
OF RIGHTS**
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The contentious *Patients' Bill of Rights* has passed the House and Senate in different versions. This means Congress must create a *Conference Committee* to hammer out the differences between both Bills. The major sticking point is liability. The House version of the bill limits damages (including pain, suffering, and punitive damages) to \$1.5 million. One could sue for punitive damages only if an insurer does not comply with the orders of an external review committee.

The Senate-passed bill provides uncapped non-economic damages, and punitive damages are capped at \$5 million. The House bill passed on a very narrow party line vote of 218-213. Democrats want a higher liability limit (or none at all), and they vow that they will not compromise in the conference committee because the House statute puts the burden of proof on patients, says Senator Ted Kennedy. Liability, he says, is "the lynchpin in guaranteeing protections" against health insurance companies. Other critics say that the House bill is unconstitutional because it preempts state laws by requiring federal rules to be followed in state courts.

PHARMACEUTICALS
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Drug Spending

A recent study by the National Institute for Health Care Management Foundation indicates that spending on prescription drugs rose 18.8 percent last year to \$131.9 billion. The large increase is mostly due to an increased number of prescriptions written for the newer more expensive drugs for common diseases such as high cholesterol, diabetes, arthritis, etc. The president of the Pharmaceutical Research & Manufacturers Association (PhRMA) says the study should be welcomed as "good news" because drugs are keeping people out of the hospital.

The Foundation study indicates that about half of the nearly 19 percent increase is due to increased prescriptions for only two dozen commonly used

products including Vioxx and Celebrex for arthritis, Lipitor for high cholesterol, Prevacid for indigestion, and Glucophage for diabetes. Antidepressants were the best selling category of drugs, up 20.9 percent over the previous year. The study also estimates that drug spending rose approximately 40 percent between 1998 and 2000; 42 percent of the increase is attributable to an increased number of prescriptions, 36 percent was due to a shift toward newer and more expensive drugs, and 22 percent was due to price increases. The 50 top selling medicines accounted for 30 percent of all prescriptions written last year. Nineteen drugs had retail sales over \$1 billion.

Drug Prices

The prices of the 50 most frequently prescribed drugs rose an average 6.1 percent last year, compared to general inflation (excluding energy) of 2.7 percent, according to Families USA. Eighteen of these drugs increased more than three times the rate of inflation. The thyroid medicine, Synthroid, increased 22.6 percent, which is 8.5 times the rate of inflation.

Professor Stephen Schondelmeyer of the University of Minnesota says the cost of making a medication is only 10 percent of the price, and about one-third of the American price covers advertising and marketing expenses. About one-third of all prescription drugs are purchased by the elderly. PhRMA insists that drug prices rose only 3.9 percent last year, but admits the industry seems to have a public relations problem over pricing.

Scandal

TAP Pharmaceuticals (owned by Abbott Laboratories and Takeda Chemical Industries) is expected to pay the government more than \$840 million to settle charges that it raised prices and bribed doctors to prescribe its prostate cancer drug, Lupron Depot. The company is accused of giving doctors free drugs and allowing them to sell the drugs to their patients; bribing an HMO with \$65,000 to switch patients from a competing drug; and manipulating the Average Wholesale Price (AWP) for government reimbursement (Medicare) to assure that doctors would earn at least \$100 profit per dose. It is estimated that Medicare may have spent \$100 million



per year more than it should have from 1993 to 1998 on Lupron. Cancer chemotherapy drugs are often sold to oncologists who then bill the patients insurance.

CME Controversy

The former editor of the *New England Journal of Medicine* (NEJM), Dr. Arnold Relman, printed a scathing editorial in the April 18 issue of the *Journal of the American Medical Association* (JAMA), decrying the influence of drug companies over Continuing Medical Education (CME) credits. "The pharmaceutical industry has gone too far," wrote Relman, "It is assuming a role in CME that is inappropriate for an industry with a vested interest in selling prescription drugs."

Relman also wrote about the growth of a new for-profit industry, CME providers, that create educational programs, choose speakers, and arrange conferences. These "hired agents of pharmaceutical companies are given authority for the content of CME programs." Eli Lilly has created Lilly CME, and Bayer has created the Bayer Institute for Health Care Communication, and both have been accredited as CME providers. Relman asserts that only medical professional societies should be accredited for CMEs because they are independent of commercial influence. He feels the "integrity and credibility" of CMEs are being questioned due to the increasing influence of companies. "There has been no effective challenge to this intrusion of for-profit businesses," says Relman, and "commercialization threatens to overwhelm us."

Unpublished Studies

Controversy is brewing over unpublished studies that are kept secret for a variety of reasons. The phenomenon is called the "file drawer effect." The investigation of the recent death of a volunteer in the Johns Hopkins asthma study revealed that the primary investigator did a literature search on the use of the investigational drug used in the study. The journal article he cited did not mention side effects. Investigative reporters contacted the author of the article, and he revealed that several patients did have serious adverse events, which he didn't mention in his journal article.

Pharmacia Upjohn sponsored three phase III studies on its nicotine inhaler several years ago, but only one study was published. The company will not reveal why they are keeping data from the other two studies secret. A scientist from the Reno Veterans Affairs Medical Center said the file drawer effect "violates scientific ethics and skews the medical literature to make treatments look overly beneficial" because negative information about the product is not published. The Public Citizen Health

Research Group says that consumers cannot believe drug companies "if they only release data from studies with results palatable to company executives, stockholders, or potential stockholders."

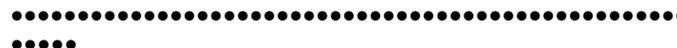
Data Confidentiality

When drug companies decide to fund a clinical trial, they sign contracts with researchers. Some of those contracts contain clauses giving the drug sponsor veto power over publication of the data. If a company does not want the study to be published, they can usually prevent it. Last year an Irish researcher asked Bayer to provide an antibiotic for a study he was doing. He was asked to sign a contract with the following clause: "We declare that we will inform Bayer AG in writing of our test results and will not publish or commercialize them without written permission of Bayer AG." The researcher objected, but Bayer refused to waive or remove the restriction.

An April, 2001 editorial in *The Lancet* reviewed a similar problem when a pharmaceutical manufacturer wanted an author to remove a sentence from a journal article that raised safety questions about a drug. *The Lancet* told the company it would publish an article naming the company and describing its attempt to manipulate the study's conclusions. The article was printed with the sentence intact.

The Lancet editorial asserts, "Doctors must look to existing institutions to challenge, on the public's behalf, forces of commercial bias that risk staining permanently the integrity of medicine."

MEDICAL JOURNALS CHANGE RULES





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Editors from eleven of the world's most prominent medical journals will announce a new policy this autumn to ensure "scientific independence" by refusing to publish drug company sponsored studies unless the authors are guaranteed to write without corporate oversight and intervention. Scientists have complained that they are sometimes prevented from publishing uncensored articles because pharmaceutical sponsors must approve manuscripts before publication, and they are prevented from publishing unfavorable study results. Henceforth, authors of articles will have to guarantee scientific independence before the article is considered for publication in a major journal.

The Autism National Committee, the Northeast Regional Conference on Autism, and the University of New Hampshire's Institute on Disability Conference: "Things that Matter": **October 12-13, 2001** (Oct. 12th Crowne Plaza Hotel, Nashua, New Hampshire; October 13th Souhegan High School in Amherst, New Hampshire).

Narcolepsy Network 2001 Annual Conference: **October 12-14, 2001** at the Long Beach Hilton Hotel in Long Beach, California. Contact: Narcolepsy Network, 10921 Reed Hartman Hwy., Suite 119, Cincinnati, Ohio 45242; phone: (513) 891-3522; Web site: <www.narcolepsynetwork.org>.

MEETINGS & PUBLICATIONS

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Depression & Related Affective Disorders Association (DRADA) Annual Meeting: "Mood Disorders: Clinical Perspectives and an update on Brain Imaging": **September 20, 2001** at the Oakland Mills Interfaith Center in Columbia, Maryland. For more information, call (410) 955-4647 (Baltimore) or (202) 884-3964 (Washington).

CT 2001 Women's Conference: "Defining a Vision for Behavioral Health Care": **October 22-23, 2001** at the Marriott Hotel in Farmington, Connecticut. Contact: The CT Women's Consortium, 205 Whitney Avenue, New Haven, CT 06511 or visit: <www.womensconsortium.org> or call (203) 498-4184.

The Society for Progressive Supranuclear Palsy (PSP) Symposium: **September 28, 2001** at the Crowne Plaza Hotel in Woburn, Massachusetts. Contact: The Society for PSP, Woodholme Medical Bldg., Suite 515, 1838 Greene Tree Rd., Baltimore, MD 21208; phone: 800-457-4777 or (410) 486-3330.

National Marrow Donor Program (NMDP) Council Meeting: "A Fusion of Hope, Harmony & Life": **November 9-11, 2001** in Minneapolis, Minnesota. Contact: NMDP, 3001 Broadway St. N.E., Suite 500, Minneapolis, MN 55413-1762, Att: Pat Valley; phone: (612) 627-5813 or (800) 526-7809; fax: (612) 627-5810; Web site: <www.marrow.org>.

NORD Annual Patient/Family Conference: **October 5-7, 2001** at the DoubleTree Hotel in Arlington, Virginia. Contact: Donna Bolton, NORD Development Associate, at the NORD office (203) 745-6518, ext. 210.

National Hemophilia Foundation 53rd Annual Meeting: **November 15-17, 2001** at the Opryland Hotel in Nashville, Tennessee. Contact: National Hemophilia Foundation, 116 West 32nd St., 11th Floor, New York, NY 10001; phone: (212) 328-3700 or (800) 424-2634; fax: (212) 328-3766.

Hereditary Colon Cancer Association (HCCA) 2001 Annual Conference: **October 7 & 8, 2001** at the DoubleTree Hotel in Arlington, Virginia. Contact: HCCA, 3601 N. 4th Ave., Suite 201, Sioux Falls, SD 57104-0787; phone: (605) 373-2067; fax: (605) 336-6699; email: <hcca@hereditarycc.org>.

NIH State-of-the-Science Conference: "Endoscopic Retrograde Cholangiopancreatography (ERCP) for Diagnosis and Therapy: **January 14-16, 2002** at the Natcher Conference Center, The William H. Natcher Bldg., National Institutes of Health, Bethesda, Maryland. To register for this conference or to obtain further information, visit the NIH Consensus Development Program Web site: <<http://consensus.nih.gov>> or contact: Heather Zeitlin, Prospect Associates, 10720 Columbia Pike, Silver

National Institutes of Health Symposium: "Celebrating 50 years of Brain Research: **October 9-10, 2001** at the Natcher Conference Center, NIH Campus, Bethesda, Maryland. For more information, call: (866) 502-7246; email: <50brain@masimax.com>.



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Spring, Maryland 20901; phone: (301) 592-2115; fax:
(301) 593-5791; email: <ercp@prospectassoc.com>.

NIH State-of-the-Science Conference: “The
Management of the Clinically Inapparent Adrenal Mass
 (“Incidentaloma”): **February 4-6, 2002** at the Natcher
Conference Center, National Institutes of Health,
Bethesda, Maryland. To register for this conference or
to obtain further information, visit the NIH Consensus
Development Program Web site:
<<http://consensus.nih.gov>> or contact: Channett
Williams, Prospect Associates, 10720 Columbia Pike,
Silver Spring, Maryland 20901; phone: (301) 592-2130;
fax: (301) 593-5791; email:
<adrenalmass@prospectassoc.com>.

Third North American Symposium: “Skeletal
Complications of Malignancy”: **April 25-27, 2002** at the
Natcher Conference Center, National Institutes of
Health,
Bethesda, Maryland. For more information, contact:
The Paget Foundation, 120 Wall Street, Suite 1602,
New York, NY 10005-4001; phone: (212) 509-5335;
fax: (212) 509-8492; email: <pagetsym@aol.com>;
Web site: <www.paget.org>.

Note: Please notify NORD of any address,
phone or fax number, or email address
changes so we can keep our contact
information current.