Dr. Julian Whitaker's
Health & Healing®

January 1996 Supplement

The FDA's Unholy War Against Dr. Burzynski

As I discussed in November, Stanislaw Burzynski, M.D., Ph.D., has been treating cancer patients for years with a non-toxic therapy he discovered called *antineoplastons*. Many patients with terminal cancers taking this therapy are now in complete remission.

Despite the obvious evidence of benefit, the Food and Drug Administration (FDA) has been trying to put Dr. Burzynski out of business for the past 12 years. This culminated on November 20, 1995 in 75 criminal charges that could put this talented physician in jail for 229 years!

It all started in 1983 when the American Cancer Society put Dr. Burzynski's therapy on their "unproven methods" blacklist. A few months later, the FDA filed a civil suit in federal court in an attempt to shut him down. Federal Judge Gabrielle McDonald ruled that Dr. Burzynski could continue his work, but did stipulate that he could not ship the therapy across state lines. The vendetta began.

The FDA Used Dirty Tactics

Robert Spiller, the FDA lawyer assigned to this case, was furious that the judge did not put Dr. Burzynski out of business, and told Dr. Burzynski's defense lawyer, "Well we did not get him that way, but we can use the criminal system."

Since 1983, Spiller, the FDA, and a parade of mindless US attorneys have terrorized Dr. Burzynski with raids on his clinic in Houston, Texas, and have used the grand jury system to harass Dr. Burzynski and his staff. In 1985, the FDA convened the first grand jury, then raided his clinic and seized virtually all of his medical records (11 filing cabinets full). Because Dr. Burzynski could not practice medicine without the charts, the court ordered the FDA to "allow him" to come to FDA offices in Houston and copy the charts at his expense. In spite of all this activity, there was no indictment.

A second grand jury in 1990 subpoenaed 100,000 more documents, but after nine months of investigation, the FDA did not convince the grand jury to indict Dr. Burzynski. To date, the FDA has not returned those medical records and subpoenaed documents.

He Did Everything by the Book

In 1991, experts from the National Cancer Institute (NCI) carefully reviewed the charts of seven patients with "incurable" brain cancer who were being treated with antineoplastons. They noted antitumor action in all seven, complete remission in five, and called for long-term trials to more accurately assess benefit. Dr. Burzynski then submitted copious data to the FDA, seeking permission to do the necessary trials.

From 1991 to 1993, while the FDA "sat" on the request, Dr. Burzynski was under constant investigation by the FDA and the US Attorney's office as they sought to demonstrate that he was sending his therapy across state lines. A third grand jury was convened in 1994—and yet again failed to indict.

The Texas Medical Board Jumped In

As if not to be outdone by Robert Spiller and the FDA, the Texas State Board of Medical Examiners is also out to get Dr. Burzynski. There has never been a patient complaint to the Board against Dr. Burzynski. In spite of that, in 1994, they tried to put him on indefinite probation. The probation requirements were hostile, restrictive, demeaning, and more appropriate for a paroled felon than a physician who had never had a complaint nor been charged with a crime.

In fact, some of the requirements were paternalistic nonsense. For instance, one was that Dr. Burzynski abide by Texas and federal law, as if he was not required to abide by the law ordinarily. More ominous, several requirements were open to subjective interpretation. Anyone reading them would conclude that it was not an effort by the Board to safeguard the public, or even uphold the law. It was more a step toward closing Dr. Burzynski's practice.

The Medical Board contended that Dr. Burzynski should be on probation in a 20-page "finding of fact" court document. In that document, it was confirmed that many of Dr. Burzynski's patients had not been helped by conventional therapy, yet were alive because of antineoplastons. In addition, *seven physicians*—including the chief of neuroradiology at the National Institutes of Health—testified that without antineoplastons many patients would die. This testimony was not contested by the State or the Board.

However, the Texas Medical Board didn't care. They wrote that "the efficacy of antineoplastons in the treatment of human cancers is not of issue in these proceedings...." and went on about their business of destroying Dr. Burzynski and the therapy.

That document was signed by Board president John M. Lewis, M.D., a Houston cardiologist. Folks, what kind of doctor would try to "get" another doctor by using as evidence a "finding of fact" document that large numbers of patients would die as a result? What has happened to our civilization?

PLEASE CALL OR WRITE PRESIDENT CLINTON AND TELL HIM TO DROP
THE SENSELESS, WRONGFUL, & WASTEFUL PROSECUTION OF DR. BURZYNSKI
The White House, 1600 Pennsylvania Ave., NW
Washington, D.C. 20500 (202) 456-1414 or 456-1111; FAX 202 456-2461

The Case Was Dismissed

Fortunately, Judge Paul Davis was both more reasonable and compassionate than the "good ol' boys" on the Board. He threw the case out, and chastised the board for being "arbitrary and capricious," and for "abuse of discretion." The Medical Board appealed, and the case is with another group of judges.

In 1994, the FDA granted Dr. Burzynski permission to do clinical trials on antineoplastons. He has begun four separate trials at his own expense.

You might imagine that since the FDA had approved the trials they would have left him alone. Not so. On March 24, 1995, Dr. Burzynski appeared on the CBS *This Morning Show*, along with three patients who had been diagnosed as terminal but were now free of cancer. The effect this TV appearance had on the FDA was like shaking a cage full of rattlesnakes and pouring them over Dr. Burzynski's head.

The FDA Vendetta Continued

That very afternoon the FDA raided Dr. Burzynski's clinic, herded employees into a closed room, and wouldn't let them out until they had given the FDA a lot of personal information. They spent seven hours ransacking the clinic, and left with boxloads of documents.

With this, the FDA kicked off the fourth and most malicious of all grand jury investigations. For eight months, there were monthly rounds of subpoenas. As with all grand jury interrogations, witnesses had to appear without a lawyer, and were at the mercy of the prosecuting attorney. After a full day of abusive questioning by an assistant US attorney, a receptionist at the clinic, Eva Vigh, collapsed with a heart attack and has yet to recover.

If you still harbor the delusion that Robert Spiller, the FDA, and the US attorneys are trying to protect you against cancer fraud, let me tell you that in June of this year, the FDA raided and seized the X-rays and MRIs of Dr. Burzynski's most responsive patients, including the "best-case" series evaluated by the NCI. This was done to prevent him from showing this evidence that the therapy works. Incredibly, as a society, we are desperately looking for a cancer cure, yet when one is found the FDA seizes the evidence, then works to put the discoverer in jail.

Federal Judge Lynn Hughes ordered the FDA to make copies of the X-rays and return the originals, which they did. Of the almost one million documents and items the FDA has seized over the past 13 years, these X-rays are the only items they have returned—and that only because of a court order. Of course, the Bill of Rights forbids arbitrary government seizure of property, but who cares?

Wouldn't You Want a Life-Saving Therapy?

Now look at your spouse, your children, and your grandchildren. Imagine that one of them had an inoperable brain tumor the size of an orange, and that with the antineoplastons developed by Dr. Burzynski, it had shrunk to the size of a pea.

I want you to know that in order to "get" Dr. Burzynski, Robert Spiller would think nothing of coming into your home and seizing the antineoplaston therapy, knowing that it was the only hope your loved one had to avoid a horrible death.

Robert Spiller has done well at the FDA. He is now Associate Chief Counsel for Enforcement.

Folks, over the past five years we have gotten involved in a variety of important causes, and have had an impact. However, our support of Dr. Stanislaw Burzynski is more important than all of them combined, because of what is at stake. If the FDA wins its unholy war with Dr. Burzynski they will not only destroy one of the most promising cancer therapies we have, they will also reinforce the message that any physician or scientist with the talent, energy, and courage to make a positive difference in the health field, had best move to another country.

Is that what you want?

Dr. Burzynski does not have the money necessary to save his therapy and himself. Without a dime from the government or any other agency, he discovered, developed, and even synthesized a truly significant breakthrough in cancer. And hounding him all the way was Robert Spiller and the FDA—*with your tax dollars*. Is Robert Spiller helping you?

Let's Get Behind Dr. Burzynski

Supporters of Dr. Burzynski have set up a legal defense fund. I encourage you to give any amount you feel you can. For a $50 donation, the defense fund has put together an information packet on antineoplastons, including the NCI report on seven cases.

For $75, the defense fund will throw in a videotape of the recent congressional hearings conducted by Congressman Joe Barton investigating the FDA's vendetta against Dr. Burzynski. Mrs. Mary Michaels offers tearful testimony. At the age of five, her son Paul had an inoperable brain cancer the size of an orange. Both the Mayo Clinic and Memorial Sloan-Kettering Cancer Center told her that nothing could be done.

Today, on Dr. Burzynski's therapy, Paul is a normal, rough-housing, skateboarding, 14-year-old-kid. The brain cancer has shrunk to the size of a pea. You can feel the emotional torture this family experiences every time Robert Spiller and his goons raid Dr. Burzynski to cut off their supply.

You can also watch Commissioner David Kessler *not* answer a single question during his testimony, and you will get to meet, in person, Robert Spiller...

Make checks payable to The Burzynski Legal Defense Fund, and mail to P.O. Box 1770, Pacific Palisades, CA 90272.

Send a copy of this supplement to your local newspaper, radio and television stations. Rest assured, the FDA is also "working" the media.

Reports on Dr. Stanislaw R. Burzynski have been featured on or in:

The New York Times
US News and World Report
Good Housekeeping
ABC News Nightline
CBS Evening News
Gabe Pressman Investigative Reports
Local TV news stations around country
Scientific American Magazine
CBS This Morning
CBS Street Stories
CBS 48 Hours
CNN, CNBC and C-SPAN
20/20
Sally Jesse Raphael
Gerry Spence

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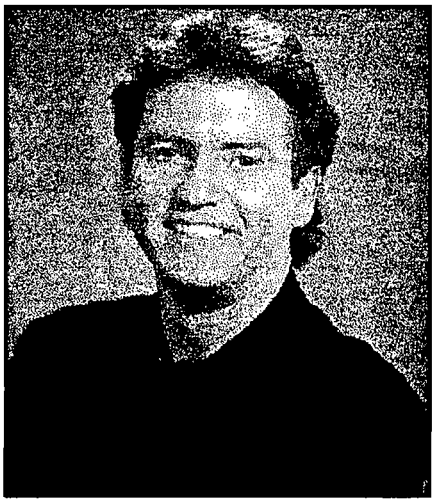
An Open Letter from
Larry Gatlin



Dear Friend:

I'm not writing to you today as a singer or as a celebrity but merely as Larry Gatlin, private citizen and proud American. I love my country and it's been very good to me but that doesn't mean that every once and a while we don't make a mistake. In fact, much of our greatness as a democracy comes from our ability to recognize and remedy our mistakes.

Well folks that's why I'm writing today- I'm very concerned that our government is about to make a mistake and if they do, some desperately ill Americans will suffer.

You know, I've been very fortunate in my life, I've been able to stay healthy and not lose any loved ones to cancer. But a good friend of mine isn't so lucky - he's fighting cancer now, and if we stop and think about it, I bet we all know somebody who's faced this terrible disease too. Lord knows it isn't easy - surviving cancer takes every bit of fight and faith a body's got and a good doctor makes all the difference.

Fortunately, my friend found a good doctor and a good treatment for his cancer but there's just one small problem - our government wants to take away his medicine and put his doctor in jail!

Who could take away a cancer patient's medicine, you ask? Well, you might have heard of a government agency called the FDA, the Food & Drug Administration, and most of the time they do a heck of a job of keeping our country safe and healthy, but every now and then they get a little carried away - and that's what's happened here.

My friend is receiving a promising new cancer therapy called "antineoplastons". They are naturally occurring, non-toxic substances which help the body to fight off cancer. They were discovered years ago and have been safely used on thousands of cancer patients with some amazing results. In fact, the FDA has approved 65 Phase 2 clinical trials of this promising therapy, *BUT* - and here's where it gets a little crazy - that very same FDA now wants to put the doctor who invented this drug in prison!

Now, this story has been on 'Nightline', '48 Hours', even on the front page of The New York Times but most people still haven't heard about it. Or maybe they have heard about it but like me they just can't understand it. Who can blame them - it's never happened before! Never before has the FDA approved an experimental drug for cancer testing while simultaneously trying to destroy the scientist that discovered it.

Why are they doing it? It seems that the FDA is a government agency that seldom forgives and never forgets. You see, my friend's doctor, Dr. Stanislaw Burzynski of Houston, Texas won a court case against the FDA back in 1983 and frankly folks, the government just doesn't like to lose. Ever since then, the FDA lawyers have vowed to settle the score.

So when Dr. Burzynski came up with his non-toxic antineoplaston cancer drug, all he ever got was the royal runaround. Despite universal agreement on it's safety and abundant evidence about it's effectiveness (including confirmation by the National Cancer Institute in 1991) the FDA put antineoplastons on terminal hold, leaving terminal cancer patients with no alternative to toxic treatments.

But the FDA didn't just want to put Dr. Burzynski on hold, they wanted to put him on ice! So even after three grand juries refused to indict him because of lack of evidence, the government still managed to indict him on a legal technicality about shipping medicine out of state. And now this beloved doctor who has saved hundreds of lives faces hundreds of years in a federal penitentiary!

Folks, when my friend told me about this situation I didn't believe it. I didn't believe that in this great country we would ever get to the point where we were letting murderers go free and putting good doctors in jail.

I have truly never seen such breathtaking bureaucratic boneheadedness. They can't even get their own story straight - on the record the FDA says antineoplastons are safe, yet off the record, they are mounting a massive public relations war against Dr. Burzynski (and guess who's paying for all this silliness?)

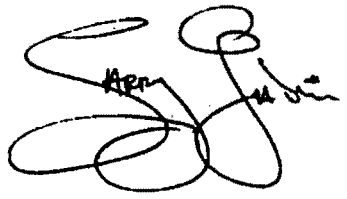
Keep in mind, this FDA's 'public enemy' is an M.D. and PHD biochemist who has treated over 3000 patients in the last 18 years with his non-toxic medicine and not one of them has ever filed a complaint! His scientific breakthrough is being studied all over the world and right now three hundred men, women and children (including my friend) are gratefully participating in the clinical trials. So who is the FDA protecting and what are they thinking?

Folks, it's time to stand up and stop this insanity now . Do you really want your tax dollars going to put a respected scientist in jail and leave hundreds of cancer patients without a doctor?

You know, the little known truth is that even after 25 years and 30 billion dollars, we are losing the war on cancer. More people are dying than ever before, chemotherapy and radiation have not done the job - we just can't afford to lock up a doctor whose breakthrough therapy is saving lives.

Doesn't it really come down to a question of personal choice? If you had a terminal illness, wouldn't you want to be able to try a safe non-toxic treatment that has helped so many others?

I know I would. I support Dr. Burzynski and I encourage you to do the same.



Larry Gatlin

Honorary Chairman
Friends of Doctor Burzynski

The Washington Times

Cancer doctor sees pope, but not about his health

By Larry Witham
THE WASHINGTON TIMES

Pope John Paul II has asked a Polish-American doctor about his alternative cure for cancer but has not discussed his own health, an associate of the doctor's said yesterday.

Dr. Stanislaw Burzynski, a Houston cancer expert who was summoned to the Vatican this week, could not be reached overseas to discuss details of his unusual visit with the pope.

But Dean Mouscher, clinical trials director of the Burzynski Research Institute in Houston, said Dr. Burzynski has called his associates since seeing the pope.

"He told me he did not discuss the pope's medical condition," Mr. Mouscher said in a telephone interview yesterday. "The pope was very interested in his cancer research."

He said nothing about the visit suggests the pope has cancer. "There was no reason to think that from Dr. Burzynski's trip. He did not say he [the pope] had cancer," he said.

A Vatican official said he had heard no rumors about the pope having cancer. "I've heard absolutely nothing," said Archbishop John Foley, a communications officer at the Holy See who was reached at his home in Rome last night. "I would be cautious. It's better to get confirmation from somewhere."

In November, a federal grand jury indicted Dr. Burzynski on charges of allowing his unapproved cancer treatment, a new drug called Antineoplastins, to cross state lines and to be sold by mail. His trial may begin next month.

The Vatican meeting took place Tuesday, a few days after John Paul returned from a pastoral visit to France, where he reportedly looked robust compared with other public appearances this year.

The pope, who was operated on in 1981 to remove a would-be assassin's bullet and in 1992 to remove an intestinal tumor, this year suffered three bouts of fever that doctors link to an inflamed appendix. It will be removed next month.

Dr. Burzynski, who has 400 patients, has said that, under clinical trials, his new drug shrunk malignant brain tumors.

"The FDA [Food and Drug Administration] are playing God," said Steven Siegel, director of the Burzynski Patient Group whose wife is a patient of Dr. Burzynski's. "They are keeping this successful treatment from people who depend upon it for their lives.

Mr. Siegel has been in Washington this week to lobby for passage of the Access to Medical Treatment Act.

NEWS RELEASE - ATTN: NEWS MANAGER, ASSIGNMENT EDITOR, OR NEWS DESK

CANCER PATIENTS MARCH ON WASHINGTON

CANCER PATIENTS PROTEST PRESIDENT'S BROKEN PROMISE, PERSECUTION OF TEXAS DOCTOR, DEMAND ACCESS TO NEW MEDICINE

Patients and supporters of a controversial cancer doctor will take their case to Washington on September 28th. A rally across from the White House in Lafayette Park is planned from noon to 3pm. Invited guests include congressmen, celebrities and cancer survivors. Organizers are hoping to focus attention on alleged FDA abuses in handling their case. Patients will demand continued access to their current cancer therapy and legal relief for their doctor. (Dr. Burzynski is currently in Rome where he was summoned for an audience with the Pope.)

Background: At the center of the debate is Dr. Stanislaw Burzynski, a Polish-born biochemist and physician who faces trial in Houston on October 15th. Dr. Burzynski uses a non-toxic drug he discovered in 1967 called "antineoplastons." While his medicine is not yet approved for general use, it has been FDA approved for 68 Phase II clinical trials for many types of cancer and also HIV. Some 300 patients are presently on antineoplastons all over the country.

The case has been drawing national attention because even though the FDA has officially approved the 68 current clinical trials, the agency has been secretly mounting a behind-the-scenes public relations blitz against the doctor and his treatment. In response, hundreds of present and former patients have come forward to support him, and his story has been on Nightline, 48 Hours, 20/20, even a recent front page New York Times article. The doctor faces trial next month on charges brought on behalf of the FDA by the Department of Justice. A multiple count indictment charges he caused interstate shipment of an unapproved drug when some of his patients carried their medicine back from Texas to their home states. The FDA's enforcement division lost a key legal fight with Dr. Burzynski in 1983 when a Texas court ruled they had no jurisdiction within the state and Burzynski was free to treat any patients in his Houston clinic.

On March 29th of this year, President Clinton and FDA Commissioner David Kessler promised faster cancer drug approval, but so far they have been unmoved by the pleas of Dr. Burzynski's patients. Hundreds of cancer sufferers around the country have been lining up for the clinical trials but now worry that their lives will be at risk if the FDA succeeds in jailing their doctor.

Doctor Burzynski developed antineoplastons almost 30 years ago and began treating patients with them in Texas in 1978. Made from synthetically-produced amino acids which occur naturally in the body, antineoplastons are non-toxic and do not have the common side effects of traditional chemotherapy such as nausea, hair loss and immune system damage. The drug is given intravenously and reportedly works by chemically reprogramming cancer cells rather than indiscriminately killings all dividing cells like chemotherapy.

Since 1978 Dr. Burzynski has treated over 3000 patients, most of whom had been given up on by their regular doctors after chemo and radiation failed to halt their disease. In 1991 experts from National Cancer Institute examined some of Dr. Burzynski's cases and confirmed the anti-cancer activity of antineoplastons. Earlier this year, following a public outcry and four Congressional Hearings, the FDA approved Dr. Burzynski's drug for Phase II clinical trials. While the doctor does not claim that his drug works on all cancers, he does report good results with brain tumors and lymphomas, two incurable types. Some of his HIV patients also have reported good results. The drug is also being tested in Japan, Israel, Australia and Holland. For more information, please contact:
Tony Martinez (201) 661-1900, Steven Siegel (310) 573-9122, or Rita Starr (305) 532-3113.

FDA RENEGES ON CLINTON'S PROMISE TO CANCER PATIENTS

On March 29, 1996, President Clinton, VP Gore and FDA Commissioner David Kessler held a nationally-televised press conference to announce "bold new initiatives" in the war against cancer. Their purpose was to expand access to experimental cancer drugs and expedite approval of promising new cancer drugs.

"For patients with refractory, hard-to-treat cancer, instead of requiring evidence of clinical benefits, such as survival, FDA will rely on objective evidence of partial response, such as tumor shrinkage, as an initial basis for approval," Dr. Kessler stated. "This will allow us to rely on smaller, shorter studies for the initial approval of cancer drugs.

"This accelerated procedure, which will be followed up by further studies on clinical safety and effectiveness in larger groups of patients, should and will simplify and speed up the evaluation and approval of drugs for advanced stages of sold tumors."

This is a standard of proof that pioneering cancer researcher and physician Dr. S. R. Burzynski of Houston can meet -- if the FDA will let him. Although Burzynski is conducting 69 FDA-approved phase II clinical trials of his experimental cancer drug antineoplaston, the FDA is trying to jail him for having used the drug in the past without FDA's blessing. FDA does not allege that any patient was ever harmed, and does not deny the drug may be an important advance in the fight against cancer.

Dr. Burzynski recently asked for a meeting with FDA officials to discuss his dramatic results with terminal brain tumor patients -- results which have been audited by an independent neurological institute. But the FDA refused to meet with Dr. Burzynski, stating candidly that the "bold new initiatives" announced in March had not changed anything.

In a letter to Dr. Burzynski, Oncology Division Director Dr. Robert DeLap wrote that "The cancer initiatives announced in March of this year by President Clinton and Vice President Gore did not set aside any laws or regulations related to the approval of new drugs for cancer treatment. In this regard, we have not changed our standards for the approval of such drugs."

DeLap's comments make a mockery of Kessler's promise that "The FDA's initiatives will allow the agency to rely on smaller trials, fewer patients if there is evidence of partial response in clinical trials... We will accept less information up front... Science really dictated this initiative. We now have the scientific evidence that demonstrates that we, in fact, can approve drugs on the basis of partial responses, and that's a responsible, scientific thing to do. That's real reform that, in the end, I believe will save patients."

If promises made to cancer patients by the Clinton Administration mean nothing, the American people need to know about it. That is why we will be demonstrating across from the White House in Lafayette Park at 12:00 noon this Saturday, September 28.

a. Sun 3/31/96 60 CENTS

PRESIDENT ORDERS FASTER APPROVAL OF CANCER DRUGS

MOVE AIMED AT THE G.O.P.

F.D.A. Acknowledges Risk but Sees Increases in Survival and Comfort of Patients

By PHILIP J. HILTS

WASHINGTON, March 29 — The Clinton Administration announced today that it would take steps to streamline the Food and Drug Administration's rules to speed cancer drugs to patients.

President Clinton said the regulatory changes would apply to at least 100 drugs now under study. "Dozens of them will get to the market sooner and that means they can help Americans suffering from cancers of the breast, lung, ovary, prostate and colon, among others," he said at the White House.

The Administration hopes that the steps announced today will blunt a Republican drive to reduce the regulatory reach of the F.D.A. For some time Republicans have been pressing for changes at agencies like the Environmental Protection Agency and the F.D.A., arguing, for example, that delays in drug approval are bad for patients, drug companies and the nation's competitive position. The Administration has already taken steps to streamline or reduce some drug approval regulations.

The reforms will go into effect immediately, said Donna E. Shalala, Secretary of Health and Human Services.

But the agency acknowledged that the new approach ran the risk of sometimes making drugs available whose safety and effectiveness had not been as thoroughly tested as they might have been previously.

Until now, makers of cancer drugs had to show that they could lengthen the survival of cancer patients or improve the quality of their lives before the drugs would be approved for marketing. Under the new rules, however, all a company has to show is that the drug can measurably shrink the size of a tumor, even for only a short time.

In another significant change, the F.D.A. will accept evidence of a cancer drug's effectiveness from 26 other countries, essentially all those with some system for reviewing and approving drugs, rather than requiring lengthy testing in the United States. Drugs approved in the 26 countries could become widely available in the United States long before companies submit applications for approval to market them.

Under this so-called expanded-access program, which already covers AIDS drugs, any doctor can get one of these drugs from its maker by promising to provide information on the outcome of the treatment.

The F.D.A. said it would monitor the approval of drugs by the 26 countries so that the agency could quick-

Continued on Page 12, Column 1

President Planning to Quicken The Approval of Cancer Drugs

Continued from Page 1

ly review data and permit such expanded access to a drug if there was evidence that it worked.

The average approval time for so-called breakthrough therapies for life-threatening diseases is six months, but it is longer for drugs that are very similar to those already on the market.

"Science has matured to the point where we can actually make much earlier decisions," Dr. Shalala said. "This is a genuine reform, not just putting an artificial time frame on the F.D.A. We are reconceptualizing the drug-approval process based on science."

Vice President Al Gore called the new initiative a "common sense approach to approving promising new cancer therapies."

But the Commissioner of Food and Drugs, David A. Kessler, said in a telephone interview: "We are taking a risk here. We are going to make mistakes in this process. There will be some drug that comes along that is not as effective as it looked like or has much more severe side effects than we thought. But that risk is worthwhile when patients are facing life-threatening illnesses, we feel."

The Pharmaceutical Research and Manufacturers Association, the industry's trade group in Washington and a leading backer of Republican efforts to modify F.D.A. procedures, applauded today's announcement as "long overdue."

The statement said, "The Administration's effort is an acknowledgment that F.D.A. must be reformed, and it draws attention to the need to pass comprehensive legislation to improve drug development."

The main measure in Congress to streamline the agency's drug-approval process was approved by the Senate Labor and Human Resources Committee on Thursday, by a vote of 12 to 4. The bill, sponsored by Senator Nancy Landon Kassebaum, the Kansas Republican who is chairwoman of the committee, would require the F.D.A. to evaluate every drug or medical device within six months. The bill also takes the first steps to turn over drug approval to private groups paid for by the pharmaceutical industry.

The bill was attacked by Senator Edward M. Kennedy, Democrat of Massachusetts, as a giveaway to industry and a threat to public safety.

Senator Kassebaum said the bill would speed approval and give Americans access to any drugs available in Europe. In response to Mr. Kennedy, she said, "No one on this committee in any way wants to damage safety." She also said she would address some of Mr. Kennedy's concerns by suggesting changes to the bill before it reached the Senate floor.

Three bills were introduced in the House today in a package similar to the Senate measure. Representative James C. Greenwood, Republican of Pennsylvania, one of the sponsors of the package, said the legislation would not conflict with the President's action but enhance it.

Dr. Sidney Wolfe, director of Public Citizen's Health Research Group in Washington, said he was concerned about the Administration proposal, saying it was pressing the limits of what was possible. "These are extremely toxic drugs in cancer," he said. "You are fighting fire with fire, so if you just misestimate the benefits versus the risk by a little bit, you could end up doing more harm than good."

He noted that AIDS groups, which have had the benefit of rapid approval for some time, are now backing away from further shortcuts because the harm of early approval has become apparent for some patients.

"The agency will have to monitor these quick access drugs very carefully," he said.

Under the plan announced today, after a drug is approved under the expanded-access program the companies will supply more detailed information on safety and effectiveness to insure that unexpected problems are discovered.

A move to blunt efforts by the G.O.P. to fight regulation.

Moreover, the agency will add a patient advocate to each of its advisory boards, beyond the one consumer member already on the boards, which play a crucial role in determining if a drug is effective and safe enough to put on the market.

There are now about 300 cancer drugs in development at companies or waiting for approval of the F.D.A. All will be eligible for the expanded access, and probably 100 will be shown to be effective enough to gain expanded access quickly.

Dr. Kessler suggested three drugs that might be approved quickly under the rules, all for cases in which the first-line drug for the cancer fails. They are irinotecan, used for colorectal cancer; taxotere, used for breast cancer resistant to doxorubicin, and topotecan, used to treat ovarian cancer.

Dr. Shalala said that 1.3 million cases of cancer would be diagnosed in the United States this year.

More national news appears on page 24.

NY Times

3-30-96

FOR RELEASE ON
JANUARY 4, 1989

PUBLIC STATEMENT
BY
FRANK E. YOUNG, M.D., PH.D.
COMMISSIONER OF FOOD AND DRUGS

NATIONAL COMMITTEE TO REVIEW CURRENT PROCEDURES
FOR APPROVAL OF NEW DRUGS FOR CANCER AND AIDS
BETHESDA, MARYLAND
JANUARY 4, 1989

INTRODUCTION

Thank you for inviting me today to describe FDA's review process for cancer and AIDS therapies. We welcome this review, and I am delighted to have FDA support this committee. This topic is of great importance to all of us who share a deep concern for the needs, hopes, and rights of the desperately ill. I believe FDA's review process helps us to provide the best possible care for patients. I know that you, as fellow physicians, would do anything within your power to help save a patient facing certain death. This basic concern that we all share must be reconciled with equally important concern to base our treatment decisions on good science and a sound analysis of benefits and risks.

It is clear that the issues this Committee has been asked to consider are complex and require input from all involved. Many questions raised are pertinent to the performance of FDA, NCI, and NIAID. We are, I assure you, quite used to having our performance reviewed and we believe in it. Agencies that have such important functions must be scrutinized and I can assure you my colleagues and I at the Food and Drug Administration will do everything we possibly can to cooperate with this committee. Our regulatory system must serve the public first and foremost.

I do want to say at the outset that we have modified our procedures extensively in the last four years, and that the changes we have made have improved our review of therapies for cancer and

AIDS. In a recent address, President Reagan said that the streamlining of the Food and Drug Administration's review of new drugs to treat AIDS, cancer, and other devastating diseases, is a prime example of regulatory reform that has been at least as significant as tax cuts.

However, we are not complacent. Improving the quality and timeliness of the review process for drugs and biologics continues to be FDA's highest priority, as reflected in our Action Plans. I will send copies of Action Plans I and II, and the Executive Summary of Action Plan III, to the committee as soon as possible. As Commissioner, I pledge that FDA will continue to do all it can to ensure that important medical advances reach the desperately ill as soon as possible. I hope today is just one of a number of occasions where we can describe what we have been doing. In order to assist in this process, I would like to appoint an FDA liaison to support the activities of this committee, and I hope that you will agree to this suggestion.

FDA has recently made significant changes to streamline the drug review process, without sacrificing our statutory requirements of safety and efficacy. The review process has considerable flexibility, and allows FDA to make sound scientific judgments concerning the risks and benefits of new therapies. When FDA reviews cancer and AIDS therapies, the fact that these are life-threatening diseases certainly enters into the risk benefit

evaluation in a major way.

I will begin my testimony with an outline of the drug development and review process. Then, I will describe changes FDA has made to clarify, streamline, and strengthen the process, and to expedite development of therapies to treat life-threatening and severely debilitating diseases. Finally, I will describe how FDA has applied these changes to cancer and AIDS therapies.

THE DRUG REVIEW PROCESS

Let me start by outlining the new drug review process because I believe this will be helpful to your understanding of much of the remainder of my remarks. (Figure 1)

Before a new drug can be tested in humans in the United States, its sponsor must give FDA the results of laboratory and animal research, as well as any information about previous human use of the drug in other countries. In addition, the sponsor must describe how the initial clinical research trials will be conducted. The animal data needed depends on the nature of the clinical trials to be carried out. This information is essential so that later, reasonably safe doses can be used in humans, and the most likely toxic effects can be carefully avoided.

This information is sent to the FDA as an

"Investigational New Drug" application, which, in the great tradition of government use of initials, becomes an "IND." Clinical testing in humans is conducted under an IND.

Clinical studies normally occur in three phases. I must emphasize, however, that there is no regulatory requirement for a three phase approach. Phase 1 studies are designed to determine pharmacologic actions of the therapy, drug metabolism, and side-effects associated with increasing doses. Usually, fewer than 100 patients are involved in these early studies, which typically are conducted over a period of from six months to one year.

Phase 2 studies are well-controlled trials which are conducted to evaluate effectiveness of the therapy for particular indications and to further evaluate safety. Since the sponsor is still learning about the therapy, no more than several hundred subjects are usually involved at this stage.

Phase 3 studies are expanded further to gather additional information about effectiveness, to establish proper dosing regimens, and to provide sufficient safety information to give a clear profile of the risk-benefit ratio of a particular drug. Phase 3 studies can involve several hundred to several thousand subjects.

Once the sponsor believes Phase III testing is completed,

the test results are submitted to FDA in the form of a new drug or biologic product license application. At this point, the agency's formal review process begins, culminating in a decision of whether to approve the product for general marketing.

FDA and the pharmaceutical industry closely monitor drug products once they are on the market. Factories are inspected regularly to ensure good manufacturing and laboratory practices. In addition, both FDA and manufacturers collect reports of adverse drug reactions and manufacturers must report all reactions to FDA. Should an important new toxicity problem be confirmed that cannot be remedied, under urgent and unusual circumstances, products may be withdrawn from the market.

I should point out that many drugs that begin the clinical testing process do not complete it. (Figure 2) The process indeed serves as proof that well-controlled clinical trials weed out drugs that would pose unacceptable risks and those that would not be effective.

Of crucial importance is how well clinical trials are designed. Where an illness of the magnitude of AIDS or cancer is concerned, FDA stresses to drug sponsors its willingness to work with them early in the process to design clinical trials that will:

- Yield data that both FDA and the sponsor agree are essential; and
- Facilitate the development and review of the drug.

I want to emphasize that our advisory committees and workshops provide us with an invaluable source of outside scientific expertise; and we rely on this outside expertise for advice on problems that develop at all stages of a drug's review.

QUALITY OF CLINICAL TRIALS

FDA has the critical responsibility of ensuring that the products of science get to the patients who can benefit from them as soon as possible. I believe that the most important contribution we can make is to help sponsors improve the quality and adequacy of clinical trials. We expend enormous efforts determining the kinds of data and studies we consider necessary, developing guidelines, and meeting with sponsors. We also listen to drug companies, to their advisors as well as to our own, and to agencies such as NCI, NIAID, NHLBI, in determining the kinds of data we need. Simply stated, the trials must be designed properly to answer the key questions.

The quality of clinical trials depends on the correct execution of those trials as well. While FDA can help with trial design, the proper execution of clinical trials depends on the work

of the on-site clinical investigators.

To help in the design and execution of clinical trials in the drug development process, FDA has made some key changes. In doing so, we have been sure to maintain appropriate standards of safety and effectiveness as we utilize our scientific knowledge about the development of clinical trials to speed the process.

THE DRUG REVIEW PROCESS -- PROGRESS REPORT

Recent years have witnessed identifiable progress in the regulation of new drugs and biologicals. A major reorganization has been accomplished; new management initiatives have been implemented; regulatory requirements have been simplified; backlogs in drug reviews have been greatly reduced; improvements have been made in the quantity and quality of staff; new technologies have been incorporated into the regulatory process; and the first drug and biological products of biotechnology have been successfully introduced. All of this has been done at a time in which FDA's resources have been severely constrained. Let me give you some examples from the past four years.

- By December 1987, total overdue new drug applications had reached their lowest level five years. In the past two years, the number of overdue NDAs dropped 47% (from 169 in 12/85 to 90 in 12/87).

- More new chemical entities were approved during the four years from 1984-87 than in any preceding four-year period.

- From 1984 through 1987, FDA reviewed 890 new drug applications, and found 523 of those to be approvable.

- The first drug to treat AIDS, (AZT) was approved for marketing in 107 days (3 1/2 months). The only other approved drug related to AIDS, pentamidine, was reviewed and approved in 6 months.

- Eight major drug or biological products of biotechnology have been approved: 1983:

  - Hepatitis B vaccine
  - Interferon for hairy cell leukemia and Kaposi's Sarcoma
  - Two human growth hormones
  - Monoclonal antibodies
  - Human insulin
  - Tissue plasminogen activator for heart attack

victims

- Factor VIII:C for treatment of hemophilia (biotechnology techniques used to purify)

Some innovations in staffing contributed to these accomplishments:

- o The staff of medical officers to review new drugs has been increased by 20 percent since 1986.

- o The first fellowship program for cooperative arrangements between FDA and academe/industry has begun, and others are in development.

- o New computer hardware for drug review staff has been purchased and put in place.

Management improvements were also needed to improve the efficiency of the drug review system. The following improvements have been implemented:

- o In October 1987, the Center for Drugs and Biologics was divided into the Center for Drug Evaluation and Research (CDER), and the Center for Biologics Evaluation and Research (CBER). Under the direction of Dr. Carl Peck and Dr. Paul Parkman respectively, the new Centers have

placed high priority on efforts to improve the drug review process and fight AIDS.

- In February 1988, CDER established a Division of Antiviral Drug Products to focus on AIDS drugs, and CBER established a Division of Cytokine Biology to review biological products that affect cellular growth and development.

- The NDA Rewrite of the new drug application regulations, published in February 1985, was implemented to clarify and streamline the application process for new drug sponsors. Fourteen sets of guidelines have been published to aid sponsors in understanding how to complete those applications. Most recently, a Guideline for the clinical and statistical sections of a NDA gives detailed guidance on putting together an application.

- The IND Rewrite of regulations governing drug testing was published in March, 1987, with the goal of helping drug sponsors do better studies of promising new drugs, giving researchers more freedom in designing studies, and encouraging closer cooperation between drug sponsors and FDA.

- Treatment INDs were authorized formally in regulations

for the first time in May, 1987 to permit widespread use of investigational drugs used to treat desperately ill patients; and 8 treatment INDs have been approved.

- Pilot efforts have begun using the electronic submission of new drug application data.

- Management information systems have been updated and automated within FDA to improve the efficiency and accountability of the drug review system.

- Working groups have been established with the Institute of Medicine and the Pharmaceutical Manufacturers Association to gather outside ideas about ways to improve the drug review process.

THE NEW REGULATIONS

This fall, FDA announced the immediate implementation of new regulations designed to make promising therapies available sooner for patients with life-threatening and severely debilitating diseases. The plan was developed at the request of Vice President Bush in his capacity as chairman of the President's Taskforce on Regulatory Relief. (Figure 3)

FDA's goal is to be able to reach a scientifically defensible decision to approve or disapprove marketing of drugs intended to improve the outcome in such diseases, based on the results of well-designed phase 2 controlled trials. In this way, it is hoped that important drugs and biologics will be developed in the minimum time, just as AZT was.

These new regulations recognize that physicians and patients are generally willing to accept greater risks or side-effects from products that provide effective treatment for life-threatening or severely debilitating diseases. The benefits clearly make the risks involved worth taking.

Ordinarily, the testing of drugs in humans takes from 3 to 7 years. For many products, such a research pace may be cost-effective and appropriate. But for treatments for AIDS and other life-threatening conditions, we want to reduce that time to the bare minimum needed to assess safety and effectiveness.

The element of the plan I want to emphasize today is the need for consultation between FDA and sponsors throughout the drug development process. Only in this way can we get the well-designed, well-controlled studies that will make this plan work. By preventing false starts and wasted effort, we can do much to save time and cut costs.

When FDA consults with sponsors during the preclinical stage, we can facilitate the start of clinical trials as early as possible, thereby reducing potential barriers to innovation at this important stage of new pharmaceutical development and limit animal studies to the minimum required to ensure safety.

At the end of early (phase 1) clinical testing, FDA and the sponsor will seek to reach agreement on the proper design of phase 2 controlled clinical trials. For cancer trials, phase 2 has a somewhat different definition, representing the first trials in a particular disease: generally open, single treatment trials. The goal is still applicable, however: to have sufficient data on the product's safety and effectiveness to support a decision on its approvability for marketing. In fact, where drugs have been strikingly effective, such trials have been the basis for approval. Three major components in the treatment of testicular cancer, cisplatin, etoposide, and ifosfamide, were approved on the basis of historically controlled phase 2 trials that showed long-term survival, often in a very small number of cases, in patients who would not have had such responses without the new agent.

If the preliminary analysis of test results appears promising, we may encourage a treatment IND. Such a treatment protocol, if submitted and granted, would allow widespread distribution of the drug while the new drug application is being

reviewed. Cancer drugs that in the past have been entered into Group C would ordinarily become treatment IND/Group C drugs.

Once phase 2 testing and analysis is completed by the sponsor and a marketing application is submitted, the agency has the difficult task of considering whether the benefits of the drug outweigh the known and potential risks in satisfying the statutory standard for safety and effectiveness. Here, we have to take into consideration the severity of the disease and the absence of satisfactory alternative therapy.

Finally, when approval or licensing of a product is being granted, FDA may work with the sponsor to determine which postmarketing studies should be done. Such studies would help to determine rare long-term side-effects, reactions in particular population groups such as the elderly, and appropriate dosage changes.

REVIEWING CANCER THERAPIES

Drugs that are developed to treat cancer are likely to represent potential life-saving therapy. The evaluation of these agents, many of which are highly toxic, has always taken into account the fact that the illnesses they are intended to treat are deadly. In our new regulations to get promising drugs to patients as soon as possible, we are considering both AIDS and cancer drugs,

as well as other life-threatening illnesses. The Group C cancer drugs program was, in a sense, the precursor for the treatment IND. The Group C program made promising drugs available while they were under development and informed the treatment community of their existence.

I am pleased to report that in the oncology area at FDA, our staff has been able to essentially eliminate backlogs and achieve rapid response times. The oncology group is very well-qualified. It has six physicians. Of the six, 4 have received with formal training in medical or radiation oncology or hematology. Four of the group are board certified in medical oncology; the other two have more than 15 years of experience in oncology therapy. All 6 have had at least 5 years of experience in oncology therapy.

The oncology group assures that almost every drug, almost every important new claim is considered by FDA's Oncology Drugs Advisory Committee, a group of distinguished nongovernment oncologists. Even though the committee's recommendations are advisory and not binding, the agency has, over the last 5 years, disagreed with a committee recommendation just once. Even in that case, while we did act contrary to the Committee's recommendation, we were aware that substantial new data were to be available soon. The new data convinced the committee to alter its recommendation. A second claim for the same drug was reviewed and approved in 3

months.

One difficult issue on which we have sought advice from our Advisory Committee is the matter of the therapeutic end points that should be used as a basis for approval of new oncologic agents. With the help of our advisors we have decided that the best approach at this time is to make decisions on a tumor-by-tumor basis. We have now considered three tumors: ovarian, colon/rectal, and urinary bladder tumors. In each case, the Advisory Committee concluded that several clinically meaningful outcomes, only one of which was survival, could be a reasonable basis for approval.

There are some misperceptions about FDA requirements. For example, one is that we insist on evidence of improved survival before approval, and on particular designs of trials, and that large numbers of patients are needed. In fact, cancer drugs have been approved in some cases on extremely small data bases, (well under 100), with responses in less than 10, and on the basis of studies whose design was anything but classic. Effects other than survival were considered.

Let me note that there is very good agreement on what endpoints are relevant. Trials supported by NCI regularly measure many endpoints including tumor response rate, time to progression, survival, and various indices of quality of life. The only debate

is about which endpoints should be a sufficient basis for approval of a new agent.

In fact, we consider all standard endpoints, not just survival. Even where survival is considered a critical endpoint, as in metastatic breast cancer, what we really seek is evidence that survival is not reduced compared to standard therapy. In such a case, we do not expect good evidence of enhanced survival. Let me illustrate here the diversity of end-points used:

o Alpha-interferon was approved last year for hairy cell leukemia based on objective response rate, decreased infections, and a decreased transfusion requirement.

o Cerubidine was approved for induction therapy of adult acute lymphocytic leukemia on the basis of an improved complete response rate of meaningful duration, compared to randomized controls. In this setting, that response was considered a valid surrogate for an improved quality of life, even though it did not result in improved survival.

o Tamoxifen was recently approved as adjuvant therapy for breast cancer on the basis of a delay to time of recurrence, which was considered a meaningful end point that had an important impact on quality of life.

o Even where survival was a crucial end-point, approval has sometimes been based on a small number of long-term survivors where this was unexpected. For example, etoposide was approved for recurrent testicular cancer on the basis of observed long-term responses in an uncontrolled study, with convincing evidence that this response was not seen with regimens not containing etoposide. A similar basis, but with still fewer cases, allowed approval last week of ifosfamide for refractory testicular cancer.

o At its most recent meeting, the Oncology Advisory Committee recommended approval of carboplatin for recurrent ovarian cancer. While there was marginal evidence of enhanced survival in two small controlled trials, the basis of approval rested equally on a small (6, altogether) number of complete histopathologic responses of good duration and a clear decrease in time to progression in the randomized trials.

In a 1987 editorial in "Cancer Treatment Reports," Dr. Robert Wittes, then Director of NCI's Cancer Therapy Evaluation Program, recognized that recent FDA approvals were based on studies of diverse design and with diverse endpoints. He also urged greater attention to evaluation of improvement in tumor-related symptoms such as weight loss, pain, nausea, or decreased exercise tolerance as a basis for approval.

Dr. Robert Temple, director of FDA's Office of Drug

Evaluation I, made a presentation to the Oncologic Drugs Advisory Committee in 1985 and commented then on the difficulty of showing improved survival for many solid tumors when overall response rates ere low, (20-25%) and complete responses were very few. He suggested that even a modest number of improvements in clear-cut tumor symptoms could be persuasive evidence of a meaningful clinical effect. However he noted that it was rare to see evaluation of such symptoms in cancer studies presented to FDA. Drs. Temple and Wittes worked together to translate these thoughts into a publication and many parts of Dr. Wittes editorial reflected this joint effort.

We also have succeeded in achieving timely action on important new drugs or new indications for already approved drugs. Several recent examples are:

- Approval of mitroxantrone to treat leukemia was approved just 2 months after the submission of data for this claim to FDA.

- On December 30, we sent an approvable letter to Schering-Plough for flutamide, to be used in combination with LHRH agonistic analogues for treatment of metastatic prostatic carcinoma. We sent this approvable letter only 3 months after receiving the key data for this indication.

o The NDA for high dose methotrexate in osteosarcoma was approved within 6 to 7 months of submission. Some delay was caused from problems concerning the integrity of one of the clinical trials, which was shown not to have been carried out as its published report indicated.

o Finally, the Treatment IND for ifosfamide in refractory germ cell tumors was approved within 1 month of submission. Marketing of ifosfamide was approved in 12 months, only a few months after a substantial submission of data. Mesna, to be used in combination with ifosfamide to protect against bladder toxicity, was approved in 7 months.

Certainly, also, there will be honest disagreements and inadvertent delays. But the point I want to make is that we place the highest priority on the review of drugs for life-threatening illness and with the help of highly qualified outside advisors, promptly look at all available data and alternative treatments. In fact, FDA's review time for 12 important cancer therapies, approved in recent years, averaged just over 10 months. The 10 months covered the period between the time a complete application was submitted and the time the product was approved. (Figure 4) We are also eager to discuss with sponsors and others, what we do and why we do it, and to consider reasonable alternatives.

PROGRESS IN THE REVIEW OF AIDS THERAPIES

I will now describe how FDA is applying these same principles to the review of AIDS therapies. As a first step, FDA developed a special designation for AIDS drugs called "1-AA." This designation recognizes that the review of potential AIDS therapies and vaccines takes top priority at the Agency. In practical terms, this means that FDA will immediately review new drug applications related to AIDS and act on them within 180 days, or less time, if possible. It also ensures that all AIDS drugs are given prompt consideration for orphan drug status, a status providing certain tax and other financial incentives to the sponsors of therapies for relatively rare diseases.

Let me underscore the importance of well-designed and well-executed clinical trials for AIDS drugs, as well as other drugs. The Institute of Medicine, in its recent report entitled, "Confronting AIDS: Update 1988," emphasized the importance of controlled clinical trials as the "fastest, most efficient way to determine what treatments work."

The Approval of Zidovudine

The review and approval of the antiviral drug most commonly known as AZT (zidovudine) shows FDA's review system at

its best. In part, we based our new regulations to speed the development and marketing of significant therapies for life-threatening and severely debilitating diseases, on zidovudine. The expedited review and approval of zidovudine served as the prototype for the then new 1-AA classification. It was approved in March of 1987, and remains the only approved antiviral treatment for AIDS.

Close consultation between FDA and the sponsor resulted in efficient preclinical animal testing lasting only 2 to 4 weeks. Early phase 1 clinical tests were focused, and the results warranted a larger trial. What followed was a well-designed and well-conducted multi-center phase 2 clinical trial, which showed dramatically that zidovudine increased survival in patients with AIDS and advanced ARC. Given such clear evidence of efficacy, we determined that further clinical studies were not required for the wide distribution of the drug. Even though significant side-effects were found, the clear benefit of prolonged survival clearly outweighed these risks.

At this time, the placebo-controlled trial was halted, and the drug was made available to over 4,000 patients through a treatment protocol approved within 5 days after the protocol was submitted.

Based on this experience, we concluded that formal

provision should be written into FDA's regulations permitting expanded use of experimental drugs in desperate situations. This was the genesis of the Treatment IND regulation.

Finally, marketing approval for zidovudine was granted in the record time of 107 days. The sponsor also agreed with us that further research, (phase 4), was needed to study the effects of zidovudine in patients at an earlier stage of the disease. In total, the drug development and evaluation process, which takes an average of 8 years from initial human testing under an IND to final marketing approval, took only 2 years for zidovudine.

Current Status of AIDS Therapies

As of December 1, 1988, FDA had approved 215 investigational new drug applications (INDs) to test 145 new AIDS drugs, biologics, vaccines, and diagnostics in humans. (Figure 5) The 215 approved IND applications include:

43 for antiviral drugs
70 for immunomodulators
4 for vaccines
6 for antineoplastics
44 for drugs to treat opportunistic infections
48 for diagnostics

We now receive close to 10 applications each month. This surge in research has come from both federal and private sources. We believe we are just beginning to see the clinical investigation of drugs that are designed specifically for AIDS, and we believe FDA's workload in this area will continue to increase, as will our overall workload in biological drugs. (Figures 6 & 7)

The determination of AIDS clinical trial endpoints to evaluate efficacy will be strongly influenced by the nature and stage of the disease and by the availability of other proven treatments. In the case of AIDS treatments, we must have scientific evidence that, at a minimum, an agent significantly delays clinical progression of the disease, prevents opportunistic infections, or controls an AIDS-related cancer. Clinical studies must define disease stages carefully and study the drug long enough so that significant effects are apparent.

The danger of reporting early clinical findings without clear evidence of safety and effectiveness was shown in the case of the immunomodulating drug ampligen. The sponsor of that drug, after reporting initial positive findings on just a few patients, recently discontinued the trial because of lack of beneficial results.

As I stated before, zidovudine remains the only approved drug to treat AIDS directly. However, an intense search is

underway to find drugs to treat opportunistic infections and cancers that are often fatal to AIDS patients. The injectable form of the drug pentamidine to treat Pneumocystis carinii pneumonia (PCP) was approved quickly, in about 6 months. This past November, the agency approved alpha interferon to treat Kaposi's Sarcoma, based in part on a study by scientists here at the National Institute of Allergy and Infectious Diseases. This marks the first recognized combination therapy for AIDS. NIAID is also conducting studies comparing treatment with alpha interferon plus zidovudine to treatment with zidovudine or alpha interferon alone.

We anticipate that combination therapies will become increasingly more important in the treatment of AIDS, in the same way that they tend to be the rule, not the exception, in the treatment of cancer. As the clinical trials expand, there will be new challenges for NIH and FDA. For example, how do we ensure appropriate representation of all affected groups in clinical trials? When do we begin trials on women, pregnant women, children and the elderly? We will need your thoughtful advice.

There are two treatment INDs for AIDS-related conditions. Trimetrexate was the first, approved for expanded distribution on February 1988, to treat pneumocystis carinii pneumonia. The Treatment IND's sponsor is NIAID.

The second treatment IND was granted for ganciclovir on

November 30, 1988 to treat patients with cytomegalovirus retinitis, a disease with infections that are immediately sight-threatening. Controlled clinical trials are also underway for patients that are newly diagnosed and not in as serious a condition. NIAID is also sponsoring treatment IND while the Syntex Corporation is supplying the drug. At present, we are attempting to negotiate a third treatment IND for an opportunistic infection that frequently accompanies AIDS.

SUMMARY

Before closing, I wish to summarize the following initiatives FDA already has underway in the areas your committee was asked by President-elect Bush to review. We would be interested in your ideas on these initiatives as we implement them. FDA is:

(1) Implementing regulations requested by Mr. Bush to expedite the development of life-threatening and seriously debilitating diseases.

(2) Systematically evaluating the therapeutic end points that should be used as a basis for product approval. In this matter, we have sought advice from our advisory committees and expert groups such as the Infectious Disease Society of America. In the area of oncology, we

have decided that the best approach at this time is to make decisions on end points on a tumor-by-tumor basis.

(3) Working closely with Dr. Broder, Dr. Fauci, and Dr. Goodwin and other NIH and ADAMHA staff to identify ways to expedite development of cancer, AIDS and neuropharmacological drugs.

(4) Examining the IND phase to identify ways for investigators to have greater flexibility, to assess the impact of clinical holds, and to evaluate why and when INDs tend to drop out of the review process. We would be glad to share our data.

(5) Actively working to improve the quality and timeliness of our review process. I have not gone into much detail on these improvements here, but our liaison, if you like, will be glad to discuss them with you.

In addition to the initiatives summarized above, we have several suggestions for better integration of basic research and clinical trials which we believe would enhance development of new therapies. I would welcome the opportunity to share these ideas with you. In addition, there are several problems I suggest that you consider.

(1) How do we assure that all affected groups have access to

clinical trials? How much information is required before women, pregnant women, children, and the elderly are included in clinical trials?

(2) What is the effect of reimbursement policies on drug development?

(3) How can we maximize the use of treatment INDs? Are there liability questions or costs that inhibit the process?

(4) Currently, there exists a great deal of encouragement for more cooperative government-industry research. How can we best prevent the appearance of conflict of interest? Although cooperation is generally good public policy and makes sense, collaborative research can raise the appearance of conflict of interest when government researchers conduct collaborative research with industry, and FDA must review the results of their research. What should the relationship be between an NIH scientist who has helped to develop a new therapy, and the FDA scientist who must review it? These are issues I hope you will address.

CONCLUSION

FDA's successful efforts over the past four years to streamline the drug and biologic review system show that FDA is an integral part of the solution to AIDS and cancer. We have the responsibility of assuring that new therapies are safe and effective and are transferred expeditiously to the public. We cannot afford to fail on either count. Accordingly we have placed the evaluation of new therapies in general and AIDS in particular as FDA's highest priority.

We are in the midst of a biomedical revolution that promises to change the face of medicine forever. The new biotechnology especially will have a large impact on the discovery and development of new therapeutic agents. Such change demands that we leave behind many of our old ideas of doing business and find new ways to work together. We must strengthen the partnership among the academic community, NIH, consumer groups, and industry so that we can work together to develop safe and effective new therapies in this time of change.

As a scientist, it gives me enormous pride and satisfaction to be serving in the federal government during this revolution in pharmaceutical therapies. As a physician and as a person who has deep compassion for people with AIDS and cancer, I ask you to work with us to provide them with safe and effective new

therapies -- <u>real</u> hope for the future.

Thank you.

DRUG DEVELOPMENT PROCESS

PRODUCTS FOR LIFE-THREATENING ILLNESSES

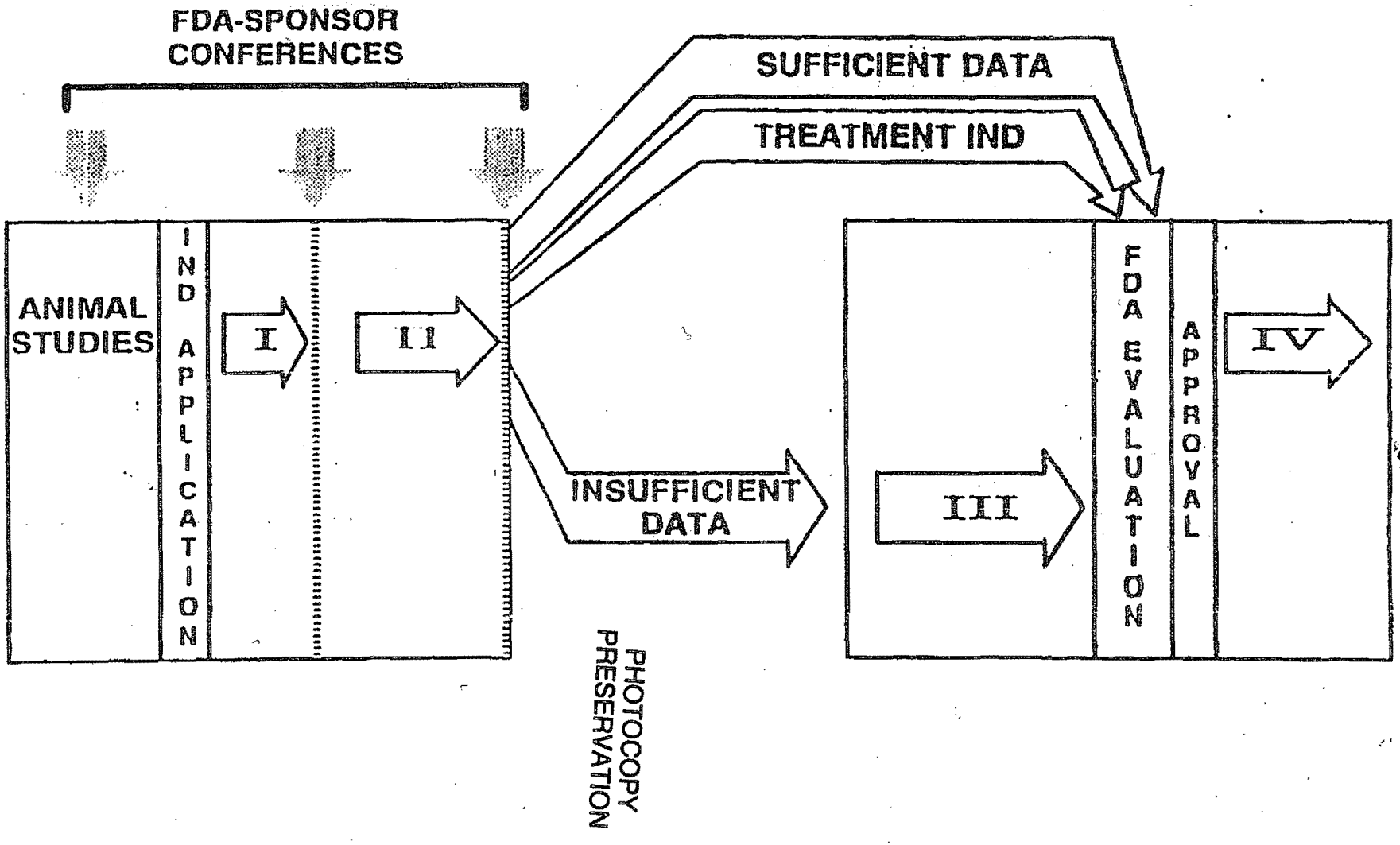


FIGURE 9

HFD-150 Oncology Treatment INDs

Drug	Indication	Date Filed	Date Approved
Ifosfamide/Mesna	refractory testicular	11-30-87	12-24-87
Pentostatin (DCF)	refractory hairy cell leukemia	7-7-88	7-28-88
Teniposide (VM-26)	childhood acute leukemia	9-7-88	10-7-88

FIGURE 4 (continued)

SUCCESS OF CLINICAL RESEARCH
(NCEs SUBMITTING FIRST INDs IN 1976-1978)

FIGURE 2

REVIEW TIMES FOR IMPORTANT RECENT CANCER APPROVALS

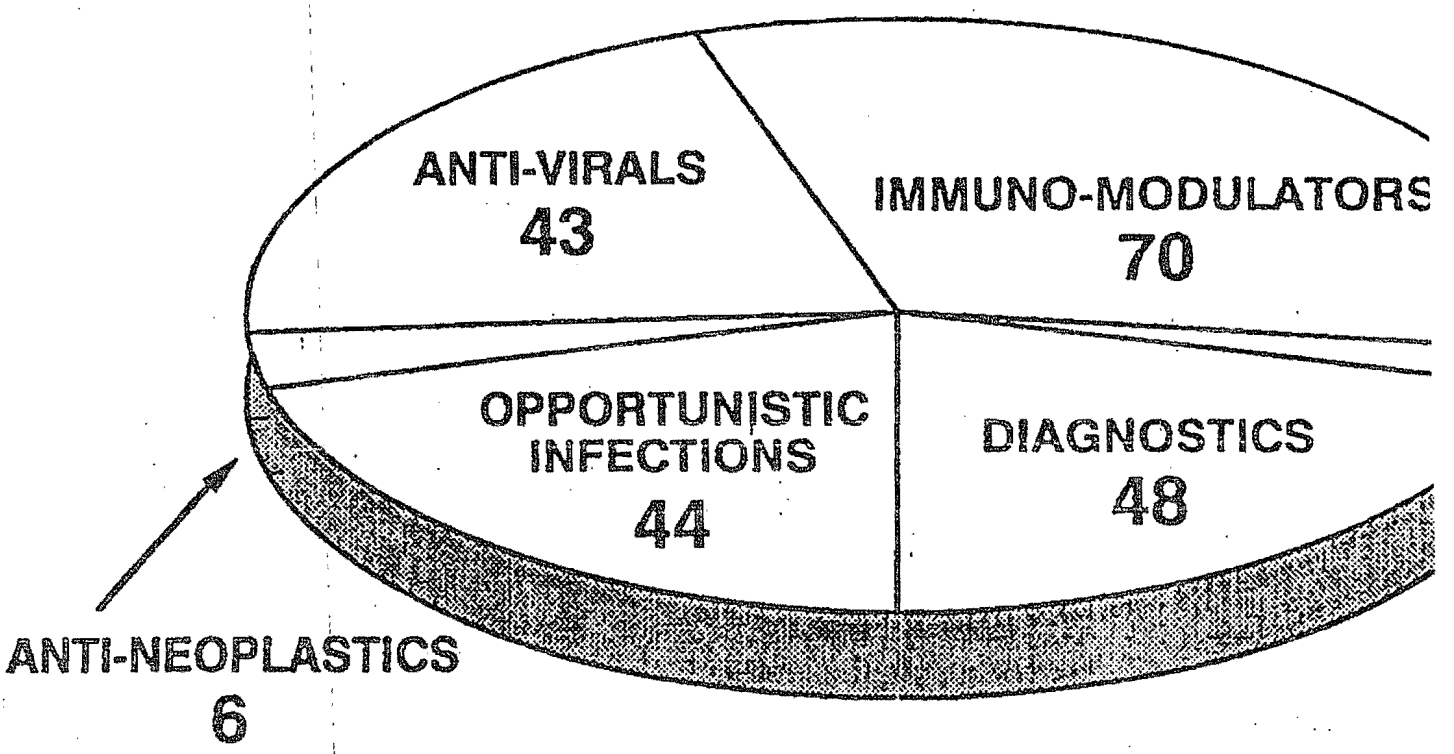
Therapy	Indication	Date Complete Application Submitted	Date Application Approved	FDA Review Time
1. Ifosfamide	Refractory Testicular	8/5/88	12/30/88	4 1/2 months
2. Mesna	Uroprotection	7/3/88	12/30/88	5 months
3. Mitoxantrone	Adult AML	10/28/87	12/23/87	2 months
4. High Dose Methotrexate	Osteosarcoma, Adjuvant	10/14/87	4/7/88	6 months
5. Intron-A	Kaposi's Sarcoma	3/18/87	11/21/88	20 months
6. Roferon-A	Kaposi's Sarcoma	7/9/87	11/21/88	16 1/2 months
7. Tamoxifen	Adjuvant single Agent	2/3/86	12/3/86	10 months
8. Etoposide	SCLC, capsules	12/31/85	12/30/86	12 months
9. Etoposide	SCLC, injection	12/31/85	9/4/86	8 months
10. Roferon-A	Hairy Cell Leukemia	8/15/85	6/4/86	10 months
11. Daunomycin	Adult ALL	7/31/85	3/11/87	20 months
12. Intron-A	Hairy Cell Leukemia	6/28/85	6/4/86	11 months

FIGURE 4

AIDS INDs

TOTAL = 215

As of December 1, 1988



CYTOKINE BIOLOGY

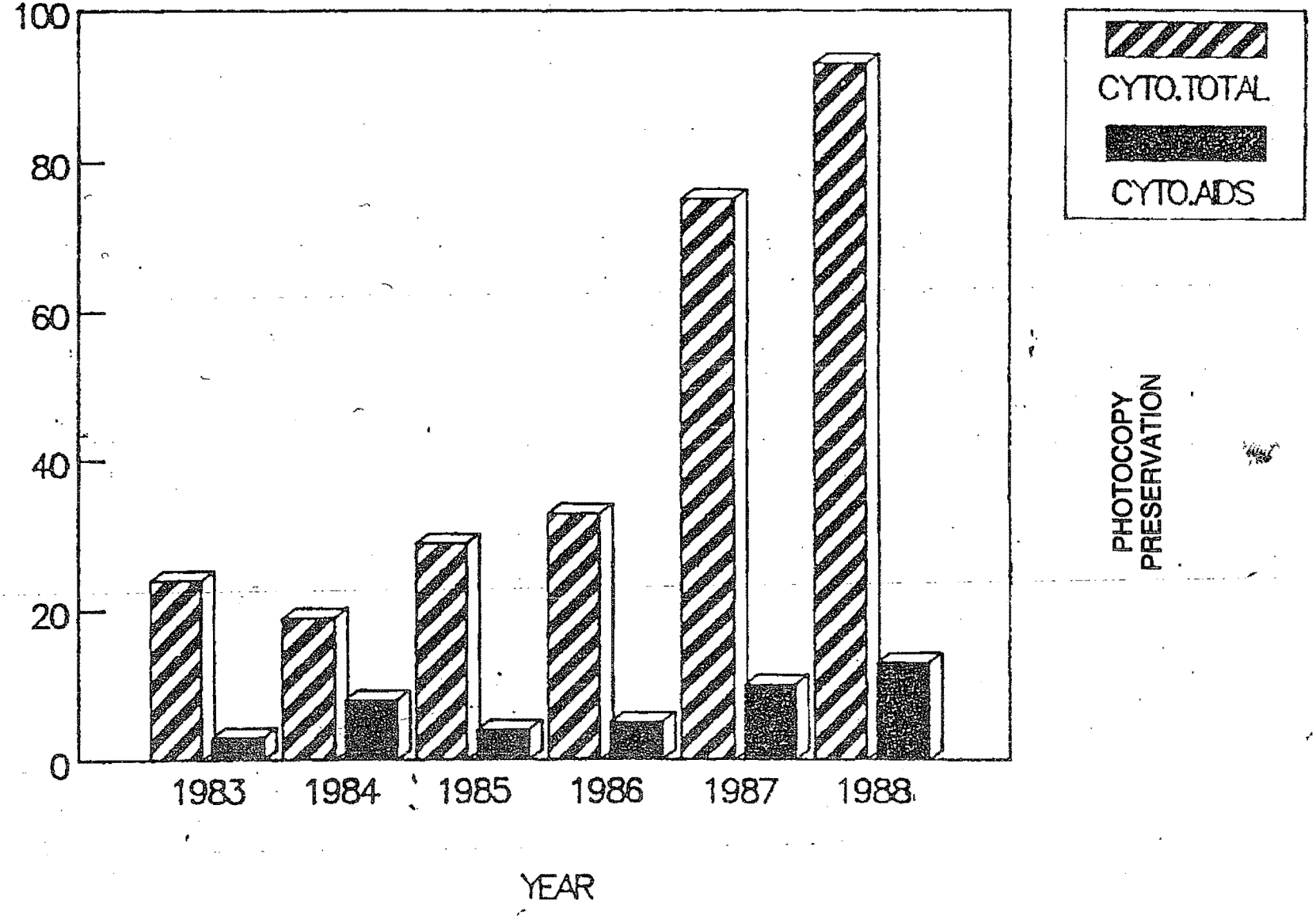


FIGURE 6

APPROVED TREATMENT IND's

Drug Indication	Date
Kidney Transplant	October 1987
Germ Cell Cancer	December 1987
AIDS Infection (PCP)	February 1988
Obsessive-Compulsive Disorder	June 1988
Parkinson's Disease	June 1988
Hairy Cell Lukemia	July 1988
Lymphoblastic Lukemia	October 1988
AIDS Infection (CMV)	December 1988

Food & Drug Administration Jan. 1989

DRUG DEVELOPMENT PROCESS: TREATMENT USE

FIGURE 1