Paul- Here's a final report on your article. I'm afraid the only clip we got was the one in The Chronicle. Thanks again! - David

DAVID JARMUL

DIRECTOR

NATIONAL ACADEMY OP-ED SERVICE

cc: Jesse, Bill

TELEPHONE: 202-334-2138

FACSIMILE: 202-334-2158

NATIONAL ACADEMY OF SCIENCES

2101 CONSTITUTION AVE., N.W.

WASHINGTON, D.C. 20418

NEWSPAPERS THAT PUBLISHED VOLBERDING, DOBSON, AND THORNE ARTICLE ON AIDS DRUG TESTING

1	Tuscaloosa News	Tuscaloosa	AL
2	Hanford Sentinel	Hanford	CA
3	San Francisco Chronicle	San Francisco	CA
4	The Daily Democrat	Woodland	CA
5	Dalton Daily Citizen-News	Dalton	GA
6	The Maui News	Wailuku	HI
7	Washington Times-Herald	Washington	IN
8	Bangor Daily News	Bangor	ME
9	Canandaigua Messenger	Canandaigua	NY
10	Newark Advocate	Newark	OH
11	Klamath Falls Herald & News	Klamath Falls	OR
12	Wheeling News-Register	Wheeling	WV

NEWSPAPERS THAT USED VOLBERDING, DOBSON, & THORNE ARTICLE FOR BACKGROUND

1	Pine Bluff Commercial	Pine Bluff	AR
2	The Phoenix Gazette	Phoenix	AZ
3	Yuma Daily Sun	Yuma	AZ
4	Orange Coast Daily Pilot	Costa Mesa	CA
5	Fresno Bee	Fresno	CA
6	Loveland Reporter Herald	Loveland	CO
7	New London Day	New London	CT
8	Orlando Sentinel	Orlando	FL
9	Pensacola News Journal	Pensacola	FL
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11	Savannah Morning News	Savannah	GA
12	Topeka Capital-Journal	Topeka	KS
13	Kentucky New Era	Hopkinsville	KY
14	Daily Iberian	New Iberia	LA
15	Shreveport Journal	Shreveport	LA
16	Fitchburg Sentinel & Enterprise	Fitchburg	MA
17	Easton Star Democrat	Easton	MD
18	Detroit News	Detroit	MI
19	Owosso Argus-Press	Owosso	MI
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21	N.E. Mississippi Daily Journal	Tupelo	MS
22	Lincoln Journal	Lincoln	NE
23	Concord Daily Monitor	Concord	NH
24	Asbury Park Press	Neptune	NJ
25	Syracuse Post-Standard	Syracuse	NY
26	Akron Beacon Journal	Akron	OH

27	Celina Standard	Celina	OH
28	Tiffin Advertiser Tribune	Tiffin	OH
29	Coos Bay World	Coos Bay	OR
30	Reading Eagle	Reading	PA
31	Clarksville Leaf Chronicle	Clarksville	TN
32	Knoxville News-Sentinel	Knoxville	TN
33	Memphis Commercial Appeal	Memphis	TN
34	Beaumont Enterprise	Beaumont	TX
35	Houston Chronicle	Houston	TX
36	Lubbock Avalanche-Journal	Lubbock	TX
37	Midland Reporter-Telegram	Midland	TX
38	San Antonio Express News	San Antonio	TX
39	Bristol Herald-Courier	Bristol	VA
40	Eau Claire Leader-Telegram	Eau Claire	WI

THE SAN FRANCISCO CHRONICLE (CA)
JANUARY 30, 1990

Expanded Access To AIDS Treatments Would Benefit All

By Paul Volberding, Jesse Dobson and Bill Thorne

A committee of the U.S. Food and Drug Administration is meeting in Washington today to weigh recommendations for major changes in FDA policies on testing new AIDS drugs.

As those drugs have emerged from laboratories and older ones have entered the market in Europe, militant groups representing people with acquired immune deficiency syndrome have demanded swifter progress in America's drug testing and approval process, and they have even organized an underground supply system for many of the drugs when early tests have indicated that they are safe.

The following article on the polarized issue was written jointly by one of the national leaders in the conventional clinical trials of new AIDS drugs, Dr. Paul Volberding, and by two members of the Aids Coalition to Unleash Power.

New policies recently were proposed to the federal Food and Drug Administration that would permit wider distribution of new AIDS drugs after toxicity trials of the drugs are completed and some evidence of benefit has been demonstrated, but while efficacy tests are still in progress.

These proposals, which are still being considered by the FDA, have generated both strong support and vocal criticism. Most advocacy organizations have supported this new "parallel track" system as a way to make drugs with limited toxicity and with at least some evidence of benefit available to people who have few or no other treatment options. Distribution would be limited to patients ineligible for ongoing clinical trials, and the drugs would be administered by the patients' physicians.

Researchers have feared that this expanded access may expose patients to potentially severe long-term toxicities and would slow the entry of candidates to necessary clinical trials. These criticisms increased after the recent early-release program for the new AIDS drug dideoxynosine.

This polarization has seemed to place paternalistic researchers against their patients, engendering mistrust exacerbated by a lack of direct communication. This dispute is unnecessary.

Indeed, both parties have much to gain from expanded access to new drugs: Patients will have greater treatment options, and research could become more effective.

Many Available Treatments

Why do we think this? First, the days when AIDS patients had to choose between experimental trials and no therapy fortunately are past. Multiple treatments are emerging, enabling patients to make choices as consumers in a "marketplace." Expanded-access policies only hasten this process. If participation in clinical trials is perceived to require compromise in the level of care, or is excessively cumbersome without ameliorating advantages, recruitment will be difficult.

Instead of making sweeping attacks on new treatment options, researchers should design trials that address these concerns, or even collect data from parallel-track drug use. Opinions on specific new approaches are bound to vary, but it simply is not realistic to rely on elegant trials. Some improvements could include setting more reasonable "end points" in studies, not only for groups of patients but also for individual participants. Patients who volunteer to be in a trial should be told in advance how their response to the drug will be determined; their consent should be well-informed.

Community Standards

Also, the supportive care provided in clinical trials must meet community standards. For example, if supportive medications are commonly prescribed by community physicians, these same treatments should be permitted for trial participants.

Not all problems with existing trials can be addressed in design; financing constraints also have slowed recruitment of patients and made participation cumbersome.

More generally, physicians and AIDS researchers, policymakers, and pharmaceutical companies should affirm that the parallel track for new AIDS drugs provides vital choices to patients, particularly while approved therapeutic options remain limited. Rather than resisting expanded access efforts, the research community should identify ways of collecting useful data from them to speed drug evaluation.

An important step to reducing resistance is ensuring that expanded access only involves patients who do not qualify for existing clinical trials, as is stated in the proposals now under consideration.

Community physicians could help in this process by collecting data in a formalized manner, when practical, and by cooperating with voluntary enforcement of eligibility guidelines so long as the resulting system clearly has the patients' best interests at heart.

AIDS researchers must maintain a dialogue with patient-advocacy groups so drug trials can quickly attract appropriate patients by ensuring excellent medical care while still gathering crucial new information.

With these steps, everyone stands to gain, and researchers, patients and their advocates can work together to overcome the many obstacles that prevent the defeat of our common enemy, AIDS.

Paul Volberding, M.D., is associate professor of medicine at the University of California at San Francisco; director of the AIDS program at San Francisco General Hospital, and a member of the AIDS review committee of the Institute of Medicine and the National Academy of Sciences. Jesse Dobson and Bill Thorne are members of the AIDS Coalition to Unleash Power in San Francisco.

F.Y.I.
Orphan Drug Amendments
Jim Russell

[redacted]

July 30, 1990

Senator Edward Kennedy
United States Senate
Washington D. C. 20515

Dear Senator Kennedy:

I am an AIDS activist in San Francisco. Last week I met with Dr. Mona Sarfaty to discuss the Waxman amendments to the Orphan Drug Act and other AIDS related matters. Dr. Sarfaty was very helpful and knowledgeable and she shared my concern about the effect of these amendments on drug research and development. Let me review the major points I made to her.

1. The Orphan Drug Act has encouraged investment in drugs for diseases with small afflicted populations: two of the valuable drugs developed as orphans are the AIDS drugs pentamidine and ddC. The Waxman amendments originated as an attempt to "remedy" what Congressman Waxman deemed the excess profits of three drug companies: Lyphomed with pentamidine and Genentech and Eli Lilly with their human growth hormones. This kind of tampering will send the wrong message to companies considering investment in orphan drugs. It will tell them that here the rules can be changed in the middle of the game because of unforeseen political factors. Moreover, Waxman's co-exclusivity clause will directly curtail incentives. The overall effect of the amendments will be to discourage development of desperately needed treatments.

2. Specifically targeting pentamidine and human growth hormone, the Waxman amendments epitomize inappropriate micromanagement on the part of Congress.

3. The Waxman amendments attempt to drive down drug prices at the expense of developing treatments for people with AIDS opportunistic

illnesses and other rare diseases. To use sick people this way is ethically wrong and discriminatory against those unfortunate minorities afflicted with rare diseases.

4. Rather than lowering orphan drug prices, the Waxman amendments would do just the opposite because pharmaceutical companies would conclude that here they need higher profit margins to compensate for the added risk of political tampering with orphan drug laws.

5. The most effective way to lower drug costs is to lower the cost of drug development by streamlining FDA approval procedures. It now costs an average of $231 million to get a drug approved and our approval procedures are among the world's slowest. FDA procedures demand total safety regardless of cost in time and money. We could seek total safety on our highways by outlawing motorcycles and requiring truly crashproof vehicles equipped with every safety feature. But the American people would not stand for such an infringement on their freedom of choice or for the tripling of auto prices. As more people realize the terrible price we are paying for "safety, damn the cost" FDA practices, a rebellion builds. AIDS activism is one dramatic expression of this rebellion.

6. Rather than curtail incentives in the Orphan Drug Act, we should expand them for diseases with very small populations, like AIDS opportunistic illnesses. For example, for an indication afflicting fewer than 10,000 people we might expand exclusivity from seven to twenty years. This would not only encourage development of drugs for truly rare diseases, it would make these drugs cheaper by letting pharmaceutical companies amortize costs over a longer time.

Sincerely yours,

James P. Driscoll, Ph. D.

DRAFT

5 January 1990

TO: Alice Trinkl

FROM: Cathy Roseberry

RE:

David Jarmul just called regarding the letter Paul co-wrote with ACT-UP. He had three main points:

1) The need to expand on the significance of the byline. To catch the average reader's attention they need to expand on what the two groups represent and that fact that they are working together.

2) The piece is too scientific for the average reader. (i.e. what is a Phase II Trial, Parallel Tracking, etc.) What have been the concerns in the past regarding the methodology.

3) Be more specific about the new proposed methodologies (how would they solve the issue.)

David Jarmul's phone # is [redacted]/fax # is [redacted]. Bill Thorn's # is [redacted]. As you know, Paul is in China until next Thursday but I reach him by fax. David (who with the National Academy of Sciences OPED services) is anxious to talk with you.

SAN FRANCISCO: SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE

[redacted]

5 January 1990

TO: Alice Trinkl

FROM: Cathy Roseberry

RE:

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[redacted] Jesse Dobson

Explain co-authors
rep. extremes of opinion – AIDS researcher
ACT UP being local rep. of AIDS pts
& critical of policy

[redacted]

MFR Private [redacted]

[redacted]

February 16, 1990

Melanie Kirkpatrick
Deputy Editor, Features
Wall Street Journal

Dear Ms. Kirkpatrick:

Please find enclosed an article intended for your op-ed page. The news behind this piece is not so much in the specific proposals outlined for the improvement in distribution of AIDS treatments or the design of clinical trials, but that former opponents on these issues have seen the inevitable need to work together and are suggesting a framework of cooperation to benefit everyone. A much truncated version of this article appeared in the San Francisco Chronicle on January 30, but this limited exposure did not provide the exposure that these ideas deserve and need to become implemented. I hope that you see fit to print it. This will be particularly timely, as there is a quarterly meeting of the AIDS Clinical Trial Group in Bethesda on March 5-7, 1990. Significantly, activists, including myself, have been invited to this meeting to help begin the process of cooperation. There is, however, substantial opposition within the group and the NIH to our presence. Publication of this article would provide a very useful starting point for changing this.

If you have any questions, please do not hesitate to call me at 415-462-2900 or Dr. Volberding at 415-476-4387. I thank you in advance for your consideration.

Sincerely,

Jesse C. Dobson
ACT UP/San Francisco

AIDS DRUG TESTING

NEW ERA/NEW OPTIONS

by Paul Volberding

UC San Francisco Associate Professor of Medicine

Director, AIDS Program, San Francisco General Hospital

Member, AIDS Clinical Trials Group, National Institute of Allergy and Infectious Diseases

and

Jesse Dobson

Bill Thorne

AIDS Coalition to Unleash Power

(ACT-UP) San Francisco

This article is co-authored by individuals who have represented two extremes of opinion on the issue of AIDS drug testing. One is an AIDS researcher who has been involved from the outset of the epidemic in testing potential drugs using classical scientific methodology; he and other AIDS researchers have criticized certain aspects of these proposals. The other authors of this article are representatives of a vocal group representing persons infected with HIV who have been openly critical of the implementation of academic-scientific method of drug testing while AIDS patients have been in extreme need of effective treatment.

When first proposed, new policies that would permit wider distribution of new AIDS drugs while strict and limited testing of the drugs was still in progress generated both strong support and vocal criticism. Trials of side effects (toxicity) of these drugs

would have been completed prior to wider distribution, but final tests of benefit (efficacy) would still be in progress.

Many AIDS advocacy organizations and patients saw this new system, called "parallel track", as one that could make drugs with at least some evidence of benefit and limited short-term toxicity available to persons with a life-threatening condition who had few or no other treatment options. Although still not finalized, the draft version of the parallel track proposal included guidelines to make drugs available to patients not eligible for ongoing or planned clinical trials. All drugs in the parallel track system would be administered under the supervision of the patient's personal physician.

The research community has feared that the parallel track system might expose patients to drugs with undefined but potentially severe long-term toxicities and that expanded access would slow the entry of appropriate candidates to necessary clinical trials. These criticisms were specifically made after Bristol-Myers Corporation began an ambitious early release program for a new drug called ddI.

The polarization has seemed to place paternalistic researchers on one side and patients on the other. This engendered mistrust that has been fueled by lack of direct communication. We believe that this dispute is not necessary. Indeed, both parties have much to gain with the expansion of access to new drugs: patients will have greater treatment options and research will become more effective and attractive.

What has led to this change in view? First, expanded access policies simply hasten the time when the testing of any new drug will have to compete with multiple existing therapies. The days when AIDS patients HAD to choose between experimental drug trials and no therapy are fortunately past. Sooner or later, new treatments will be approved with or without expanded access policies. Researchers and sponsors of new therapies must appreciate that this will allow patients to approach the options as consumers in a "marketplace" as opposed to desperate, dying individuals willing to do almost anything for a chance to survive. If participation in a clinical trial is perceived to require compromise in the level of otherwise available care or is excessively cumbersome without ameliorating advantages, recruitment of participants will be difficult. Rather than making sweeping attacks on the availability of new treatment options, however, researchers might do better to design trials that address these concerns or even help design these alternative treatment protocols to enhance their research. Opinions of what these changes should be are bound to vary from researcher to researcher, but this is also true for existing clinical trials. Methods to resolve these disputes already exist. But the underlying choice seems simple--design attractive trials that can still efficiently answer key questions or see elegant but unrealistic trials move so slowly that the disease changes more rapidly than the research. Some improvements in clinical trials could include setting reasonable end points for studies and ensuring that supportive care in

clinical trials meets community standards. For example, if supportive medications are commonly prescribed by expert community physicians for patients not in clinical trials, these same treatments should be permitted for patients in a drug test. Also, researchers could more clearly inform potential volunteers when the experimental study will end and what follow-up treatment will be available after the study is finished.

No important issue is, of course, as straightforward as this short analysis might paint this one; nor are solutions necessarily easy. Not all of the problems with existing trials can be addressed in design, as funding constraints also play a role in slowing the recruitment of patients and make participation in these trials cumbersome. Carefully controlled clinical trials should be powerful weapons in the battle against AIDS and need to proceed at an even faster pace than ever. This is the best way to evaluate the potential risks and benefits for any treatment.

What immediate steps do we propose? First, physicians and AIDS researchers, pharmaceutical companies and those who establish drug approval policy should affirm that expanded, early access to new AIDS drugs provides vital choices to patients, particularly when approved therapy options are so limited. Expanded access would be more acceptable to those opposed if it is clearly articulated that it is designed for patients who do not qualify for existing clinical trials. This has been already stated in existing parallel track proposals.

Second, AIDS researchers must maintain an active dialogue with

patient advocacy groups to design trials of new drugs that can quickly attract appropriate patients and that ensure state-of-the-art medical management while still gathering absolutely crucial new information. Finally, the researchers, pharmaceutical companies, regulatory agencies, community doctors and patients should work together to identify ways that useful and valid data to speed drug evaluation and approval can be collected from the expanded access programs. Community physicians could when practical collect data in a formalized manner and cooperate with a policy of voluntary enforcement of the guidelines on eligibility for early access to treatment, if it became clear to the community physicians and their patients that the resulting system had the patients' best interest at heart.

If we can accomplish these things, everyone stands to gain and the resources of the researchers, patients and their advocates can work together to overcome the many obstacles that prevent the defeat of our common enemy, AIDS.

February 15, 1990

Melanie Kirkpatrick
Deputy Editor, Features
Wall Street Journal

Dear Ms. Kirkpatrick:

Please find enclosed an article intended for your op-ed page. The news behind this piece is not so much in the specific proposals outlined for the improvement in distribution of AIDS treatments or the design of clinical trials, but that former opponents on these issues have seen the inevitable need to work together and are suggesting a framework of cooperation to benefit everyone. A much truncated version of this article appeared in the San Francisco Chronicle on January 30, but this limited exposure did not provide the exposure that these ideas deserve and need to become implemented. I hope that you see fit to print it. This will be particularly timely, as there is a quarterly meeting of the Aids Clinical Trial Group in Bethesda on March 5-7, 1990. Significantly, activists, including myself, have been invited to this meeting to help begin the process of cooperation. There is, however, substantial opposition within the group and the NIH to our presence. Publication of this article would provide a very useful starting point for changing this.

If you have any questions, please do not hesitate to call me at 415-462-2900 or Dr. Volberding at 415-476-4387. I thank you in advance for your consideration.

Sincerely,

Jesse C. Dobson
ACT UP/San Francisco

NATIONAL ACADEMY OP-ED SERVICE

2101 Constitution Avenue, N.W., Washington, D.C. 20418
Telephone: (202) 334-2138; Facsimile: (202) 334-2158

Nov. 9, 1989

Dr. Volberding:

You may recall that I slipped you a copy of the attached brochure when you were at the Academy a few weeks ago. Since you were in the middle of a conference, I didn't want to burden you with a lengthy description of our op-ed service.

I am writing you now just to remind you that this service exists and to share some sample clips from previous articles. We now mail to 406 newspapers weekly, and we are eager to develop an article on the practical and ethical problems of AIDS drug testing. I am sure many papers would publish such an article, helping readers to understand some of the complex issues involved.

The article would need to be only 750 words, and we can help with drafts. I do hope you will consider working with us on such a piece in the near future.

Again, many thanks.

Sincerely,

David

David Jarmul
Director

The National Academy Op-Ed Service provides daily newspapers with timely opinion articles authored by prominent members of the scientific, technical, and health-care communities. It is affiliated with the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council.

UCSF/SFGH

FAX

AIDS PROGRAM

Fax (415) 821-8859

TO: DAVID JARMUL FAX# 202 334 2158

FROM: PAUL VOLBERDING MD

RE: OP-ED DATE: 1/4/89

Message:

MY ASSISTANTS NAME IS CATHY ROSEBERRY. SHE CAN RELAY YOUR THOUGHTS TO ME AND THE ACT-UP AUTHORS.

AIDS DRUG TESTING

NEW ERA/NEW OPTIONS

When first proposed, new policies that would permit wider distribution of new AIDS drugs while strict and limited Phase 2 (efficacy) experiments of these drugs were still in progress generated both support and criticism. Many AIDS advocacy organizations and patients saw this new system -the "parallel track"- as one that could make drugs with at least some evidence of benefit and limited short-term toxicity available to persons with a life-threatening condition who had few or no other treatment options. Although still not finalized, the draft version of the parallel track proposal includes guidelines to make drugs available to patients not eligible for ongoing or planned Phase 2 studies. Drugs in this system would be administered under the supervision of the patient's personal physician.

Many AIDS researchers, including one of the coauthors of this article, have criticized certain aspects of these proposals. They have feared that this system might expose patients to drugs with undefined but potentially severe long-term toxicities and that expanded access would slow the entry of appropriate candidates to necessary clinical trials. These criticism were specifically made after Bristol-Myers' ambitious early release program for ddI began.

This polarization has seemed to place paternalistic researchers an one end and patients on the other. This has engendered mistrust that has been fueled by lack of direct communication. We believe that this dispute is not necessary. Indeed both parties have much to gain with the expansion of access to new drugs: patients will have greater treatment options and research will become more effective and attractive.

What has led to this change in view? First, expanded access policies simply hasten the time when the testing of any new drug will have to compete with multiple existing therapies. The days when AIDS patients had to choose between experimental AZT trials and no therapy are fortunately past. Sooner or later, new treatments will be approved with or without expanded access policies. Researchers and sponsors of new therapies must appreciate that this will allow patients to approach the options as consumers in a "marketplace" as opposed to desperate, dying individuals. If participation in a clinical trial is perceived to require compromise in the level of otherwise available care or is excessively cumbersome without ameliorating advantages, recruitment of participants will be difficult. Rather than making sweeping attacks on the availability of new treatment options, researchers might do better to design trials that address these concerns or even help design these alternative treatment protocols to enhance their research. The opinions of what these changes should be are bound to vary from researcher to researcher, but this is also true for existing clinical trials. Methods to resolve these disputes already exist. But the underlying choice seems simple - design attractive trials that can still efficiently answer key questions or see elegant but unrealistic trials move so slowly that the disease changes more rapidly than the research. Some improvements in clinical trials could include setting reasonable end points for

studies and ensuring supportive care in clinical trials meets community standards.

No important issue is, of course, as straightforward as this short analysis might paint this one; nor are solutions necessarily easy. Not all of the problems with existing trials can be addressed in design, as funding constraints also play a role in slowing the recruitment of patients and make participation in these trials cumbersome. Carefully controlled clinical trials should be powerful weapons in the battle against AIDS and need to proceed at an even faster pace than ever. This is the best way to evaluate the potential risks and benefits for any treatment.

What immediate steps do we propose? First, physicians and AIDS researchers, pharmaceutical companies and those who establish drug approval policy should affirm that expanded, early access to new AIDS drugs provides vital choices to patients, particularly when approved therapy options are so limited. Second, AIDS researchers must maintain an active dialogue with patient advocacy groups to design trials of new drugs that can quickly attract appropriate patients and that ensure state-of-the-art medical management while still gathering absolutely crucial new information. Finally, the researchers, pharmaceutical companies, regulatory agencies, community doctors and patients should work together to identify ways that useful and valid data to speed drug evaluation and approval can be collected from the expanded access programs.

If we can accomplish these things, everyone stands to gain and the resources of the researchers, patients and their advocates can work together to overcome the many other obstacles that prevent the defeat of our common enemy, AIDS.

Dr. Paul Volberding
Director AIDS Program SFGH
Member ACTG

Jesse Dobson
Bill Thorne
ACT-UP/San Francisco
Treatment Issues Committee

This paper is the result of a collaborative effort by ACT-UP activists and an ACTG researcher following Gina Kolata's article in the New York Times 11-21-89 (see enclosed).

AIDS Plan May Hinder Testing

Continued From Page A1

AIDS, the Bristol-Myers Company announced that it would put its promising new AIDS drug, DDI, on a parallel track. The drug is intended to slow the progress of the disease by interfering with reproduction of the AIDS virus. The human immunodeficiency virus that causes AIDS attacks the body's immune system and makes patients susceptible to a wide array of diseases, including cancers.

Objection of Patients

Some patients object to participating in clinical trials because they usually have just a 50 percent chance of receiving the new drug. For example, to test the Bristol-Myers drug, researchers would recruit about 1,900 patients for three trials. In two of them, half the 1,540 patients would receive AZT, the standard drug for AIDS, and the others would receive DDI. The third trial, whose recruitment goal is 360 patients, is for patients who cannot tolerate AZT.

As the trials progressed, the drug was also to be made available in an "expanded use" program to patients who did not qualify for the trials or who lived too far away from trial sites to participate.

While the National Institute of Allergy and Infectious Diseases, which runs the testing program, provided the figure of 75 patients enrolled in the trials, Bristol-Myers did not provide its own figures. But Dr. Douglas D. Richman of the University of California at San Diego, said the company disclosed at a private meeting with researchers two weeks ago that more than 1,300 patients had enrolled in the expanded access program and that the number was increasing by 100 a day.

Seriousness of Problem

Dr. Daniel Hoth, who administers the clinical trials program at the institute, which is part of the National Institutes of Health in Bethesda, Md., said "it is entirely too early to say" whether the experience so far with the parallel track method indicated a serious problem. "Of course we're concerned, and we are looking at this very closely," he added.

Dr. Fauci said he was optimistic that the clinical trials would soon start to attract many more patients. "I don't want to say that I am concerned and I don't want to say that I am not concerned," he said, and echoed Dr. Hoth's statement that it is too early to draw any conclusions. He noted that the expanded access to the new drug had begun before it was available for clinical trials, so "this was not, strictly speaking, parallel track."

Jerry Parrott, a Bristol-Myers spokesman, said the company was pleased with the enrollment so far in both clinical trials and the expanded access programs.

Patients participate in the expanded access program if their doctors request the drug for them and assert that they fulfill the criteria. Mr. Parrott said that the company does not try to verify whether patients belong in expanded access rather than clinical trials. He said, though, that it would begin auditing patient enrollments in its programs, and this "should reveal problems if they exist."

But researchers who are trying to recruit patients for the clinical trials have a different perception. "A lot of us are very concerned," said Dr. Fred Valentine, who heads the DDI trials at New York University Medical Center. "There is a real issue here."

Dr. Richman said: "As it is designed, parallel track will not work. What was actually put in place is an invitation to disaster. It will prevent us from finding drugs that will help people."

DDI is a toxic drug, and the only way to know if its benefits outweigh its risks is to assess it in clinical trials with large numbers of people that compare it to the standard treatment, experts said.

"Without appropriate clinical trials, the only consensus that will be possible will relate to the drug's side effects," said Dr. Samuel Broder, director of the National Cancer Institute. In fact, he said that if the only data available on AZT were from programs like the expanded access ones, "AZT would have been completely dismissed as a drug that's too toxic." That is because AZT has so many negative effects that without the statistical comparisons that clinincal trials provide, it would have been impossible to prove that taking the drug was better than not taking it.

Dr. Richman and others said that if the parallel track worked the way it was supposed to, patients could get the drug outside the trial groups only if they did not qualify for the tests. But Dr. Richman said, "It is not clear that the rules are being adhered to." He added that he knows of a number of patients who entered expanded access programs when they should have been in clinical trials.

Dr. Groopman agreed. "Patients basically didn't want to enter a clinical trial comparing AZT with DDI," he said. "That is a major issue."

Defense of Program

Advocates for people with AIDS defend the expanded access concept. The real problem, they say, is with the clinical trials. Mark Harrington, a member of the AIDS Coalition to Unleash Power, said that because of bureaucratic problems the DDI trials started supplying the drug several weeks after it was available through expanded access programs.

~~Inno~~vative AIDS Drug Plan May Be Undermining Testing

NYT 11-21-89

By GINA KOLATA

The Federal Government's bold new plan to make promising but unproven AIDS drugs widely available at the same time that they are undergoing clinical trials appears to be foundering.

In the first test of the new system, almost 20 times as many people have flocked to free distributions of the new drug DDI than have signed up for the clinical trial, leaving researchers in despair over whether they will ever be able to complete the formal study.

Although Federal officials and a drug company spokesman said it was too soon to tell if the new method would work, the mood among many researchers is grim. At latest counts, only 75 patients had volunteered for the clinical trial, which requires 1,900 people, but 1,300 had applied to receive the drug outside the trial, and that number was increasing by 100 a day.

New Approach Is Announced

The new approach, called the parallel track, was announced in June by Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, as a significant new direction in drug testing. After numerous discussions with advocates for people with AIDS, Dr. Fauci said he favored the concept.

In the parallel track method, standard clinical trials would test a drug's safety and usefulness but, at the same time, the drug would be made available to patients who could not participate in the trials. Dr. Fauci said he had decided it was not necessary to force patients with acquired immune deficiency syndrome to enter testing programs so they could receive a promising drug. He added that if the parallel track proved effective, it would be used in testing drugs for other diseases as well.

In September, after weeks of meetings with advocates for people with

Continued on Page B9, Column 1