In the

# Supreme Court of the United States

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| CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION AND WELFARE, et al., as Petitioners and as Respondents, | ) | |
| HYNSON, WESTCOTT AND DUNNING, INC., as Respondent and as Petitioner, | ) | Consolidated cases |
| CIBA CORPORATION, as Petitioner, | ) | 72-394 |
| BENTEX PHARMACEUTICALS, INC., et al., as Respondents, | ) | 72-414<br>72-528<br>72-555 |
| USV PHARMACEUTICAL CORPORATION, as Petitioner. | ) | 72-666 |

Washington, D. C.
April 17, 1973

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IN THE SUPREME COURT OF THE UNITED STATES

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| CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, et al., Petitioners, v. HYNSON, WESTCOTT AND DUNNING, INC., Respondent. | No. 72-394 |
| HYNSON, WESTCOTT AND DUNNING, INC., Petitioner, v. CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, et al., Respondents. | No. 72-414 |
| CIBA CORPORATION, Petitioner, v. CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, et al., Respondents. | No. 72-528 |

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| CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, et al., | : | |
| Petitioners, | : | |
| v. | : | No. 72-555 |
| BENTEX PHAEMACEUTICALS, INC., et al., | : | |
| Respondents. | : | |
| - - - - - - - - - - - - - - - - - - - - - - | : | |
| USV PHARMACEUTICAL CORPORATION, | : | |
| Petitioner, | : | |
| v. | : | No. 72-666 |
| CASPAR W. WEINBERGER, SECRETARY OF HEALTH, EDUCATION, AND WELFARE, et al., | : | |
| Respondents. | : | |
| - - - - - - - - - - - - - - - - - - - - - - | : | |

Washington, D. C.,

Tuesday, April 17, 1973.

The above-entitled matters came on for argument at 10:13 o'clock, a.m.

BEFORE:

WARREN E. BURGER, Chief Justice of the United States
WILLIAM O. DOUGLAS, Associate Justice
POTTER STEWART, Associate Justice
BYRON R. WHITE, Associate Justice
THURGOOD MARSHALL, Associate Justice
HARRY A. BLACKMUN, Associate Justice
LEWIS F. POWELL, JR., Asrociate Justice
WILLIAM H. REHNQUIST, Associate Justice

APPEARANCES:

DANIEL M. FRIEDMAN, ESQ., Office of the Solicitor General, Department of Justice, Washington, D. C. 20530; for the Government.

APPEARANCES [Cont'd.]:

ANDREW L. FREY, ESQ., Assistant to the Solicitor General, Department of Justice, Washington, D. C. 20530; for the Government in re: Hynson and USV.

CLYDE A. SZUCH, ESQ., 570 Broad Street, Newark, New Jersey 07102; for CIBA Corporation.

GEORGE F. TOWNES, ESQ., Greenville, South Carolina; for Bentex Pharmaceuticals, Inc., et al.

EDWARD BROWN WILLIAMS, ESQ., Marter, Calhoun & Williams, 423 Washington Building, Washington, D. C. 20005; for Hynson, Westcoot and Dunning, Inc.

JOEL E. HOFFMAN, ESQ., 1320 Nineteenth Street, N.W., Washington, D. C. 20036; for USV Pharmaceutical Corporation.

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C O N T E N T S

P R O C E E D I N G S

MR. CHIEF JUSTICE BURGER: We will hear arguments first this morning in a series of related cases, which I'll indicate only by numbers: 72-394; 72-414; 72-528, 555, and 666.

Mr. Friedman, you may proceed.

ORAL ARGUMENT OF DANIEL M. FRIEDMAN, ESQ.,

ON BEHALF OF THE GOVERNMENT

MR. FRIEDMAN: Mr. Chief Justice, and may it please the Court:

These five consolidated cases present important questions under the 1962 amendments to the Federal Food, Drug, and Cosmetic law. Under the predecessor statute, the Food and Drug Administration, in granting premarketing clearance to new drugs, is limited to considering the safety of those drugs; that's all it viewed, whether the drug was safe. And the major change made in the 1962 amendments, insofar as these cases are concerned, is that this premarketing clearance was extended to cover the effectiveness of drugs as well as their safety.

These cases present before the Court the questions of the standards under the statute and the procedures by which the Food and Drug Administration is to determine the effectiveness of the alrge number of drugs now on the market and thereby to protect the public against the distribution in

interstate commerce of ineffective drugs.

The statutory provisions are quite detailed and complicated, and in order to put the issues in the proper perspective and indicate the interrelationship among the issues in the cases, before discussing the particular cases, I would like to make a rather generalized statement that is applicable to all the cases, in which I will first describe the background and history of the statute, then deal with its particular provisions and finally explain the administrative steps that the Food and Drug Administration has taken to implement this statute.

After this opening statement which, according to my best estimate, should take around twenty minutes, the cases will then be argued in three separate segments. The first segments will consist of the Bentex and CIBA cases, which I will argue for the government; and in each segment the case will be viewed as a separate case, that is, the opening argument will be made by the government in the first two and by respondents, petitioners' counsel, the drug company, in the third; then there will be an answering argument, and this in turn will be followed by rebuttal.

So the Court will have, in the way of an oral presentation, an opening statement applicable to all of the cases, followed in effect by three separate consecutive arguments, in which, as I think it will develop, the issues are

somewhat interrelated.

Now, the starting point in the analysis of this statute is the 1906 Food and Drug Act. That Act prohibited the distribution in interstate commerce of adulterated and misbranded drugs. But the Act had no provision for premarketing clearance of the drugs by any administrative agency. The only sanctions under that Act were proceeding to forfeit the misbranded or adulterated drugs and criminal prosecutions.

In 1938, as the result of a tragic accident in which a number of people died as the result of taking a drug that had not been tested and proved to be unsafe, Congress passed the Federal Food, Drug, and Cosmetic Act, which, for the first time, provided for premarketing clearance of drugs before the drugs could be distributed in interstate commerce.

The statute prohibited the introduction of any new drug unless there was in effect an application that had been filed with and permitted to become effective by the Secretary of Agriculture. These applications for the marketing of new drugs are known in the industry as NDA's, new drug applications, and both the government and the counsel for respondents will use that term to describe them.

The statute also provided that after notice and opportunity for hearing, the Secretary could deny any application for new drug approval if he found either that the drug was not safe, or that he was unable to find that it was safe;

and, finally, it permitted the suspension of an approved new drug application if subsequent evidence developed to show that the drug was unsafe.

The 1938 statute also substantially expanded the enforcement authority of the Food and Drug Administration, it gave the -- correction; the Secretary of Agriculture. The statute in turn delegates the powers to the Secretary of Agriculture and that was transferred to the Secretary of Health, Education, and Welfare, but he has delegated virtually all of his powers under the statute to the Food and Drug Administration; and I will use the term "Secretary" and "Food and Drug Administration" interchangeably.

The statute authorized the Secretary to promulgate regulations for the efficient enforcement of the Act, gave the agency authority to conduct investigations, and finally expanded the district court authority to include suits for injunction in addition to forfeiture and criminal proceedings.

Now, the processing of these new drug applications is a --

QUESTION: Mr. Friedman, before you go on to that. Prior to the 1962 amendments, if you'll tell me again, what was the mechanism, the enforcement mechanism? Was it only a cease and desist order?

MR. FRIEDMAN: No. No, the --

QUESTION: Or injunction?

MR. FRIEDMAN: No. In addition to that, under the -- before the 1962 Act, the Secretary had authority to deny approval to a new drug application if he either found that the new drug application, that the drug was not safe or that they had failed to find it was safe; and, in addition to that, he had the authority to withdraw approval after notice and opportunity for hearing if subsequent developments after the NDA had become effective indicated the drug was not safe.

Then, in addition to that, there were the ancillaries, we believe the ancillary remedies of proceedings in the district court, under which, under the 1938 Act -- prior to the 1938 Act, they could only proceed through criminal proceedings or forfeiture, but the 1938 Act expanded this to give Food and Drug, the government, the authority to seek injunctive relief in the district court.

But, as a practical matter, as a practical matter because of the nature of drugs and public concern, it's a rare instance in which a drug manufacturer would attempt to market the drug if the Food and Drug Administration concluded that it could not permit the new drug application to become effective.

In other words, our basic position here is that the primary enforcement method that Congress selected in the 1938 Act as increased and improved in the 1962 Act was the administrative procedure of premarketing clearance for drugs.

That is, that the agency would stand at the gateway before the drugs could get into the channels of interstate commerce and say whether or not they would permit these drugs to be distributed.

QUESTION: With respect to NDA, the new drug applications?

MR. FRIEDMAN: That is right.

QUESTION: And you are going to deal, I suppose, with the so-called "me-too" drugs?

MR. FRIEDMAN: Yes, sir, I will come to that in one or two minutes, Mr. Justice.

QUESTION: Right.

MR. FRIEDMAN: After just making this one point, that the processing of these new drug applications is an extremely time-consuming and difficult task. They're huge things. They are filed with a mountain of scientific information. They may have statements from as many as several hundred doctors giving their views on these drugs. They are papers, lengthy analysis, I am told that they sometimes occupy as much as several hundred volumes. They may fill half of a room, and obviously it would have been an enormous task for Food and Drug just to process these applications as they were filed.

And I would mention that in the period between the 1938 Act and the 1962 Act, Food and Drug processed and permitted to become effective almost 10,000 of these applica-

tions, and at the time the 1962 Act was passed, it was estimated there were approximately 4,000 of these applications covering drugs that were then being distributed.

Now, the fact of life in the drug industry is that there are a large number of drugs on the market which are basically the same generic drug, but with various chemical differences. They are fundamentally the same, but they have slight variations. Most of these drugs would come on the market after a new drug application had become effective. What would happen is, one or two new drug applications would come on the market, the drug would be in use for two or three years, and it turned out to be safe; and of course under the 1938 Act, safety was the sole criteria for passing on new drug applications.

And following this, a number of other large pharmaceutical firms would put on the market similar products for normally labeled -- label goes of course to the doctor, we're not talking of the label on a package of patent medicine; this is the label that tells the doctor what the drug will do -- labeled basically, making the same, or very similar claims to those in the drugs where the new drug applications were outstanding.

Since, under the 1938 statute, the test of a new drug was whether the drug was safe, and since by definition, after the new drug applications had been determined to be safe,

the so-called "me-too" drugs, which is what the industry calls the drugs that are patterned after the NDA drugs, for which no NDA is in effect, they came to be recognized as not new drugs or old drugs, and they came on the market.

The estimates are that in the prescription drug field there's anywhere from five to thirteen "me-too's" for every drug with respect to which an NDA is outstanding.

So that by 1962, when the amendments were passed, the best estimate is that there were probably 30 to 50 thousand drugs outstanding in the me-too category, and that is just in the prescription drug field. In addition, the over-the-counter drug field has a vastly greater number. It's impossible to know, but the best estimate of Food and Drug is probably there were 200,000 drugs in the over-the-counter market.

QUESTION: Now, NDA means new drug application --

MR. FRIEDMAN: Application.

QUESTION: -- applications.

MR. FRIEDMAN: Application, but it's also used --

QUESTION: In one of the -- in the Court of Appeals opinion in one of these cases, I think there seems to be some confusion, that court thought it meant "new drug approval".

MR. FRIEDMAN: Well, we -- it's used interchangeably.

QUESTION: Oh. Well, how do you mean it -- how are you going to use it?

MR. FRIEDMAN: I'm going to use it primarily as new

drug approval; that is a new drug application that has been approved. And the phrase is sometimes used as NDA, but what I think I will do, when I am speaking of the application, refer to it as the application, and when I'm speaking of the approval, I will use the short phrase, NDA.

QUESTION: So NDA is going to be your code for new drug approval.

MR. FRIEDMAN: Approval. That is the approved application; the approve application.

QUESTION: Yes.

QUESTION: Mr. Friedman, when you talk about "me-too" drugs, you mean something more than just an identical chemical compound that has a different trade name, you mean something that has a similar but not identical chemical compound and a different trade name?

MR. FRIEDMAN: Well, it may be identical, it may actually be identical, but at least it's similar. The --

QUESTION: Well, Mr. Friedman, doesn't it also include just any drug that's not covered by an NDA?

MR. FRIEDMAN: No, Mr. Justice, it's used in the trade -- it's used in the trade to relate just to drugs which are similar to the drugs which are NDA.

QUESTION: And yet there are a lot of other drugs that are not covered by NDA?

MR. FRIEDMAN: Oh, yes, there are --

QUESTION: What do you call them?

MR. FRIEDMAN: Just --

QUESTION: Just drugs.

MR. FRIEDMAN: -- drugs. They're mostly in the over-the-counter market, and there are many, many --

QUESTION: Are those involved in this case?

MR. FRIEDMAN: They're not directly involved in this case, but some of the principals involved in this case will be significant when Food and Drug implements its recently established procedure to determine the effectiveness of the over-the-counter drugs.

QUESTION: Would you apply that to common aspirin, to illustrate how it relates to it?

MR. FRIEDMAN: Well, common aspirin, at the moment, I assume, is viewed as a drug that is both safe and effective. Now --

QUESTION: It long predates 1938.

MR. FRIEDMAN: It long predates -- it's not a prescription drug, it's over-the-counter; there is, of course, no NDA for common aspirin.

Now, there are various compounds of aspirin. There's Bufferin, various types of analgesics. They are advertised, many of them are advertised perhaps as effective for various things. Food and Drug may want to consider whether in fact the claims made for aspirin and related aspirin drugs, whether

these claims are valid in the sense that the drug is effective for the particular condition it is alleged that it can alleviate.

Now, let me take it one step beyond that. Suppose one of the aspirin companies came out and announced that they had discovered that if you took four tablets of aspirin four times a day it would cure acne. This would be a new claim, and under the statute, even though there's no NDA, it would be necessary for the -- excuse me -- Food and Drug could consider whether the drug would be effective for that particular new claim.

QUESTION: If they put it on the label.

MR. FRIEDMAN: If they actually -- if they put it on the label.

QUESTION: Yes.

MR. FRIEDMAN: Now, with the limited staff that Food and Drug has, it was obviously impossible for it to police this vast number of new drug applications -- of these drugs, particularly the me-too's, occasionally they brought a proceeding against a violator which was a sporadic thing, but, by and large, in this period the Food and Drug Administration could not deal with the vast number of me-too's.

QUESTION: Mr. Friedman, just how limited is the staff? Is it a small staff?

MR. FRIEDMAN: Relatively small. At the time of the

statute in, I think in 1962, the budget was just a few million dollars, it's expanded somewhat -- a good bit now, but, nevertheless, it seems the staff is still inadequate to handle the policing job, if you were trying to police this on a drug-to-drug basis. A hearing, if you have a full hearing on a single drug, it can take three or four months, and when I point out that there are thousands of these drugs, and one of our points is that it would be impractical for Food and Drug Administration to deal with them on a single drug-to-drug basis.

QUESTION: Well, I fail to find anything specific in the record. Is it a staff of 60 or 5,000, or does anybody know?

MR. FRIEDMAN: I am advised 6,000 altogether; but this includes all the scientific people, the technical people, the statistical people, and so on. It may seem like a large staff, Mr. Justice, but it's an enormous problem. They assure me the staff is quite inadequate to deal effectively with the problem.

QUESTION: Are the 6,000 in the drug part of FDA?

MR. FRIEDMAN: No, no, that's the whole agency.

QUESTION: Oh, that's quite different.

QUESTION: I can assure you I'm aware of the enormity of the problem.

This also involves people involved with food and

cosmetics.

MR. FRIEDMAN: Food and cosmetics.

QUESTION: And the various aspects of the FDA jurisdiction over all these.

MR. FRIEDMAN: Yes, color additive, -- and all of its chemists and so on.

QUESTION: Right.

MR. FRIEDMAN: Yes. The actual number of people working on the drug phase of the activity --

QUESTION: And on the drug applications.

MR. FRIEDMAN: The drug applications.

QUESTION: -- specifically, would be much smaller.

MR. FRIEDMAN: Much smaller, oh, yes.

QUESTION: And then just think of the lawyers.

MR. FRIEDMAN: Unfortunately, they don't have enough lawyers, either, Mr. Justice.

Now, between 1959 and 1961, the Senate conducted lengthy hearings on the drug industry, and one of the things that came out in these hearings was that the Food and Drug Administration was powerless to deal with the fact that many, many drugs were ineffective to accomplish the claim made for them. And the problem was recognized as a serious one, there was a great deal of testimony. But Food and Drug, of course, at this time had no authority to provide preclearance approval for marketing drugs on the grounds of ineffectiveness.

And Congress, in 1962, closed this regulatory gap by giving Food and Drug, for the first time, the authority to apply the preclearance technique to the effectiveness of drugs as well as their safety.

Under the amended statute in Section 505, the Secretary is required to disapprove an application for a new drug if he finds there is substantial evidence -- I'm sorry, if he finds there is a lack of substantial evidence that the drug will be able to have the effect and do the things claimed for the drug on the label.

Congress also heard at these hearings of the importance in ascertaining the effectiveness of drugs that there be adequate clinical, scientific studies. There was repeated testimony, much of which we have summarized in our brief in the Hynson case; repeated testimony that you cannot determine how effective a drug is merely because various doctors state that they use it in their practice and they have found it works. There has to be some kind of a control.

otal QUESTION: Is that what's called the anecdotal reports in the --

MR. FRIEDMAN: The anecdotal testimony.

QUESTION: -- in the briefs.

MR. FRIEDMAN: Yes.

QUESTION: That's what anecdotal reports are.

MR. FRIEDMAN: Yes, the doctor said he treated six

patients for this condition and they recovered.

QUESTION: And they got well.

MR. FRIEDMAN: Yes.

Now, Congress did a very unusual -- excuse me?

QUESTION: Four died.

MR. FRIEDMAN: Normally the doctor's --

QUESTION: But the anecdotal evidence --

MR. FRIEDMAN: -- anecdotal evidence doesn't bring that out.

QUESTION: Right. Right.

But that's what is meant by the anecdotal?

MR. FRIEDMAN: Anecdotal, as distinguished from the scientific, clinical study.

QUESTION: Right.

MR. FRIEDMAN: Congress did a rather unusual thing in this statute, because of the evidence before it that clinical studies were important. It said in the statute that the Secretary should not approve a new drug application unless he found by substantial evidence it was effective, it went on and defined in the statute what it meant by substantial evidence. And substantial evidence, under this statute, means something very different than substantial evidence in the traditional administrative statute.

It defines substantial evidence in the statute as constituting, meaning adequate and well-controlled investiga-

tions, including clinical investigations by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved.

And Congress also expanded the definition of new drugs to cover effectiveness, so that a new drug is now defined as one not generally recognized among the experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs.

Two other things that the statute did in the way of strengthening the administrative authority of the Food and Drug Authority: First, under the predecessor statute in 1938, a new drug application became effective automatically unless the Secretary affirmatively disapproved it. This was changed in the 1962 Act to provide that the application did not become effective unless the Secretary affirmatively approved it.

The statute also provided that after an interim period of two years, the Secretary was required, if, on the basis of new information before it, there was a lack of substantial evidence that the drug will have the effect it proposes to have, but in that situation the Secretary was to withdraw the approval of the new drug application.

Finally, there is in the statute a grandfather clause, which I will not go into because that will be discussed in some of the succeeding cases, under which certain

drugs that were being distributed on the effective date of the statute are exempt from the effectiveness requirements, this could be expected as a sharp disagreement between the government and the companies as to the meaning of that exemption.

Now, --

QUESTION: This two-year grace period began to run with the enactment of the statute?

MR. FRIEDMAN: From October 10, 1962.

QUESTION: Yes.

MR. FRIEDMAN: So that it meant that until October 10th, 1964, Food and Drug could not begin proceedings --

QUESTION: Right.

MR. FRIEDMAN: -- to withdraw the new drug approvals on the ground that the drugs would be ineffective.

Now, the Food and Drug Administration recognized immediately that with 4,000 new drug applications outstanding, approved applications, NDA's, it just couldn't itself undertake, with its limited staff, to evaluate every one of these. So what it did was it called upon a group of eminent scientists of the National Academy of Sciences and its constituent, National Research Council, for aid in determining the validity of the effectiveness claims of this large number of drugs.

And what the National Academy of Sciences did was it set up panels, thirty panels, each panel containing six

experts with respect to the particular type of drug involved. The companies were requested to submit all evidence they had concerning the effectiveness of their drugs as claimed to these panels; the panels then evaluated each of these drugs and made recommendations to Food and Drug with respect to their effectiveness.

They evaluated the drugs, and what happened was as follows: The panels found, of all of these drugs, of these 4,000 NDA's that were reviewed, 7 percent were ineffective, a considerable number were described as effective, and the balance was somewhere in between; they described them as possibly effective, probably effective, effective but, effective with respect to some claims and not all.

Many of the labels, of course, suggested the drug was suitable for more than one condition, and of the 4,000 NDA's, there were approximately 16,000 claims, and the National Academy of Sciences panels found that only 19 percent of these alleged claims of effectiveness were valid.

After these studies were made, the Food and Drug Administration had a large conference with the industry in January of 1968, and it announced that its policy would be to apply the conclusions of the National Academy of Sciences to all drugs, not only to the drugs that were covered by the NDA's, but also by the me-too drugs. And what they announced they said they would do is that they would issue notices and

opportunity for hearing with respect to all of the NDA manufacturers whose drugs were found ineffective, and that they would permit the me-too's to come in to those hearings to be heard.

Following -- the best estimate was that as a result of these procedures they would have to conduct something like a thousand hearings. And in 1969, in the hope of making this problem manageable, they issued further regulations in which they defined what would constitute an adequate and well-controlled study, very specific, they told exactly what it had to be, and they also said that if a manufacturer requested a hearing, they would not grant a hearing unless he produced, as indicated as the substantial evidence that he would produce, that type of evidence; that is, the well-controlled studies, the validity of this regulation is at issue in another one of these cases.

And then finally, in 1972, the Food and Drug Administration issued another regulation which more specifically put the me-too's on notice that the withdrawal of the NDA for the so-called pioneer drugs would also apply to the me-too drugs.

QUESTION: Mr. Friedman, does the statute give the Commissioner expressly authority to define by regulation the statutory language in 505(d) pertaining to substantial evidence?

MR. FRIEDMAN: There is a specific general authority to promulgate rules and regulations. Section 701; and it's a very broad statute. It authorizes him to promulgate rules and regulations necessary for the effective implementation of the Act.

There is no specific provision giving the Commissioner authority to define further what constitutes substantial evidence, but we believe that as a general exercise of administrative authority, this broad rule-making power does permit him further to define and particularize the standard of substantial evidence which Congress provided. He's not changing it, he's merely explaining what is meant by a well-conducted clinical study and investigations.

Now, we think that this legislative history that I've given drmmatizes and brings home three things, which I'd just like to reiterate now, because they are critical to the legal issues in the cases.

First, by the 1962 amendments Congress intended to take off the market, to take off the market, drugs that had not been shown to be effective. And Congress decided to do this primarily by expanding the authority of the Food and Drug Administration's premarketing clearance authority to cover effectiveness as well as safety. It required that the definition of whether a drug be effective be put in terms of high probative scientific studies.

Secondly, as I think I have indicated, Food and Drug was faced with this enormous administrative problem, and it couldn't possibly deal with the situation on the basis of a drug-by-drug procedure, of bringing 4,000 separate proceedings. It had to deal with it on a more comprehensive basis.

And finally, we think the method it has selected, the use of the National Academy, with its panels of experts, the opportunity given to the manufacturers to come in after the scientific studies had been made and to show why in effect, in fact, their drugs were effective in accordance with their claims under principles of adequate and well-controlled clinical investigations was a reasonable and fair method of dealing with the problem.

And with this as a background, I'd now like to turn to the two cases I'm going to argue, the Bentex case, which is here on certiorari to the Fourth Circuit, and the CIBA case, which is here on certiorari to the Third Circuit.

The question in each of these cases is whether the Food and Drug Administration has jurisdiction to determine whether a product is a new drug to which the premarketing clearance procedures and the withdrawal procedures of Section 505 of the statute are applicable.

Our contention is that the Secretary and the FDA does have that authority. The Fourth Circuit held and the respondents contend that he does not; and as they view his

authority, the only thing he can do is pass upon applications for new drug approvals or withdraw previously effective applications. He cannot, according to their theory, decide the threshold question whether or not something is a new drug.

Bentex involves a drug to deal with the mental problems of senility. Bentex is a me-too manufacturer. There is no NDA outstanding for Bentex's product. But prior to 1962 there were three NDA's outstanding for a similar product.

Upon its review of these drugs, the National Science Foundation panel concluded that these drugs were ineffective for their stated purposes.

After evaluating the Academy's studies, Food and Drug concluded preliminarily that there was not substantial evidence of effectiveness, and put out a notice of hearing, so stating, and giving the manufacturers of these three drugs the opportunity to request a hearing to show why the drug was effective, and it also invited any interested persons who might be adversely affected by the removal of these drugs from the market to participate. And finally, the notices stated that the withdrawal of the NDA's for these three drugs will cause any such drug on the market to be a new drug for which an approved new drug application is not in effect, and will make it subject to regulatory action.

One of the three NDA holders submitted some material which Food and Drug found was not substantial evidence as

defined by the statute. And after a second notice published in the Federal Register, which again gave interested parties the opportunity to come in, and which again pointed out that withdrawal of the NDA would cause the me-too's to be new drugs, Food and Drug Administration withdrew its approval of the three NDA's covering this drug.

No court review was sought of that action by the three NDA manufacturers.

Now, under Food and Drug's view of the law, the withdrawal of the NDA also had the effect of making the me-too's into new drugs subject to the premarketing clearance. And, accordingly, Food and Drug sent out letters to a number of manufacturers of the me-too drugs, pointing this out to them, and it specifically sent such a letter to Bentex, that is reprinted in the opinion of the Court of Appeals, and asking what Bentex what its intentions were with respect to removing this drug from the market.

QUESTION: How could the administration know about what all the me-too drugs were, --

MR. FRIEDMAN: Well, we don't know --

QUESTION: -- at least until the 1972 legislation, that you haven't mentioned.

MR. FRIEDMAN: We don't know -- we're not sure that these are all the me-too drugs. We do know that 22 of these people brought this lawsuit. They sent out to those that they

knew about, I think. You know, they are informed people, they have some knowledge. They may not have gotten all the me-too's.

QUESTION: There was no real way except --

MR. FRIEDMAN: There's no real way --

QUESTION: -- for their general knowledge of the industry.

MR. FRIEDMAN: -- except for the drug registration statute, and that will not be effective until June of this year.

QUESTION: It was not enacted until 1972.

MR. FRIEDMAN: That's right.

They had no way -- but they did know, they did know at least that Bentex and some of the others were manufacturing this drug.

Now, the response of Bentex to this request for information as to what it was going to do to remove the drug from the market was to bring a lawsuit for a declaratory judgment, in which Bentex, joined by 22 other me-too manufacturers, they sought a declaratory judgment that they, their products were not new drugs and were not subject to the application procedures of Section 505.

Then the government, in the district court, moved to dismiss the suit on the ground that the district court had no jurisdiction to determine this question, that this was -- we

made two arguments: one, that this was a matter within the exclusive primary jurisdiction of Food and Drug; and, secondly, that since Bentex had had the opportunity to come in to the proceedings for the withdrawal of the NDA's, Bentex as barred from litigating this question in the district court.

The district court rejected those arguments, and held that it and Food and Drug had concurrent jurisdiction, but it also rejected the plaintiff's contention in that lawsuit that the district court had exclusive jurisdiction to determine the question of new drug status.

And what it said was that the authority of the Food and Drug Administration to approve or withhold approval of the NDA's necessarily implies authority for Food and Drug to determine the threshold question of whether the article involved is a drug which requires an approved new drug application for lawful interstate shipment.

And the court then said that it thought it was appropriate that the Food and Drug Administration should decide this question in the first instance, because, it said, the nature of the proof relevant to that issue makes Food and Drug the more able arbiter of the question. So the evaluation of conflicting reports in the field is not a matter well left to a court without chemical or medical background.

And, accordingly, the district court deferred any proceedings in the case until Food and Drug had an opportunity

to conduct a hearing on the new drug issue.

The government did not appeal that aspect of the case, and has accepted the remand. But I want to make it quite clear to the Court that while we do, if the Court agrees with us in this case, plan to hold a hearing, we do not contemplate that the hearing will be the typical evidentiary trial type hearing; we think it appropriate to conduct a hearing along the rule-making lines, which the agency is now using in this case.

QUESTION: What is the specific -- tell me again, the specific issue is to whether or not a drug is a new drug?

MR. FRIEDMAN: Yes.

QUESTION: What is the underlying question?

MR. FRIEDMAN: Well, there is -- there --

QUESTION: Is this the -- this is its reputation or its actual quality? Or do you think there's any difference?

MR. FRIEDMAN: Well, that's a matter of disagreement again. It's the statutory definition of new drug, one which is generally recognized among this group of experts as being effective for uses. And that, we think -- as Mr. Frey will develop -- we think that the general recognition standard in the statute is something in addition to the substantial evidence.

That is, we think that if a panel of experts concludes that there's not substantial evidence based on well-

conducted clinical studies to show that a drug is effective, the same experts could not --

QUESTION: Why couldn't they?

MR. FRIEDMAN: -- possibly be recognized, its general effectiveness. We think the recognition is something else. That's the issue. And, for example, there may be questions in these cases; they claim that they are not a new drug because the NDA drugs contained an additional element that their drug doesn't contain. They say one of the drugs was administered intravenously, another is orally; that's the distinction.

So that there are two questions, really: one, --

QUESTION: Well, don't they really claim that no me-too drug can be a new drug?

MR. FRIEDMAN: That is another claim. That is a claim. They also claim they are covered by the grandfather exemption.

QUESTION: Right. Right.

MR. FRIEDMAN: Yes.

QUESTION: That's another question; that's another problem.

MR. FRIEDMAN: That's another problem, yes.

QUESTION: But you say for the new drug thing you're contemplating a rule-making type of proceeding?

MR. FRIEDMAN: Not a rule-making type of proceeding,

what I'm suggesting, Mr. Justice, is we do not contemplate that there would be a hearing in the sense of a trial type hearing at which a large number of doctors will take the stand and give their opinion. They will have full opportunity to bring to the attention of the Commissioner all pertinent material bearing on their claim that their drug is not a new drug because it is effective or because it's covered by the grandfather exemption.

QUESTION: The type of hearing required for that purpose, is that at issue here? In this case?

MR. FRIEDMAN: That is -- I think that is in issue because of the fact that ine one of the other cases a hearing was denied --

QUESTION: Right.

MR. FRIEDMAN: -- because of the failure of the parties to produce the kind of evidence requisite.

QUESTION: Well, when you say a rule-making hearing, Mr. Friedman, you're not talking about a hearing whose ultimate object is to promulgate a rule, are you? You're talking about a hearing for the purpose of adjudicating particular facts with respect to these drugs?

MR. FRIEDMAN: To these drugs. I use the word "rule-making" perhaps too loosely. What I would suggest it would be is a hearing appropriate, considering all the circumstances, for determining this question, which is not the

same thing as the kind of a hearing to decide, for instance, whether an employer fired a man for his union activities or for inefficiency.

QUESTION: Well, but it would still be -- but it would be a hearing for the purpose of making an adjudication?

MR. FRIEDMAN: Yes, it would be a hearing to determine --

QUESTION: And one to be made on the record.

MR. FRIEDMAN: On the record. And would be judicially reviewable.

QUESTION: Yes.

QUESTION: But that would be to fix a definition basically, would it not?

MR. FRIEDMAN: Well, I don't think so, Mr. Chief Justice, because the statute has --

QUESTION: Well, wouldn't it have two prongs? One would affect the particular parties involved now, and the other would be to establish a definition.

MR. FRIEDMAN: Well, it would be to establish a definition, a determination as to whether this type of drug, whether this type of drug is effective; and there would be, I suppose, two issues. One would be the issue as to whether or not these people's drugs are -- they would have the opportunity under this particular hearing procedure to come in and produce any additional evidence not before, for example,

the National Academy proceedings, why their drug is effective. That is, if they had well-established studies that had not been presented, they could present those to the Commissioner.

In addition, they could come in and explain why they think their drug is different from the FDA drug, so that their drug, whatever one might say as to the NDA drug, as to why the me-too drugs are not new drugs, why their drugs are effective even though the me-too drugs have been -- though the FDA drugs have been determined not to be effective.

If I may just --

QUESTION: What worries me about this new drug -- No. 1, it's not a new drug.

MR. FRIEDMAN: That's a word of art, Mr. Justice.

QUESTION: I know, but that's what gets me confused. Suppose the me-too drug has an additional ingredient in it, which makes it effective?

MR. FRIEDMAN: If it makes it effective, under the standards -- if it makes it effective under the standards, then it would not be a new drug. In other words, if it was effective, if it's effective, then it does not have to meet the --

QUESTION: Well, where does he get a chance -- as I understand, as soon as the NDA three people lose theirs, he automatically loses his?

MR. FRIEDMAN: That's under the theory because he

had the opportunity to come in. Now, we're not arguing that in this case. In this case we're not arguing, because that is --

QUESTION: Well, it's in one of them.

MR. FRIEDMAN: Pardon?

QUESTION: Isn't it in one of them?

MR. FRIEDMAN: No, no, it's not in one of them: what is, is the question, is whether the kind of evidence they have to produce. They have to produce that.

QUESTION: That's what I mean.

MR. FRIEDMAN: Yes. But we're not contending in this case, we're not contending in this case that they're barred. That's what we argued in the district court; the district court rejected that. We didn't appeal it.

Well, for the future we're going to take that position, that they had the opportunity to come in and produce all the evidence in the proceeding; and if they don't do it, they're barred.

Now, the Court of Appeals, just briefly, held in this case that the --

QUESTION: Which court?

MR. FRIEDMAN: The Fourth Circuit, in the Bentex case, held that the Food and Drug Administration has no jurisdiction to decide new drug applications. It said basically that the statute has two different procedures. Food and Drug can do

nothing but pass on applications for approval, and withdraw approved applications if it finds that they are not, the drug isn't effective. But it cannot do anything in the way of trying to determine the threshold question of whether something is a new drug. That, they said, is a question solely for the district court, to be decided either in a declaratory judgment suit brought by the manufacturers or to be decided by the district court when the government moves against the drug.

Now, I may just very briefly turn to the facts in the CIBA case, which presents the same issue, though in a different context.

CIBA did have an NDA, and its drug was reviewed by the National Academy of Sciences, the claims were found ineffective. They went through a whole series of procedures, notices were given. The climax of this was that Food and Drug withdrew the NDA for CIBA's drug.

CIBA took that question to the Court of Appeals for the Second Circuit. The Second Circuit affirmed. At this point -- in the interval, CIBA then filed a district court suit in New Jersey, in which CIBA claimed that it was not a new drug and that it was exempt, and it wanted to have that issue determined. The district court dismissed. The Third Circuit affirmed, basically following the reasoning of the district court in the Bentex case, saying that when Food and Drug undertook to withdraw the new drug application, that it

necessarily had -- must have decided the threshold question of whether it was a new drug; that CIBA challenged the order of Food and Drug in the Court of Appeals, and when the Court of Appeals upheld that decision, it also upheld the determination that this was a new drug.

Now, the problem in this case, and the reason we think that the Third Circuit is correct, and the Fourth Circuit is in error is that --

QUESTION: Did you say the Third Circuit agreed on -- said concurrent or --

MR. FRIEDMAN: No, no. The Third Circuit said that the Food and Drug Administration had jurisdiction to decide the new drug question, that it had necessarily decided it when it withdrew the application, that that was affirmed by the Second Circuit, and there was no occasion for CIBA to be permitted to relitigate the new drug question in an independent suit brought --

QUESTION: So it didn't say whether a district court would have jurisdiction to consider a declaratory judgment action?

MR. FRIEDMAN: No, it did not. All that it held was that Food and Drug did have jurisdiction, and that of course is the only issue directly involved in these cases where the Food and Drug has jurisdiction.

Now, the problem we have with the decisions of the

Fourth Circuit in this case, and the contentions of the respondent is that it would basically transfer to the district courts, to the district courts, the primary enforcement responsibility. That is, it would bar Food and Drug from making these threshold determinations, even though Congress in the 1972 statute made its intention quite clear that it intended to strengthen the hand of Food and Drug in withdrawing from the market the drugs asserted to be ineffective.

QUESTION: What are the --

QUESTION: Under the Fourth --

QUESTION: Would that be a de novo proceeding in the district court?

MR. FRIEDMAN: Oh, yes. Under their theory, it would be a de novo proceeding.

QUESTION: Under the Fourth Circuit rule, though, Food and Drug can refer for prosecution, it can initiate in that manner, can't it?

MR. FRIEDMAN: It can initiate in that manner, Mr. Justice, but it cannot deal with the vast bulk of these applications, because prosecution in this field is not really an effective method. It's not an effective method for getting off the market these thousands of drugs which seemingly, on the basis of the National Academy of Sciences' studies, are ineffective.

That is the whole purpose -- the whole purpose of

this statute was to give Food and Drug administrative authority to do the job it had not been able to do under the 1938 Act. And the issues, the issues, for example, in defining a new drug, as distinguished from determining whether there was substantial evidence of effectiveness, there's a disagreement between the parties as to exactly what the standard is, but however one defines the standard, it seems to me it's the kind of question, it's the kind of question that calls for expert skills and knowledge. It needs an analysis of detailed scientific information, pharmacological studies. It's the kind of thing, it's the kind of thing, the kind of expert issue that traditionally is for the administrative agencies.

And we think the district court, in the Bentex case, was well warranted in sending this matter to Food and Drug. It's traditional that administrative agencies have authority to determine their own jurisdiction. That's the threshold question.

When a claim is made that somebody -- to an agency that someone is doing something in violation of a statute the agency administers, the first question the agency has to decide is whether or not the thing is covered by the statute. Before you decide whether there's a violation, you decide whether the statute is covered.

And before you can decide whether or not a new drug application is required, you have to find out whether it's a

new drug. And it seems to us rather incongruous to suggest that Congress, which attempted to strengthen FDA's authority in the 1962 amendments, intended to deny to FDA this kind of authority to determine its own jurisdiction, that agencies traditionally have.

MR. CHIEF JUSTICE BURGER: Thank you, Mr. Friedman.

Mr. Szuch.

ORAL ARGUMENT OF CLYDE A. SZUCH, ESQ.,

ON BEHALF OF CIBA CORPORATION

MR. SZUCH: Mr. Chief Justice, and may it please the Court:

The government continues to refer to a threshold issue in connection with approvals of the new drug applications.

In order for there to be a threshold issue, something must be decided.

It would be our position that in connection with the prosecutions and filings of new drug applications, there is, in fact, no threshold issue, because there is no jurisdictional issue for the Food and Drug Administration to decide.

QUESTION: Then you agree that the district court would have a de novo proceeding to resolve these questions?

MR. SZUCH: We would take the position that the issue of new drug/old drug only comes about in connection with

actions of enforcement, such as seizures, prosecutions, criminal natures, or injunctions brought by the Food and Drug Administration after it has included, independent of a new drug application, that the product out there on the market is in fact a new product within the meaning of Section 201(p) as opposed to Section 505 of the Act.

If one looks at Section 505 and one examines what actually happens, I believe that the threshold issue will disappear.

When a manufacturer has a drug which it wishes to market, it has the initial obligation of determining whether the drug is new or old.

If he decides, or it decides that the drug is in fact a new drug, it then goes to the administration and files a new drug application, seeking approval of that application. Once the new drug application has been presented to the administration, there is no longer any issue before it as to whether that drug is a new or an old drug. The manufacturer says nothing in its application to the Food and Drug Administration on that issue. The statute calls for nothing on that issue.

The matter is put before the authority, it decides, and then we're off.

Taking the other situation of the withdrawal, the fact that the drug is new or old is irrelevant to whether the

Food and Drug should withdraw its approval of the NDA which may be filed.

For example, even if one were to assume and concede, the government and the manufacturer, that the drug were an old drug, if the manufacturer were not filing the requisite reports required by 505, it seems mandatory that approval of the new drug application be withdrawn for that reason.

There does not seem to be any option in the statute, we would submit, which would authorize the Administrator to decide that he's not going to act in this particular instance, to not withdraw because the drug is old.

Similarly, there --

QUESTION: But that has been done, he has done it, hasn't he?

MR. SZUCH: Well, --

QUESTION: Don't I remember reading that in the briefs?

MR. SZUCH: -- he may do it, but the fact --

QUESTION: And he has done it?

MR. SZUCH: And he has done it.

QUESTION: Yes.

MR. SZUCH: But the fact he has done it does not mean that the statute would permit him --

QUESTION: No.

MR. SZUCH: -- to do it, we would suggest, Mr.

Justice.

QUESTION: But it doesn't mean, either, that the mere fact of an application waives any right on the part of the applicant, or concedes that it is a new drug, either, does it?

MR. SZUCH: No, it does not.

QUESTION: Yes.

MR.SZUCH: Because a manufacturer with an old drug may choose to file a new drug application with the authority, to get the comfort of the approval of the --

QUESTION: To say, We're filing this for a ruling that this is not a new drug?

MR. SZUCH: No, would file this for a ruling that the material -- for approval of the new drug application.

QUESTION: Yes.

MR. SZUCH: Which would not involve the issue of whether the drug were new or not new.

QUESTION: Or not new. But I'd understood from -- this is a mass of material, I must say, --

MR. SZUCH: There is a mass.

QUESTION: Sorry the weather wasn't a little worse over the weekend, because I'd have stayed inside the whole weekend.

[Laughter.]

I thought I remembered reading in here that sometimes the administration had said, This is not a new drug; you don't

need to --

MR. SZUCH: Well, --

QUESTION: Hasn't that been its response?

MR. SZUCH: Well, if you go to them, they are prepared, apparently, to give you an advisory opinion on whether you have an old drug or a new drug.

QUESTION: That's what I understood. And they have done so?

MR. SZUCH: And they have done so.

On the other hand, if a manufacturer simply comes in with a new drug application and lays it down and says, I want approval of this, then, whether it's new or old, has in effect been determined by the manufacturer, and in that approval procedure he puts nothing forward on the issue, as I understand it, the Food and Drug Administration has never requested any information on that subject in connection with the approval process.

QUESTION: On the issue of whether or not it's a new drug.

MR. SZUCH: New or old drug.

QUESTION: Right.

MR. SZUCH: It is only when the advisory opinion has been sought that that issue seems to have been determined by the government.

QUESTION: I see. Thank you.

MR. SZUCH: Therefore, we would submit that to discuss threshold is wrong. 505 does not in any way involve the issue of whether the drug is new or old. The approval of a new drug application, we submit, has to be approved or disapproved, whether the drug involved is new or old.

On the other hand, once a manufacturer puts into commerce his product and there is not an approved new drug application on file for that product, the FDA may decide for itself that the product is in fact a new product. This decision would be under Section 201(p) of the statute, which defines whether a product is a new or an old drug.

Now, here, under 201(p), proof is required that there is not general recognition among experts that the product is safe and effective. If that proof does not exist, the product is new.

The government suggests that it's incongruous that there be two different schemes and two different approaches to this issue. We would submit, however, that there is logic to this dual route on this issue.

No. 1, the statute doesn't put this issue before the government under 505.

No. 2, the 201(p) test applies to a limited number of drugs, those that were being marketed between '38 and '62.

Now, as to those drugs, Congress could well have concluded that the field of expertise present in the people

out in the countryside, working with the products that were out there every day, that there were experts comparable to the kinds of experts that the administration could find in their own administrative proceedings. And we would suggest that it was concluded that the field of expertise was not exclusive to the agency, we're not dealing with products or items that are peculiar to an agency's expertise. After all, this is medicine. Worldly expertise on that subject is not vested in the FDA; there's a vast reservoir, a storehouse of knowledge in this area in the hospitals, in the colleges and universities.

And we would submit that Congress, in effect, said that if those people that are out there working with the products, not the lay people but people who are expert in their field, if those people concluded that this product was generally recognized as safe and effective, then that product could be marketed, and that a manufacturer need not go before FDA and produce reams of evidence on useless issues.

QUESTION: Is there any other regulatory scheme, Mr. Szuch, that functions on that kind of structure, that you can suggest?

MR. SZUCH: No, I cannot, because essentially, I think that the structure here is peculiar because of the subject matter with which we're dealing. SEC, Labor Board, and agencies of that type are dealing with statutory problems, statutorily created agencies; they're dealing with statutory

problems that have gained expertise and knowledge over the years in a limited area. Medicine was being practiced long before we decided we ought to have an FDA or government regulation.

For that reason, I think it is different, and I don't believe there is a counterpart to it in any other agency.

QUESTION: Well, do you think that squares with the 1962 purposes underlying the 1962 amendments?

MR. SZUCH: Yes, I do. Because I don't think that the 1962 amendments, Mr. Chief Justice, change the procedure with respect to how the FDA processed new drug applications, other than to add the one issue of efficacy. But the procedural mechanisms of how the inquiry by the FDA began is identical pre-'62 as post-'62. Pre-'62 it only involved the issue of safety, but it was the manufacturer that triggered the process of the NDA by coming in and asking for approval of it. Post-'62, the situation procedurally is exactly the same.

QUESTION: Well, I've seen various figures, some of them in here and some elsewhere, about the number, the estimated number of drugs on the market today as compared with 30 or 40 years ago, and it's an enormous multiplier, isn't it?

MR. SZUCH: It is that.

QUESTION: Yes.

MR. SZUCH: It has gone up dramatically for all kinds of reasons.

But the fact that the number of drugs has gone up, I would submit, does not negate the fact that there are people who are just as equipped to determine whether a drug is safe and effective under the 201(p) standard as the NAS people were under the substantial evidence of efficacy standard in 505.

QUESTION: That's something of a self-regulatory system in effect, then, you're suggesting?

MR. SZUCH: No, not exactly. Because under the 201(p) standard, where you must establish general recognition of safety and efficacy. It is still incumbent upon a manufacturer to produce evidence through experts, recognized experts, presumably, to testify to the proposition that this particular product is safe and effective.

QUESTION: Well, when you say testify, you mean testify in the traditional sense, or to give a testimonial?

MR. SZUCH: No, no, no, no. We are not talking about the so-called anecdotal evidence.

QUESTION: I just wanted to be sure we sorted those two out.

MR. SZUCH: Right. I think the anecdotal evidence would be on a totally different plane, as I would understand it; it's either the local pharmacist, the local patient, or a

particular doctor who is not qualified -- qualified generally, but not qualified particularly, from an expert point of view, to testify. It is not that type of evidence that 201(p) is looking for under the test.

In 201(p), as set forth at page 475 of the Joint Appendix, it says that the experts must be qualified "by scientific training and experience to evaluate the safety and effectiveness of the drugs, as safe and effective for use under the conditions prescribed."

So that it is incumbent to produce people with this high level of skill which we would submit will result in no lesser consideration of whether the drug is in fact safe or effective than the standard which is found under 505. It is just an alternate method of arriving at the same result, if you would.

I'd like to turn over any further questions from the Court, the balance of this argument, to Mr. Townes.

MR. CHIEF JUSTICE BURGER: Mr. Townes.

ORAL ARGUMENT OF GEORGE P. TOWNES, ESQ.,

ON BEHALF OF BENTEX PHARMACEUTICALS, INC., ET AL.

MR. TOWNES: Mr. Chief Justice, and may it please the Court:

First, regarding our products. They are not me-too products, we have contended throughout; and that issue is not before you.

The issue before you in our case is whether the question, whether our products are old drugs, and when I use the term "old drug", I include a drug which may currently be generally recognized both as safe and effective, and drugs which enjoy the grandfather provisions. As to whether that determination can validly be made by the Food and Drug Administration in some sort of administrative procedure, or whether Congress designated that determination in an appropriate case to be made solely by the federal judiciary, starting with an action in the district court.

QUESTION: The term "old", the phrase "old drug" is not in the statute, is it?

MR. TOWNES: No, sir, it is not. It's used in the trade --

QUESTION: I mean, the question is whether or not these are new drugs, and that is what's in the statute, and that's kind of a term of art, is it not?

MR. TOWNES: The term "old" --

QUESTION: So we can't talk loosely about old drugs and new drugs in the generic, familiar meaning of those words; but the question here is whether or not this is a, quote, "new drug", unquote, within the meaning of the statute.

MR. TOWNES: Yes, sir.

QUESTION: And the phrase "old drug" is not in the

statute anywhere, is it?

MR. TOWNES: It is not.

QUESTION: Right. Thank you.

MR. TOWNES: Now, let me illustrate the great difference that is involved in determining whether a drug is new and determining whether a new drug application should be approved.

If my clients had sat back and awaited enforcement proceedings in a district court, as they had the right to do, it would have been incumbent on the government, as prosecutor against them for selling an unapproved new drug, to prove that the drug was in fact new. Now, under the definition and under a number of court decisions, the most widely respected being the "Quick-O-Ver" case, which is also a very entertaining case to read, the government would produce two or three or four qualified experts, typically chairmen of a particular medical department, well-recognized specialists.

They would be placed on the stand and asked, after their qualifications were illustrated, to what extent were they familiar with the reputation among qualified experts in this field as to the safety of this product for the uses that the product is supposed to be for. And they would explain how they kept day-to-day track of the literature, they subscribed to many journals, they went to many symposia, they read many books, they converse with their colleagues, they attended the

meetings, and they were familiar with the reputation.

And then you would ask them, What is that reputation? And he would say, Well, nobody -- most drugs are pretty safe, so let's let this expert say that this is recognized as safe. And then he would be asked, Is it recognized as effective? And he would say, Well, frankly, no, it used to be, a long time ago, a few people thought it did pretty good and tried it, but there never were any good studies of it, and as time went on we realized that it really didn't work; and nobody pays any attention to it now.

Now, that is the government's case, really, in so many words.

The manufacturer, if he is attempting to defend this case, and very, very, very few of these cases either have been defended or will be defended, because the burden on the manufacturer is extremely great.

Once that testimony has been put up against him, he's got to, by his own experts of equal stature really, if you want -- you have to have them of equal stature -- so that for some reason the government experts were mistaken in their estimate of their colleagues' general opinion.

Now, very few of these cases, in fact, arise for that simple reason. It would be rare, and it is rare, that you would not immediately apprciate what the consensus of informed opinion was concerning a product.

The "Quick-O-Ver" case is a case in which the manufacturer did prevail. It was a Virginia case. The man had a headache remedy. He thought "Quick-O-Ver" was a cute name for it. It consisted of aspirin and caffein and a few other things; and it was the government's position that he was in some way representing this to be effective for alcoholism.

And the court said, No, he's just saying a hangover. A hangover is symptoms. And aspirin is effective for a headache; you have a headache when you have a hangover, and so forth and so on.

So, out of a number of variations of this product, the court did feel that in one instance the government was really being too extreme, and that this was safe and effective for that limited use.

Now, that is the type of issue, this flood of litigation is not going to appear, very few cases have been litigated in the past, the industry has always understood this to be a district court issue. And the issue is this reputation of the drug among the scientific community.

Now, granted, in a trial the reputation would be discussed and explored, and Why do your colleagues think it's not working?

But all the court has to pass on is that reputation.

Now, that is an entirely, entirely different issue from the issue of whether a drug in fact has been demonstrated

to be safe and effective under the criteria of Section 505, the new drug application proceeding. That is a scientific question. But, as a matter of fact, under misbranding procedures, for example, Congress itself puts on the court certain burdens of passing on scientific questions.

You are prosecuted for representing this drug to be effective for a particular use; the government must prove it's ineffective, if they are claiming misbranding.

Now, the FDA started out as a police agency -- I say the FDA, its predecessors -- under the 1906 Act. In 1938, Congress said, Well, for new drugs -- for new drugs -- let's require premarketing clearance.

Now, Congress was talking about a new drug, something new. And it came up with the definition which is as good a definition as you can come up with, at that point a new drug was defined as a drug which qualified experts generally did not regard as safe. And it's a difficult definition to apply at times, but I don't see how you can improve on it.

Now, as to everything else in the '38 Act pertaining to this general situation, there were these police powers created. If you ship a new drug without approval, if you misbrand a drug, if you adulterate a drug, the product can be seized in a district court; you can be enjoined in a district court, and you can demand a jury; or you can be prosecuted in a district court.

QUESTION: Would that proceeding affect just the particular drug involved and the particular party before the court, or would it affect all the so-called me-too or piggyback drugs?

MR. TOWNES: It would affect only the drug and the party.

Now, in a seizure action, the marshal goes and takes a quantity of the goods.

QUESTION: It's a typical forfeiture --

MR. TOWNES: Right.

QUESTION: -- like a lot of others. Yes.

MR. TOWNES: And you may or may not choose to defend it. The true owner may by this time be the druggist, the manufacturer may defend it, he may not. An injunction, again, would be addressed towards such persons as may be made parties to the injunction. I conlcude that you can make a number of persons parties other than the manufacturers.

QUESTION: If you could identify all the people who had the comparable material?

MR. TOWNES: Yes, or as many as possible.

Actually, the Food and Drug, I think, knows more than it would admit as to who makes what, because, for a generation now, its inspectors have regularly gone to plants, picked up the labels and everything, I just don't think they've had the opportunity to collate the information as fully as the

new Information Act would allow. But the information is there in the archives somewhere.

QUESTION: But this proceeding that you're talking about is one in which you test out the issue on the general reputation as distinguished from clinical --

MR. TOWNES: From clinical data, yes.

QUESTION: -- testing.

MR. TOWNES: Scientific studies.

QUESTION: Well, which -- I'm trying to sort these two out. You said you bring in people who have used it, who heard about it, who've read about it, this is what might be called the general reputation in the scientific medical community.

MR. TOWNES: Yes, sir.

QUESTION: Relating to this material.

MR. TOWNES: Yes.

QUESTION: Now, is that something that's different from the controlled clinical laboratory testing process?

MR. TOWNES: Yes,sir, it is entirely different.

QUESTION: And you don't think that second, that is, the controlled clinical or laboratory approach is involved in this district court approach?

MR. TOWNES: Not at all. If I may be so bold, I not only don't think it is, but we have a number of cases of this type, not a declaratory judgment, -- this is an inverse

seizure action, or an inverse injunction action. Instead of waiting for them to come for us, I think, as a public service, if we take the position that we are right, we bound together, we got twenty people in one suit, we're saying, You say you are [we] doing wrong, we're not going to wait for you to come after us, we want to find out right now.

And we should not -- jurisdiction should not depend on whether we wait for our product to be seized, or we wait to be prosecuted; jurisdiction should be the same, whether the action is for declaratory judgment on these issues or whether it's an enforcement action. There can't be any difference.

If there is a difference, there is a penalty, in effect, to the bringing of a declaratory judgment action, which this should never be.

QUESTION: Does the Food and Drug Administration have any authority to issue a cease and desist order?

MR. TOWNES: No, sir; not as such. They write you letters that in their opinion you're doing wrong.

Now, the ordinary response is that you quit doing wrong. If you have a violent disagreement with them, and feel that the matter is capable of litigation, then you await their seizure, you await their injunction, or you bring a declaratory judgment action.

QUESTION: All of those proceedings are in the district court?

MR. TOWNES: Those are all district court proceedings.

But the issues are so different in a new drug application. You are supposed -- every criteria relates to the results of scientific tests, and in the question of whether a drug is new or old, you're talking about Professor So-and-so, Yes, I am familiar with aspirin, I know its reputation in the scientific world, I've read volumes about it, I've discussed it, and everyone in the scientific community, in my opinion, recognizes aspirin to be safe for this purpose.

On the other hand, I'm further familiar with acne remedies, to use the gentleman's example, and I'm familiar with aspirin; and in my opinion no one in the scientific community recognizes aspirin to be effective for acne.

So, the resulting holding by the court is that aspirin is generally recognized as safe for the treatment of acne, aspirin is not generally recognized as effective for the treatment of acne.

QUESTION: But don't you agree that the '62 Act was to strengthen FDA?

MR. TOWNES: The '62 Act made no change as to jurisdiction; absolutely none. It said, from now on new drug applications must contain evidence of effectiveness.

QUESTION: But it did change the procedure by putting in specifically what they meant by the evidence.

MR. TOWNES: They changed what they meant by

evidence of effectiveness, as relates to the criterion in a new drug application. They added effectiveness, they added the criteria of effectiveness.

Now, let me point out what those criteria -- those criteria are quite interesting.

QUESTION: Well, they're the opposite of what you have in the district court.

MR. TOWNES: They're the opposite in more senses than one, Mr. Justice. Congress was concerned that a drug like Jenner's vaccine or penicillin in its early days might be generally effective but repudiated by the medical community, which does have its academic biases.

So what it said was, If you can produce proper tests which will lead a competent observer to come to a -- I forget the exact phrase; but a proper conclusion that this is effective, then everybody may disagree with it, the scientific community may not reach the results he reached, but if in good faith he could reach these results, the drug should be allowed to be marketed.

So, actually, the substantial evidence test, in many senses of the word, is an expansion of the right of innovation and experiment.

QUESTION: But in the district court could you use the same criteria?

MR. TOWNES: No, sir; in the district court the

question is: Do experts generally, in the field --

QUESTION: Well, that's where I'm confused. You say that you want to go to the district court --

MR. TOWNES: Yes, sir.

QUESTION: -- but couldn't you do better with the FDA under those rules?

MR. TOWNES: Well, you've got two problems, Mr. Justice: One is that these are not the people, my clients are not the people that developed these products originally.

QUESTION: I see.

MR. TOWNES: While they have conducted certain little tests of their own, they are not tests adequate to meet these standards.

QUESTION: I see.

MR. TOWNES: Now, if we can show that the community generally recognizes this product to be both safe and effective, then our whole task is much simplified.

Now, this general-reputation proof is both a terrible burden, in the sense that you've got to get qualified academic people to say, Yes, everybody knows this drug, it's good, it works, this is the way it's regarded. If you can get that, which is a terrific burden, then the method of proof is very simple. You pull in your three witnesses, they testify for a morning or so, and you do not have to go through all these elaborate testing procedures and so forth, because

the community accepts the drug.

QUESTION: Mr. Townes, let me go back to that illustration which you've both accepted, about aspirin being a cure for acne; this is a new claim that's made?

MR. TOWNES: Yes, sir.

QUESTION: Now, is it your position that this can be tested out only in the district court in the first instance?

MR. TOWNES: Well, sir, if I were to start advertising aspirin for sale for acne today, and I would be prosecuted for having a new drug without application; if I resisted, it would be tried in the district court. But if I wanted to get it approved, I'd have to go through the new drug approval method.

QUESTION: But the FDA cannot, to use the term used here, have assertial authority to say, No,you can't, that claim is patently invalid and you can't market it?

MR. TOWNES: They have the prosecutorial authority --

QUESTION: Yes.

MR. TOWNES: -- to do so.

QUESTION: But that takes them into the district court route?

MR. TOWNES: Correct.

QUESTION: Yes.

REBUTTAL ARGUMENT OF DANIEL M. FRIEDMAN, ESQ.,

ON BEHALF OF THE GOVERNMENT PARTIES

MR. FRIEDMAN: Mr. Chief Justice, may it please the Court:

I just would like to say two things briefly in rebuttal:

First, in response to a colloquy that Justice Stewart had with Mr. Szuch, the FDA on many occasions has sent back applications that have been filed for new drugs on the ground that nobody -- that it was not needed, i.e., that it wasn't a new drug.

Secondly, I just want to stress the -- it seems to us that the anomaly of the respondents' position here is well illustrated by the facts of the CIBA case itself.

The reason Food and Drug initiated a withdrawal proceeding in the CIBA case was because it had reason to believe that CIBA's drug was ineffective and it wanted to stop CIBA from marketing that. It held a full proceeding, it concluded that CIBA's drug was ineffective; it withdrew the NDA, and that action was upheld by the Court of Appeals.

Now, under this theory that Food and Drug has no authority to determine the new drug status, this whole proceeding would amount to basically a nullity, because CIBA now claims it can turn around and relitigate under the new drug standard in the district court the question whether or

not it's able to market it at all.

QUESTION: But in the meantime it could be prosecuted, even by a confession?

MR. FRIEDMAN: It could be prosecuted, Mr. Justice, but again I come back to the fact that --

QUESTION: Well, it could be a seizure, I suppose --

MR. FRIEDMAN: It could be a seizure.

QUESTION: -- even by its own confession.

MR. FRIEDMAN: But I come back to the fact, once again, that that is just not a practical method of dealing with this large number of drugs that we have. You just cannot accomplish the congressional purpose of getting these ineffective drugs off the market. The only thing that Food and Drug can do is, when it finds one that it thinks is ineffective, is to bring a suit in the district court to enjoin them, to seize the drug, or to prosecute them criminally.

QUESTION: Mr. Friedman, is appellate review of the action of the FDA based on some section of the Food and Drug Act or on the Administrative Procedure Act?

MR. FRIEDMAN: It depends on the type of action. If it's the action in either denying a new drug application or withdrawing an effective NDA, that would be under Section 505(h) which permits court review in the Court of Appeals, which is the route, of course, CIBA followed. If it's a determination by the Food and Drug Administration for a

declaratory judgment, that will be reviewable, we think, in the district court under the Administrative Procedure Act.

Mr. Frey will now continue the argument.

MR. CHIEF JUSTICE BURGER: Mr. Frey.

ORAL ARGUMENT OF ANDREW L. FREY, ESQ.,

ON BEHALF OF THE GOVERNMENT IN RE

HYNSON, WESTCOTT AND DUNNING

MR. FREY: Mr. Chief Justice, and may it please the Court:

The Hynson cases, No. 394 and 414, are here on writ of certiorari to review a judgment of the Fourth Circuit, holding that the Commissioner acted improperly in withdrawing approval for Hynson's product Lutrexin without a hearing.

Lutrexin is a drug product whose active ingredient, lututrin, is an extract from sow ovaries. It's offered for the treatment of dysmenorrhea, threatened and habitual abortion, and to prevent premature labor.

Hynson filed a new drug application for Lutrexin in 1953, at which time safety was the sole criterion for evaluation of such applications. The agency allowed the application to go into effect, although it wrote Hynson, advising it at that time that the study submitted did not indicate that the drug was effective for these purposes, and urging him not to market it, particularly for threatened and habitual abortion.

Now, after the 1962 amendments, Lutrexin was reviewed by the National Academy of Sciences, which concluded -- the panel concluded that Hynson's claims for Lutrexin were inappropriate and unwarranted in the absence of adequate scientific studies to support them. Lutrexin was rated possibly effective, which was a rating that specifically means that the panel found there was a lack of substantial evidence supporting Lutrexin's effectiveness.

After receiving the National Academy of Sciences' rating and making his own review of the information before him, and giving Hynson the opportunity to submit further information, the Commissioner tentatively concluded that there was no substantial evidence of the effectiveness of Lutrexin, and in March 1969 published a notice of his intent to withdraw approval for Lutrexin's new drug application.

He offered an opportunity for hearing, which Lutrexin at that time -- Hynson at that time accepted.

Then in August 1969 Hynson filed suit in the district court seeking to block further proceedings before the agency. A yeat later this suit was dismissed on primary jurisdiction and exhaustion grounds, and Hynson was remitted to the agency.

In the meanwhile, FDA had adopted the regulations which Mr. Friedman described to you, carefully defining what kinds of studies would be considered adequate and well-controlled, so that they could qualify as substantial evidence

of effective under the 1962 amendments.

The regulations further dealt with the question of when a hearing would be made available, and it required the manufacturer in requesting a hearing to submit, and I'm quoting from the regulation as it appears at page 491 of the Appendix, "a well-organized and full-factual analysis of the clinical and other investigational data he is prepared to prove in support of his opposition to the notice of opportunity for a hearing. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. When it clearly appears from the data in the application and from the reasons and factual analysis in the request for the hearing that there is no genuine and substantial issue of fact which precludes the refusal to approve the application or the withdrawal of approval of the applicent, that is, no adequate and well-controlled clinical investigations to support the claims of effectiveness which have been identified, the Commissioner will enter an order on this data, making findings and conclusions on such data."

Now, the Commissioner wrote to Hynson and advised them of the new regulations and asked them to make a new submission in conformity with the requirements of the regulations. Hynson made a further submission, after it had lost the

district court action.

In this submission it made three contentions to the Commissioner, which are here before you in these petition and cross-petition here.

First, it contended that Lutrexin is today generally recognized as both safe and effective and therefore not a new drug and not within the regulatory jurisdiction of the Commissioner.

Secondly, it contended that because Lutrexin was generally recognized as safe in October 1962, it was exempted under Section 107(c)(4) of the 1962 amendments.

Thirdly, it contended that in fact there was substantial evidence to support Lutrexin's claims of effectiveness.

The Commissioner reviewed the material submitted by Hynson, and he rejected, he refused a hearing on all three of these issues.

On review, the Court of Appeals reversed. It purported not to question the validity of the Commissioner's regulations defining what would constitute or qualify as substantial evidence, and not to question the regulations providng for a hearing only when there is a genuine and substantial issue of fact regarding whether such evidence exists.

Nevertheless, it held that the material submitted by Hynson was sufficient to raise a genuine issue as to the

drug's effectiveness. It dismissed the Commissioner's evaluations of the studies, which he had carefully made in his order, noting that while this was perhaps valid, it was the kind of thing that should only be done after a hearing.

QUESTION: Mr. Frey, the Commissioner's regulations dealing with the existence of grounds for summary judgment, do they, as interpreted, exclude only the possibility of an evidentiary hearing in such a situation, or do they also exclude the possibility of oral argument?

MR. FREY: Well, I'm not certain. Normally, the procedure is designed to give the manufacturer a full opportunity to submit any data he has to be considered.

Now, I think that -- well, let me just see.

I'm advised that if there were a request for oral presentation with regard to these matters, it would be heard before the Bureau of Drugs and not by the Commissioner personally. The Bureau of Drugs being an administrative arm which reviews the medical issues involved.

QUESTION: So the manufacturer, then, could have had an oral argument at least before the Bureau of Drugs, --

MR. FREY: I think --

QUESTION: -- although he might have been precluded from offering any evidence?

MR. FREY: That's correct. And in addition, if the manufacturer felt that the Commissioner's order withdrawing

approval of the NDA for Lutrexin was erroneous because he had in fact identified some studies that might qualify as adequate and well-controlled, he could have petitioned for reconsideration and pointed out that the order was defective and there here, indeed, is something that warrants a hearing, which you've overlooked.

QUESTION: But that would have been subsequently discovered evidence, I take it?

MR. FREY: Well, the --

QUESTION: That he had located the evidence in the meanwhile, he couldn't go back in on the same stuff he had before and get any more than he did the first time.

MR. FREY: Well, one of the issues here is the complaint by the industry that somehow maybe the manufacturer doesn't know what it is that the Commissioner is driving at when he is going to withdraw approval of the NDA. Maybe he doesn't know what the Commissioner finds to be wrong, and the Commissioner ought to have the burden of coming forward with some explanation of why he's withdrawing approval. And with respect to that contention, we don't think that has any merit, but certainly by the time he issues his order withdrawing approval he has explained his grounds for finding Hynson's material unacceptable.

And if there is something wrong with those grounds, which I've yet to hear anybody indicate in any concrete terms,

there would be an opportunity to go back to the Commissioner and say, You've made a mistake.

QUESTION: Well, you say you could get oral argument and argue with the Commission as to whether or not the material submitted did comply before the Bureau of Drugs?

MR. FREY: Yes, I think that there were requests.

QUESTION: You could go there and disagree with the Commission that the materials submitted did not meet the threshold requirements?

MR. FREY: That's right, you could --

QUESTION: But your --

MR. FREY: -- but you couldn't persude them.

QUESTION: But your lawyer could go there, whoever would appear, but you could not put in the record an expert's opinion that this material did meet the threshold requirements?

MR. FREY: No, on the contrary, you could certainly bring in anyone who you wanted to. I mean, the FDA --

QUESTION: As I said, put in the record as a matter of evidence, put him on the stand and introduce his evidence.

MR. FREY: Well, I'm not sure that there is a significant difference. I mean, that --

QUESTION: There isn't?

MR. FREY: -- this record contains --

QUESTION: There isn't? You mean -- you could submit,

even though the Commission determines there there is no issue of fact, you could submit -- have a hearing?

MR. FREY: Well, the question is whether or not there is an issue of fact, that is, has Hynson identified investigations that might possibly, conceivably be considered adequate and well-controlled investigations within the meaning of the statute.

Now, you could bring in an expert, a pharmacologist, who designs these investigations and who would say, Look, this is a good investigation because it meets the criteria of the regulation; it has sound experimental compliance.

QUESTION: But you could have submitted that ahead of time in writing?

MR. FREY: Could have submitted that ahead of time in writing or orally --

QUESTION: Well, I didn't understand that, under your submission, that you could, to use my brother White's phrase, put anybody on the stand; you just submit it, don't you?

MR. FREY: Well, that's right. We're not --

QUESTION: Really, there's no evidentiary hearing under your submission.

MR. FREY: This is not an adversary proceeding in that sense. There isn't somebody who is going to grow a manufacturer's --

QUESTION: Well, that's not a hearing, either;

adversary or otherwise. It's the submission, isn't it?

MR. FREY: It's a submission --

QUESTION: In writing.

MR. FREY: -- in writing or orally.

QUESTION: Or oral argument, perhaps, you're now telling us, but --

MR. FREY: Well, but --

QUESTION: But you don't put people on the stand, under your submission, do you?

MR. FREY: No, but you --

QUESTION: That's the point.

MR. FREY: -- but you come into the office, or you come in to meet with the Bureau of Drugs, and you can bring in your experts and have them talk, --

QUESTION: Try to convince whoever is there, whatever bureaucrat is there, that this does -- this does comply with your standards, with the statute's standards.

MR. FREY: That's right.

QUESTION: Well, what are all these people fighting about, then? I mean, I thought they were asking for a hearing of some kind, of some dimension. And what is it they want that you won't give them?

MR. FREY: Well, I think there is a question as to the nature of the hearing that would be conducted,--

QUESTION: There must be.

MR. FREY: -- if you affirmed the Fourth Circuit's --

[Laughter.]

MR. FREY: -- the Fourth Circuit's opinion.

QUESTION: So what is the difference? You say they can submit anything they want to, all the experts they want to, only in writing, though; but if the Commission then says, You haven't submitted anything to create an issue of fact, in our judgment you haven't met the threshold requirements. That's the end of the matter.

MR. FREY: That's the end of the matter. There is, in this case Hynson has simply not submitted anything about which there can be --

QUESTION: Now, what does Hynson want to be able to do in addition to what you want to permit them to do? What do they want to do?

MR. FREY: Well, I think what they have in mind is they want to bring in witnesses and they want the agency to establish an adversary to oppose them, to have their witnesses and cross-examine --

QUESTION: They would like, for example, to be able to talk, like lawyers do, with the other side's witnesses?

MR. FREY: Yes, they would like to have formal proceedings --

QUESTION: Yes, they would like to know: What do you mean? And what's your opinion based on? Things like that.

Like lawyers do. And like parties do, to have their interest determined in an adversary adjudicatory proceeding.

MR. FREY: The difficulty is to get into the nature of the issue. I think that Food and Drug would try to shape a proceeding, assume that there were some issue to be resolved, my understanding of the procedure that they would consider would be to establish a panel of independent, non-agency people to resolve the factual question; that is, prominent scientists who are knowledgeable in the particular area.

And I suppose that there is a problem in the sense that what they're saying, You're not fighting us, you're not putting somebody -- you're not cross-examining our witnesses, and you're not putting somebody on the stand to say what's wrong with our studies. And of course, at this stage of the proceeding, what the Commissioner has done is he's looked at the studies and he's said, Here is a whole bunch of things that are wrong on their face.

QUESTION: What you're saying is that you're doing no more than -- to these people than what courts normally do --

MR. FREY: Every day.

QUESTION: -- to lawyers and parties every day in granting summary judgment.

MR. FREY: Every day.

QUESTION: And except for, in summary judgment you can submit counter affidavits, which you say you can do in

this case, but you can go and argue with the judge.

MR. FREY: Well, there is one --

QUESTION: Can't you? Can't you? You normally go argue with a judge.

MR. FREY: Well, you can argue here with the agency, however; that is, you can present --

QUESTION: To a bureau; you can't argue with the body that finally makes the decision, I guess?

MR. FREY: On the question of whether there should be a hearing?

QUESTION: On the question whether the --

MR. FREY: Well, the regulations say, show us something that we can hold a hearing about.

QUESTION: Yes.

QUESTION: In other words, it's something like a prima facie showing in the conventional sense.

MR. FREY: Some service.

QUESTION: Who do you argue with when you want to tell them, Well, I haven't submitted something enough, but I want to argue -- I want to try to convince you that I have? Orally. You say we forget it --

MR. FREY: Well, this didn't happen in this case. That is, nobody said, We want some more, you're wrong, we have shown adequate and well-controlled investigations, and we want some opportunity to talk to somebody about it. I'm just not

sure, had they said so, whether the Commissioner himself would grant them an opportunity to be heard on that issue.

But I don't think we get anywhere near that in this case, because they haven't come close to raising any kind of issue.

QUESTION: But your whole summary judgment procedure, in accord, although it's premised exactly on the type of reasoning you use, the judge doesn't simply say, I've decided to grant summary judgment in this case. Someone makes a motion for summary judgment, and the parties come in and argue as to whether there is or is not a substantial issue, issue of fact.

MR. FREY: Well, but this is an administrative proceeding, and the Commissioner is not the adversary of this party. I mean, he is not setting out to take these drugs off the market. What he is doing is setting out to enforce the congressional mandate that has been imposed upon him. He has a duty to foster the distribution of useful drugs as well as a duty to take ineffective ones off the market. He is not an adversary in the sense that in a judicial summary judgment proceeding you have parties A and B, who have conflicting interests with one another and who are fighting one another.

Now, here --

QUESTION: As soon as the FDA disagrees with an

applicant, then the applicant views him as an adversary.

MR. FREY: Yes. It's understandable that Hynson would view the Commissioner in some real sense as an adversary, because he has the power to take action which is adverse to their interests.

But it seems to me perfectly reasonable for him to say that statute -- Congress imposed the standard, and it imposed the standard of substantial evidence. This is an objective, scientific standard, and his regulations implement this standard and set out the criteria, and it certainly is reasonable to ask the manufacturer to come in and make some showing of something, anything that could possibly qualify under these regulations and under the statutory standards.

QUESTION: Is there some parallel here, Mr. Frey, possibly between this situation and Section 2255, where a district judge may dispense with a hearing if he finds that it conclusively appears on the face of the record that there's nothing to have a hearing about? Is it something like that?

MR. FREY: No, I don't think I would go that far, because normally in a 2255, the judge has some prior experience, the issues may have been previously litigated before the judge.

QUESTION: But you believe it's practical, that the drug companies have, sometimes at least, filed some papers and some opinions and some records about the merits of this drug.

MR. FREY: Well, they have filed what they have to say

in support of the merits of the drug, and the Commissioner has looked at it.

QUESTION: And you're saying that the Secretary, the FDA can say, There is nothing here on the face of what you have submitted that requires us to have any hearing at all?

MR. FREY: Absolutely. And this is analogous to summary judgment, except that it doesn't have this adversary procedure and therefore -- that is, it doesn't have an active lawyer advocate/adversary, and therefore, in that respect, it's somewhat different from the judicial summary judgment.

But it still, I think, even in the case of a default in a judicial proceeding, if the plaintiff has not, on his face or on the face of the testimony that he might submit, simply doesn't make out a case. The judge will throw him out even though there's no opposition.

QUESTION: So if the Commissioner contrues the Act to say that -- and he's administering it in this way: I'm going to withdraw NDA's unless you people who hold them submit sufficient evidence to me?

MR. FREY: That's what Congress has required him to do.

QUESTION: Yes.

MR. FREY: And he has been told in this case by the National Academy of Sciences that there is no substantial

evidence to support Lutrexin --

QUESTION: What he merely says is that you haven't shown anything to change my mind.

MR. FREY: Well, he's reviewed -- the National Academy of Sciences has reviewed the drug, and they have come up with a conclusion.

QUESTION: And they came up with the conclusion "not effective" or --

MR. FREY: "Possibly" --

QUESTION: -- "possibly effective." "Probably" --

MR. FREY: -- in that case of Lutrexin.

But that means, as we show in our brief, under the instructions that they were given by FDA, that means there is no substantial evidence, no adequate and well-controlled --

QUESTION: What is the difference between that or "possibly effective"?

MR. FREY: "Possibly effective" means that if they were to conduct scientific tests, it's the clinical judgment of the people on the panel that "possibly" these tests would show the drug to be effective. And "probably effective", it's their judgment that if scientific tests were conducted, they "probably" would show it to be effective.

But it's based on their general experience and not on the kind of evidence the Congress required.

QUESTION: Thank you.

QUESTION: My only quarrel is that you keep saying that this person who makes the decision is so unbiased, et cetera, et cetera. He's already made up his mind, hasn't he?

MR. FREY: Well, he's made up his mind in the sense that the FTC, when it issues a complaint, for instance, has made up its mind that there may have been violations.

QUESTION: I'm not talking about any place else, I'm talking about this one. He has made up his mind, and your burden is to give him something that --

MR. FREY: He's made up his mind that the evidence --

QUESTION: Well, let me finish.

MR. FREY: Yes, sir.

QUESTION: And the burden on you is to show something that will make his mind be neutral.

MR. FREY: No, not at all. The --

QUESTION: Isn't that really what it is?

MR. FREY: No, because the inquiry is: Does there exist a certain kind of evidence? This is an objective question. He looks in his files, he gets his recommendation from the National Academy of Sciences, and he says, So far I haven't seen anything --

QUESTION: And then you produce something, and he might say, Ahhh, I might have made a mistake.

MR. FREY: Well, there are --

QUESTION: Is that right?

MR. FREY: Yes, absolutely. In fact, there are 56 cases so far of new drug applications where he had proposed to withdraw, they had been rated less than effective by the NAS panel --

QUESTION: Well, I would assume that this one is not in that category; this one is --

MR. FREY: In those fifty- --

QUESTION: This is the one where it's 50/60 or 50/40, or something like that; this is a close one.

MR. FREY: This one? It's not --

QUESTION: No, no, I'm talking about if there is a close one and you're up against a man who has made up his mind, you've got a problem.

MR. FREY: No.

QUESTION: You don't agree with that?

MR. FREY: If you submit a study, there are objective criteria for evaluating --

QUESTION: Well, if I've got a real close case, I wouldn't want the burden of convincing the man that he was wrong.

MR. FREY: Well, he has not made up his mind that the drug is ineffective. All that he has concluded is that so far he hasn't been shown adequate and well-controlled clinical investigations.

Now, that may mean that there's nothing in the file. Now, if the manufactuer comes forward with a study, he'll look at that study and he'll match it against the requirements of the regulations, and if the study meets the requirements of the regulations, he'll act in accordance with the study. I think this is a completely -- this notion that he is somehow biased and out to drive these people off the market is a completely fictitious element that's been injected in this case.

QUESTION: Does he match it against the regulations or against the statute?

MR. FREY: Well, the regulations -- the statute simply says adequate and well-controlled investigations including clinical investigations.

QUESTION: Right.

MR. FREY: The regulations augment that by incorporating a scientifically recognized body of principles; --

QUESTION: Yes.

MR. FREY: -- and in our brief in 414, in the appendices, we have indicated what some of these principles are in more detail.

QUESTION: With some of these drugs, indeed with this one, how responsible is it to carry on controlled investigations and to use placebos for people who are -- in the circumstances?

MR. FREY: Well, there is a suggestion that has been made on the other side, and in fact the only issue that they have raised of a concrete nature, by the way, of disagreement with the Commissioner's findings, or suggesting that he may have been wrong, that there may be an issue, is this ethical suggestion.

QUESTION: Yes, exactly.

MR. FREY: Our position is that exactly the opposite is true, and that sound ethics absolutely require scientific testing. And this point has been recently and tragically brought home by a drug called di-ethyl-stilbestrol, which is offered for threatened and habitual abortion, premature labor, and was widely used in the past. It was tested in a number of controlled clinical studies and found to be ineffective.

It turned out that 16 years afterpregnant women received this drug, their female offspring contracted vaginal cancer.

There are safety problems with these drugs that FDA simply cannot anticipate, because they only show up in one case in a million, or because they only show up twenty years later. The least, from an ethical standpoint, that can be required is that these drugs be effective for what they're being offered for.

QUESTION: Well, I'm reminded of what was revealed last summer, and it's been pressed since, the experimentation

of -- as I say, using placebos or using nothing with people who had syphilis. Now, how -- don't you run into ethical and moral and difficult philosophical problems if you're going to insist on this kind of experimentation?

MR. FREY: Well, we don't insist on it. For instance, you may have a disease or condition which has a predictable course, in which a great deal is known, and threatened and habitual abortion and premature labor is not in this category, but you may have -- for instance, in somebody had been bitten by a rabid animal, and you want to test the vaccine for rabies, you don't need a controlled experiment; all you need to do is give them your vaccine and if he doesn't die, you know it's effective.

But that's because you know the course of rabies.

MR. CHIEF JUSTICE BURGER: We'll continue with that right after lunch.

[Whereupon, at 12:00 noon, the Court was recessed, to reconvene at 1:00 p.m., the same day.]

AFTERNOON SESSION

[1:00 p.m.]

MR. CHIEF JUSTICE BURGER: Before you go on, Mr. Frey, it may seem to you that we've been asking a lot of questions here and taking up some of the time of counsel; to compensate for that, we'll enlarge the time of each side for ten minutes, and you gentlemen will work out the allocation of that bonus.

ORAL ARGUMENT OF ANDREW L. FREY, ESQ.,

ON BEHALF OF THE GOVERNMENT PARTIES - [Resumed]

MR. FREY: Thank you, Mr. Chief Justice.

Let me go back and try to place some of the problems that seem to be concerning the Court in the context of what FDA's regulatory problem was.

It reviewed these 4,000 or so new drug applications that had been filed between 1938 and 1962, and that were for products that were still being marketed, and the National Academy of Sciences submitted recommendations and reports showing that there were somewhere between 12 and 13 thousand claims that appeared not to be supported by substantial evidence of effectiveness.

Now, if any significant proportion of the manufacturers of drugs making these claims asked for full dress evidentiary hearings, each of which could last two, three, four months, just in order to keep their product on the market until FDA could act, the mission of withdrawing ineffective drugs from the

market would be totally sabotaged; it would simply be impossible for the agency to deal with this.

And I think a question that was asked earlier in the argument, there are 24 lawyers available to enforce the Food and Drug laws; that's court actions and administrative proceedings. That is the size of the general counsel's office at Food and Drug.

Now, the way that the agency responded to this problem, and the reason it was able to respond this way was that there was in the statute an objective standard, which said if you don't have adequate and well-controlled investigations, you can't stay on the market.

So the Commissioner adopted what, in effect, is a screening procedure. He said to the manufacturer: You come to me, you can show me anything that you want, bring me your data, bring me your studies, whatever you have, put that on the administrative record, and if you have something that looks like it could possibly be an adequate and well-controlled investigation supporting the effectiveness claims, then we'll give you a hearing.

If you don't have it --

QUESTION: With regard to this clinical testing, I thought it was a precondition to going on the market.

MR. FREY: It's certainly for a new compound that was newly developed after '62, it would certainly be a pre-

condition for going on the market.

Now, of course, if you're already on the market, the question becomes your right to stay on the market; and as to this, Congress also clearly intended that there would be this kind of clinical testing. That's why they gave the two-year grace period to the manufacturer, so he could do this testing.

QUESTION: Well, do you read 505(d) then, in its definition of substantial evidence, to say that nothing that does not include clinical investigation can be substantial evidence?

MR. FREY: Well, the answer to that is yes. Now, on the issue of historical controls, which has come up in this case, it is possible that you could have an investigation that would be considered adequate and well-controlled within the meaning of the statute, even though it didn't use concurrent controls and placebos and so on. That is, as the regulations indicate, there are circumstances in which what constitutes an adequate and well-controlled investigation may depend in part on what it is that you're investigating.

QUESTION: So it doesn't necessarily have to be clinical investigation, if it meets the other definitions of adequate and well-controlled?

MR. FREY: But it has to be a well-controlled, scientifically sound investigation, and if there is no such investigation, then no parade of doctors, swearing by the

product, can save it.

QUESTION: What is the provision under -- for withdrawing approval, it's (e), subsection (e)?

MR. FREY: Yes. 505(e)(3) in the case of --

QUESTION: Is this what you're proceeding under, 505(e)(3)?

MR. FREY: That's what we're proceeding under against Lutrexin; that's right.

QUESTION: That there is a lack of substantial evidence that the drug will have the effect it purports to have?

MR. FREY: That's correct.

QUESTION: "On the basis of new information before him with respect to such drug, evaluated together with the evidence available to hem when the application was approved, that there is a lack of substantial evidence".

MR. FREY: That means that there must be some substantial evidence, and if there is not some substantial evidence, that the approval must be withdrawn.

QUESTION: Automatically.

MR. FREY: If there's no substantial evidence. If there is no adequate and well-controlled clinical investigation.

QUESTION: As defined. Substantial evidence as defined in 505(d).

MR. FREY: And as augmented —

QUESTION: Augmented by the regulations.

MR. FREY: -- by the regulations.

QUESTION: You say the regulations make clear, do they, that controlled experiment does not necessarily imply a control group in the experiment?

MR. FREY: Does not necessarily imply a concurrent control group. That is, you could use historical controls. If you have a disease, the course of which is so well known, if you have appropriate pairing of the people in the treatment group that you're studying against your historical control group, so that you can exclude the possibility that the difference in results is due to something other than the drug that you're testing.

But you need some scientifically sound way of attributing the results of your test, of your treatment, to the drug that you're testing. And if you don't have that, you simply don't have the kind of evidence that Congress requires.

I'd like to point out, if you would look for a minute at the Appendix, at page 103, none of the materials that Hynson submitted has anybody ever suggested could possibly constitute adequate and well-controlled investigations, except for the Majewski and Jennings studies and the Gratton study. That's three studies.

Now, if you look at the Majewski and Jennings study, which starts at page 99, he sets up to study the ability of Lutrexin to halt contractions, and he comes up with a statistic as to the number of people in whom the contractions were halted. He never compares that with anybody or anything, there is simply no comparison whatsoever. There's obviously no way to tell whether Lutrexin halted the contractions. For all we know from this study, contractions spontaneously halt at the same rate.

That's what I mean by the lack of a controlled, and that's what the Commissioner meant.

Now, if you look at page 103, he had 88 patients in his study group. All 88 of these patients gave birth prematurely, according to this study.

Now, does this study demonstrate that Lutrexin is effective to stop prematurity?

He has no statistical analysis of this Table 4, at the top of 103; no showing that there's any significant difference, statistically different between group II and group I.

He then goes down to Table 5, he compares the 88 patients who were treated with Lutrexin --

QUESTION: Mr. Frey, this sounds to me like -- the kind of analysis you're engaging in sounds to me like it would be a very legitimate type of thing for the Commissioner

to do after a hearing, weighing this test against the other. But I have some doubt as to just excluding it at the threshold.

MR. FREY: Well, the regulations, I think, make it quite clear. It's clear on the face. If you look at this, there is nothing that could be done at a hearing to cure the fact -- for instance, in the Gratton study -- I haven't got time to go into these in detail.

But in the Gratton study, the patients received concomitant medication in addition to Lutrexin.

Now, there is simply nothing that you could do at a hearing to make that study into an adequate and well-controlled investigation.

QUESTION: That's what a lot of lawyers have said right after they've lost cases. Isn't it?

MR. FREY: Well, if -- I believe that if you look at the Commissioner's order, and that if you look at the studies, if you look at this study of Majewski and Jennings, and you compare that against the regulations, I think it is clear that the study does not come close to complying, and that there is simply no way that it could be salvaged or reconstituted.

If this kind of material is sufficient to require the Commissioner to hold an evidentiary hearing, then anything is. Because this is just grossly inadequate. There simply is no way to compare the people who were studied with the prior

experience. You don't know what kind of medical treatment the other people who are being compared had. You don't know whether they had bed rest. You don't know what other drugs they received. You don't, on its face, --

QUESTION: Let me ask you again, what was the other -- what do your opponents want a hearing about, then? To convince somebody of what?

MR. FREY: Well, I think it's not exactly clear. And I think they have not really come forward and said, Look, the Commissioner is wrong because here is the factual issue.

What factual issue?

The only factual issue that they have suggested is whether historical controls are appropriate. And since it's quite clear on the face that even if historical controls were theoretically appropriate, these are not historically controlled studies. And I don't believe that they have suggested that they are historically controlled studied. I'm not clear what the hearing would be about.

Presumably they would put Dr. Majewski and Dr. Gratton on the stand and have them try to explain what they were doing in their studies and what the results were. But if they don't say anything more than they have here --

QUESTION: What did the court think the hearing would be about?

MR. FREY: I don't believe that it made clear in its

opinion what the hearing would be about.

The issue is whether there would be substantial evidence of effectiveness. The Commissioner looked at these studies and he said: On their face, these studies do not conform with the regulations in numerous ways. They don't include concomitant medication; they don't have comparability between the patients. These are things that appear on the face of the study.

There simply -- there is nothing --

QUESTION: Aren't they judgments? Aren't they judgments of -- aren't they sort of ultimate or intermediate judgments of underlying facts?

MR. FREY: Not at all. They are completely objective things that appear on the face of the study. If the doctor says that these people got multivitamins, they got delalutin, they got DES, in addition to getting Lutrexin, that appears on the face of the study. There isn't anything to hold a hearing about.

These patients received concomitant medication, you can't attribute whatever results were obtained to Lutrexin. That's what the regulations say.

QUESTION: But might it not be at least possible that Dr. Majewski, having set up these studies, would have some defense for them?

MR. FREY: I think it's inconceivable. In fact, it's

clear that the Majewski, for instance the '68 Majewski study is not even a study. It's a collection of his experience over the preceding ten years. He went back to his files and pulled together the results that he got in treating patients with Lutrexin.

They had never even set out to be a study, a study has to have an experimental design, a plan, or protocol. It has to have things that are spelled out in the regulations and in the appendix in our brief in 414, these are objective requirements. These studies simply are miles, light years away from meeting these requirements.

I think I, in view of the time, would like to move on to another point, if there are no further questions on this point.

I'd like to turn to the question which was touched upon earlier and which involves the correctness of the Commissioner's denial of a hearing on the question of whether Lutrexin is today generally recognized as safe and effective, and therefore not a new drug, and therefore not subject to this regulatory jurisdiction.

What the Commissioner said was if there is no substantial evidence of effectiveness, if there isn't the kind of scientific evidence that Congress said was required, then these qualified experts, that Section 201(p) talks about, couldn't possibly arrive at the conclusion that the drug is

effective. They could not have that general recognition of effectiveness, because it would be based on the precise kind of unscientific clinical impressions, uncontrolled studies, the very kind of thing that Congress had been told was an unreliable basis for evaluating drug effectiveness.

Congress had the foremost experts in the country before it, and they were uniform in their testimony that you need controlled tests, you need scientifically sound evaluation; and Congress heeded their advice. And Congress enacted in the statute a specific requirement of adequate and well-controlled investigations, a concrete objective requirement.

Now, it simply seems to us totally irrational to suppose that after Congress went to all the trouble of adopting this standard and rejecting these kinds of unscientific impressions that people have, because they used the drug a few times and it seemed good to them, and so did their colleagues, that the drug should turn around and be able to stay on the market, that is, the Commissioner has evaluated, he's found it wanting; the drug doesn't have scientifically sound evidence of effectiveness.

Now the manufacturer turns around and says, Well, that's very interesting, that's fine, I'm going to go ahead and market it anyway, and I can produce 10 or 15 doctors who will tell you that they think it's effective on the basis of their uncontrolled, unscientific experience.

If there are no further questions, I'll sit down.

MR. CHIEF JUSTICE BURGER: Is Mr. Williams on next?

Mr. Williams.

ORAL ARGUMENT OF EDWARD BROWN WILLIAMS, ESQ.,

ON BEHALF OF HYNSON, WESTCOTT & DUNNING, INC.

MR. WILLIAMS: Mr. Chief Justice, may it please the Court:

I've heard so much, I don't know where to begin.

There's been a good deal of talk about the NAS/NRC report, this National Research Council report, which evaluated a number of drugs for the Food and Drug Administration. The conclusions of those panels were, in many cases, and certainly in the case of Lutrexin, as the Court of Appeals for the District of Columbia recently said in the USV case, conclusory and cryptic. They certainly were that in the case of Lutrexin.

In fact, out of the 14 studies which we eventually submitted to the Food and Drug Administration, the NAS/NRC, insofar as its report shows, considered only four.

Now, there has been considerable talk about whether the issue here is the existence of adequate and well-controlled studies.

QUESTION: Could I ask you first, is it your understanding of (e)(3) that the Commissioner is authorized to set aside an NDA if there's a lack of substantial evidence of

effectiveness and safety, and that he may put the burden on you to submit evidence, to submit that substantial evidence?

MR. WILLIAMS: No, sir. May I --

QUESTION: What do you say, No, that is not your understanding?

MR. WILLIAMS: No. No. May I approach it this way: The issue is not, as has been suggested in the withdrawal proceeding under that section which you cited, whether there are adequate and well-controlled studies, that is, substantial evidence to support the effectiveness of the drug.

The issue is, under these regulations which are alleged by FDA to follow the summary judgment procedure of the Rules of Civil Procedure, whether under those regulations there is a material, an issue of material fact raised by the evidence before the Commissioner.

QUESTION: Well, let me put it to you this way: Let's assume that the Commissioner does give you a hearing. He asks you to submit evidence, he says, I think that is a question about this drug, and he ask you to submit evidence and you submit none, for example. May he then withdraw the NDA without making any finding other than that there is a failure to produce any evidence?

MR. WILLIAMS: It is our view, sir, that under the summary judgment practice, in other agencies as well as in the courts, that he must at least put forth prima facie evidence

to show that he's got a basis for saying --

QUESTION: So he must -- you think he's got the burden of going forward with some evidence --

MR. WILLIAMS: We do.

QUESTION: -- and the burden of proof?

MR. WILLIAMS: We do. And we've argued it extensively in our briefs.

QUESTION: Well, that's a little bit in conflict, isn't it, with the idea that Congress has very broad power to set up hurdles to any drug getting on the market; is it not?

MR. WILLIAMS: I don't see why the necessity of showing there is no issue of material fact before the Commissioner is fertile --

QUESTION: Well, if I understood your response correctly, Mr. Williams, it was that you have a drug on the market, and this question arises, and you say that you need bear no burden at all in response to this question, this issue being raised, and if you default in traditional terms, the FDA must assume the role that a plaintiff assumes in default case and prove something?

MR. WILLIAMS: It must assume the same rule under its own regulations, which --

QUESTION: What specific regulation do you rely on?

MR. WILLIAMS: I'm talking here about the May 1970 regulation, which has been discussed this morning, --

QUESTION: Where do we find that specific one?

MR. WILLIAMS: -- which defines substantial evidence and the right to a hearing.

QUESTION: Where do we find that, at what page?

MR. WILLIAMS: Well, that's Section 130.12 and .14 of the 21 C.F.R., and it's at the very back of the Appendix, on page 487 and following.

QUESTION: Well, let me ask you this: Let's suppose he gives you this notice and says, please submit evidence; and you submit evidence, and he says there's a question, now let's have a hearing -- that you do submit and he thinks there's a question, so you have a hearing.

Now, if that hearing -- well, you have the hearing. And he then revokes the NDA; what must he find?

Must he find only that there's a lack of substantial evidence of effectiveness?

MR. WILLIAMS: That is correct, but he must produce some kind of evidence to --

QUESTION: But he needn't conclude that the drug is ineffective?

MR. WILLIAMS: No. Wait a minute now. Lack of substantial evidence of effectiveness is the equivalent of ineffectiveness in this context. This particular context.

QUESTION: And you think -- and at the hearing you would think that he carries the burden of going -- if you have

a hearing, that he puts on evidence first, if you're going to have an evidentiary hearing?

MR. WILLIAMS: He has always had the burden, and I don't see that it's changed here. He wouldn't have to put on much if we submitted very fragile materials, obviously.

QUESTION: But wouldn't the report of the board or that -- the scientific commission, about Lutrexin, for example, if he just says, Here is what I have, here is the report I have. Would that be a prima facie case for him, as far as you're concerned?

MR. WILLIAMS: It might in some cases, but in the case of Lutrexin they didn't even consider all the materials.

Now, we of course must deny, and do so at length in our briefs, that there were not historical controls used by Dr. Majewski and Dr. Gratton in their four studies. We consider them historical controls. Our briefs analyzed and attempted to show that they are. And as for their not having concomitant medication necessarily excluded, naturally they were.

But Dr. Gratton, who did use concomitant medication, found that with that concomitant medication without Lutrexin he lost far more babies than with Lutrexin. Therefore, he concluded, Lutrexin had some effect because he was using as controls patients whom he knew were at attendance at the premature labor or were in premature labor or had previously

aborted or had previously gone through premature labor.

So that we must look at these things directly, and in that connection I should like to refer to the government's reply brief, on page 29, in footnotes 33 and 34, it cites reports by Hinsworth and Deakman as examples of adequate and well-controlled studies of a drug used to treat cases of threatened and habitual abortion.

QUESTION: What page is that?

MR. WILLIAMS: Page 29.

These studies are alleged to stand in stark contrast to the supposedly uncontrolled studies of Hynson, Westcott and Dunning.

It is significant to note,however, that the studies cited by the government suffer from many of the alleged defects the Commissioner referred to in his order withdrawing approval of the new drug application of Lutrexin; namely, in the first place, in neither study, the Hinsworth or Deakman study is the use of concomitant medication ruled out. That was a complaint of the Commissioner against the Majewski and Gratton studies.

Secondly, certain patients were excluded from these studies which are heralded by the government without specific explanation. Again, a repeat of the Commissioner's complaint in the Hynson matter.

Third, patients with medical complications were

included in the studies. The same.

In the Deakman paper there was no method for determining how many tablets of the drug under investigation the patient took per day or per week. Another complaint of the Commissioner against the Hynson studies.

Five, in the Hinsworth study, which was conducted by the unidentified staff of nine different hospitals, the Majewski studies submitted by Hynson -- just as in the Majewski studies, the historical instance of abortion in the Deakman study, and premature deliveries in the hospital involved was compared with the incidence of such complication among patients under study.

QUESTION: Is it true, Mr. Williams --

MR. WILLIAMS: In other words, they're doing the same thing, which they say is bad.

QUESTION: Is it true that Dr. Majewski, or whatever his name, he didn't make a study but just went back in his files?

MR. WILLIAMS: No, sir.

QUESTION: Well, show me where --

MR. WILLIAMS: No, he selected physicians who had premature labor or abortion cases.

QUESTION: Other physicians?

MR. WILLIAMS: Other physicians, yes. Just as Deakman did.

QUESTION: Were they making a study?

MR. WILLIAMS: They made a study according to his instruction.

QUESTION: Sort of a nunc pro tunc study?

MR. WILLIAMS: No, according to his instructions.

QUESTION: Well, the study was a study of their files of past cases.

MR. WILLIAMS: No. His study was a study of their files on the cases which he had asked them to make records on, so he could make the study.

QUESTION: How long did he work on this study?

MR. WILLIAMS: There were three of them, and I'm sorry, I can't remember.

QUESTION: Mr. Williams, part of your complaint here is that were denied certain procedural rights before the Commission that you thought you ought to have?

MR. WILLIAMS: We were denied a hearing.

QUESTION: What would you have sought to show at the hearing, had you been accorded it?

MR. WILLIAMS: We would have sought to show that the historical controls used by these people were valid, and that they constituted adequate and well-controlled studies in the sense of the Food and Drug regulations.

QUESTION: When you say a hearing, do you mean an opportunity to put these witnesses on the stand?

MR. WILLIAMS: Yes, sir.

QUESTION: And do you also mean, or alternatively mean, an opportunity to orally argue your contentions about your written submissions before the Administrator?

MR. WILLIAMS: Well, Food and Drug hearings don't ordinarily include oral arguments, per se; but written submissions after the evidence has been submitted. But we would, of course, expect also to be able to cross-examine the government witnesses. That's essential.

QUESTION: Well, but not -- there have been cases from this Court, and I think one of the most recent was United States vs. Florida East Coast Railroad, that certainly intimate that you don't necessarily have the right to cross-examine government staff agency personnel. Now, this was in --

MR. WILLIAMS: Whatever witnesses they put on. I wouldn't expect to cross-examine anybody who wasn't put on as a witness.

QUESTION: But you would --

MR. WILLIAMS: We would not have the subpoena power under the present statute.

QUESTION: Right.

QUESTION: But if the government were relying, for example, on some conclusions of a -- of some outside specialist, you would want to --

MR. WILLIAMS: We'd like to tear into it.

QUESTION: Yes.

QUESTION: And would you regard the Academy findings here as being basically analogous to outside specialists, as opposed to staff personnel of the agency?

MR. WILLIAMS: Yes. Then, of course, we had no opportunity to examine them whatsoever.

QUESTION: But you're -- but that would -- your point was substance, only if the statute puts the burden of going forward on the -- and the proof, some kind of a burden on the Administrator rather than upon you to convince him of something?

MR. WILLIAMS: My point about a hearing, you mean?

QUESTION: Yes.

MR. WILLIAMS: Well, I think we'd be entitled to a hearing in any event. And I think I can show that by comparison of the 505(e)(3) provision, the withdrawal provision, with the provision of 505(c) which deals with an application for a new drug approval, where it is specifically said that a hearing must proceed within a certain period after the request, the offer is accepted, unless there is contrary agreement by the parties.

Now, I'd like to just conclude this one point, since so much is made of it. It is also significant to note, in any event, the government studies did not involve, as do

Hynson's, treatment of patients with histories of prior pregnancy, prior pregnancy problems, or patients in imminent danger of premature delivery or abortion; all of the Majewski and Gratton cases did.

They cannot, therefore, -- that is, these submitted by the government in its reply brief at the last minute -- which we had never seen, by the way. They cannot, therefore, be compared with HW&D's investigation, where a high risk of the fetal mortality existed. In such a case, the use of the double-blind placebo type study would be unethical according to Drs. Rezek, Gratton, Majewski and Allen. Allen, the latter -- Allen, being a member of the panel of NAS/NRC, which evaluated Lutrexin.

It was his opinion, stated in a notarized document to us, that Lutrexin should not be taken off the market, that they never had any such intention.

Now, I should think it might help if I listed the issues which I think are in these two cases.

In 72-394, which involves primarily the hearing issue, the questions are: whether Hynson is entitled to a hearing on the question of whether there is substantial evidence of safety and efficacy as distinguished from a hearing on the jurisdictional questions, which I shall refer to.

Secondly, whether the new May 1970 regulations,

which are in the back part of the Appendix, under which a hearing was denied, are valid as applied to FDA by FDA to Lutrexin.

And, finally, whether HW&D, Hynson's, right to a hearing, vested under the former regulations which preceded these, when Hynson accepted the offer of a hearing by letter to the Food and Drug Administration.

In No. 72-414, which is in support of -- in which we filed a brief in support of the cross-petition, the basic question is: whether the Court of Appeals was right in its conclusion that the Commissioner was unauthorized initially to determine his own jurisdiction under Section 201(p), the definition of new drugs.

That is, whether the drug, Lutrexin, is generally recognized as safe and effective under the Act as amended in 1962; whether it was deemed approved under Section 107(c)(2) of the Act. If it was, it is not subject to administrative withdrawal proceedings under Section 505(e).

Three, whether the drug was exempt from the effectiveness requirements of Section 107(c)(4), the so-called grandfather clause. If so, then it is our view that none of the effectiveness provisions of the statute are applicable to that drug.

There has been considerable discussion of the matter of general recognition of safety and effectiveness. And, as I

understand the government's position, and I think I do understand it, they maintain that general recognition of safety and effectiveness, which is the test of new drug status, is dependent upon the existence of substantial evidence of effectiveness as defined in the 1962 amendments in an entirely different section of the statute, not the coverage section in 505(d).

And that, in effect, the substantial evidence definition is a part of Section 201(n), and there is no real difference between a determination of new drug status and a determination of whether the drug is safe and effective.

MR. CHIEF JUSTICE BURGER: Would you keep your voice up a little bit, Mr. Williams.

MR. WILLIAMS: Sorry.

Now, it so happens that 201(n) wasn't even amended when this definition of substantial evidence was placed, written into Section 505(d), the substantial evidence definition.

Section 201(n) -- (p), the definition of new drugs, was amended in 1962 only to include the requirement of effectiveness in the definition of new drugs, not the requirement of substantial evidence of effectiveness.

Section 201(p) is a jurisdictional test which governs the application of Section 505.

QUESTION: What do you say the standard is, the

standard of proof on effectiveness?

MR. WILLIAMS: General recognition of safety and effectiveness among experts. That's specified in the statute.

QUESTION: By that you mean what is called the anecdotal, but the testimony, the testimonials of people who used it?

MR. WILLIAMS: No, I would concede to the government, and to anybody, that evidence of clinical studies published in the literature is relevant on the question of whether there could be general recognition of effectiveness or of safety. But I don't think that's the final test. Some of these drugs which have been on the market for years are obviously generally recognized as safe and effective, and they may or may not have published studies upon which that conclusion was -- by which that conclusion was arrived at.

It is only after a drug is found to be new -- in sum, it is only after a drug is found to be new under section 201(p) that one looks to section 505, to determine what the obligations of its manufacture may be.

I think it's important that distinction be made. It has always been accepted by FDA, and the industry, and FDA changed its view only after,some years after the effective date of the 1962 amendments, which did not even touch that section.

Now, the right to a hearing on the question of substantial evidence. The briefs of the government in these cases place great if not primary emphasis upon the alleged incapacity of FDA to administer Section 505, as amended in 1962. If the anticipated demands for hearings, that is the hearings anticipated by the government, and withdrawal proceedings had to be met by the agency.

We explain, however, in our brief in No. 72-394, beginning at page 33, that only if there is an issue of material fact need a hearing be granted by the Food and Drug Administration.

In the case of an application for approval of the drug, as distinguished from the question of whether it's generally recognized as safe and effective, in the case of such an application it is expressly provided in the statute that if the applicant accepts an opportunity for a hearing within thirty days of notice of such opportunity, such hearing shall commence not more than ninety days after the expiration of such thirty days, unless the Secretary and the applicant otherwise agree.

That is explicit. I don't see how an ex parte decision, such as was made in this case, denying a hearing, could be made under such a provision.

The right to a hearing in a withdrawal proceeding must be no less firm, both as I read the statute and as I read

the legislative history. In fact, Senator Eastland expressly stated, in explaining this withdrawl provision to the Senate, and I quote: "Withdrawl of approval of a new drug application . . . would be preceded by a hearing . . . with findings on the basis of the record."

That's rather explicit. Certainly, in this situation, where, as I think we show in our briefs, the likelihood of an overpowering number of required hearings seems in reality remote. The cases are applicable which hold that inconvenience or lack of staff or lack of money or the prospect of delay is no good reason for dispensing with the minimum requirement of a hearing in an adjudicatory matter.

The cases are cited in our brief in No. 394, and they include the Ohio Bell Telephone case and the Wong Yang Sung case. That's at pages 37 and 38.

So, despite the express fears of the government of a multiplicity of hearings, we think it is safe to say that the necessary showing of the existence of a material fact, and that is all that has to be shown, will drastically curb even the tendency to request such hearings the government fears, based on speculation not on evidence. In any event, we believe we have shown in our brief in No. 394 that an issue of material fact exists with respect to the efficacy of Lutrexin.

We do not deny that Section 701(a) of the Act authorizes the Food and Drug Administration to make general

rules for its enforcement. Obviously, it does. Such regulations have the status of law, if they are reasonable and in accordance with the statute.

The new drug regulations of May 8, 1970, to which we referred earlier, relating to substantial evidence of effectiveness and the right to a hearing, were issued under Section 701(a) to implement the definition of new drug in Section 201(p) and the definition in Section 505, the operative new drug section.

It is those regulations with which these cases are concerned, not the regulations published in the Federal Register of May 21, 1972, for classification of over-the-counter drugs as to their new drug status. We do not consider those OTC drugs are valid, because they represent an attempt to circumvent the provisions of Section 505 of the Act by a classification system instead of by the adjudication procedure contemplated by that section. But they are not before the Court today in any event.

The Storer Broadcasting case, which is cited by the government in support of its proposition that a rule can always be substituted for adjudication, did not circumvent a basic statutory provision, such as Section 505. The relatively simple ownership rule, station ownership rule there involved could be readily applied, and did not concern a variety of different articles or drugs or stations with different

labeling and different characteristics, as this Court recognized in Securities and Exchange Commission vs. Chenery. The problam may be so specialized and varying in nature as to be impossible of capture within the boundaries of the general rule.

Our basic position with respect to the May 1970 regulations is this:

First, as they have been applied to Hynson's drug, Lutrexin, they're invalid. Because the Commissioner refused to recognize that the evidence submitted by Hynson raises a substantial issue of material fact as to whether there is a substantial evidence of effectiveness of Lutrexin. And failed to produce prima facie evidence to the contrary.

Under such circumstances, a hearing is required by the statute, we submit, before the Commissioner may legally withdraw approval of the drug under Section 503(e)(3) on the ground of lack of substantial evidence.

Under the summary judgment rule of the RCP, as I've said, upon which these FDA rules are allegedly patterned, it is clearly the burden of the proponent to show, by prima facie evidence, that there is no issue of material fact presented by such evidence.

Moreover, under that rule, the opposing party is entitled to depose or examine the witnesses of the other party.

It is clear that, aside from the burden of proof

rules in the summary judgment procedures, the Administrative Procedure Act requires that FDA, as the proponent of the order, shoulder the burden of proof to show a lack of substantial evidence; and this it did not do.

Also, this is clear from the language of Section 505.

The second basic objection to the May 1970 regulation is that they combine in the Commissioner both the prosecutorial function and the judging function.

We recognize that the Commissioner must make the eventual and final decision as to whether a drug should be withdrawn, but it is unfair, we think, to provide for an ex parte decision by the Commissioner without the submission by him of any evidence whatsoever to rebut the studies and affidavits of the distinguished obstetricians and gynecologists which Hynson, Westcott and Dunning presented.

QUESTION: Well, even if you had had all sorts of witnesses in an evidentiary hearing, the Commissioner still would have been prosecutor and judge, wouldn't he? I mean, that wouldn't have changed that.

MR. WILLIAMS: Well, I go on to point out, and I can do it more briefly that -- well, I did say, if you'll recall, that we recognize that the Commissioner must make the final decision; but as the Attorney General's committee said in 1941, one way to eliminate the possibility of unfairness in summary judgment proceedings, or any other proceedings, for

that matter, is to have an impartial judge do the original judging. And that is the burden of the cases, I don't think there's any doubt about that, so far as I know.

QUESTION: Would you say the statute, then, or that the statute or Constitution would have required not only a hearing but before a federal administrative judge?

MR. WILLIAMS: Well, customarily, Food and Drug new drug hearings have been held before an examiner, who is now called an administrative judge. And that's the way it should be in this case, according to our view.

QUESTION: Well, what supports your view, though? I mean, is there any specific version of the statute that you rely on?

MR. WILLIAMS: Yes. We have -- specific provision?

QUESTION: Yes.

MR. WILLIAMS: Well, I just went into the hearing question. It seemed perfectly clear for -- oh, you mean about an administrative judge?

QUESTION: Yes.

MR. WILLIAMS: Oh, well, I think that we cited Goldberg vs. Kelly, one of this Court's cases, and ICC vs. Louisville & National Railroad Company in our brief at page 32 in support of that position. And in that case --

QUESTION: Goldberg v. Kelly didn't provide for a hearing examiner, it was a person writing --

MR. WILLIAMS: No, but how can you have a fair hearing if you don't have one.

QUESTION: No, we're talking now about what your authority is. Goldberg v. Kelly, that you rely on, did not call for an independent hearing examiner, in the sense that you're arguing, but merely a different person within the Social Security hierarchy from the man who had made the original decision. That's all.

MR. WILLIAMS: Oh, that's so. But I really don't contend --

QUESTION: That's quite different from a hearing examiner.

MR. WILLIAMS: Mr. Chief Justice, I don't contend any more than that. But I might point out that this Court said, through Justice Brennan, that in almost every setting where important decisions turn on questions of fact, due process requires an opportunity to confront and cross-examine witnesses. And that we didn't get here.

Thank you.

MR. CHIEF JUSTICE BURGER: Thank you, Mr. Williams.

Mr. Frey?

REBUTTAL ARGUMENT OF ANDREW L. FREY, ESQ.,

ON BEHALF OF THE GOVERNMENT PARTIES

MR. FREY: Just a word or two with respect to Mr. Williams, and then I will turn it over to Mr. Hoffman.

The Hinsworth and Deakman studies were significantly different, in the sense that they were controlled. And I think if you understand, and look at the studies, you will see this. They took the group of patients in the studies and they split them into two groups, and they paired them in order to eliminate the differences between the two groups.

It's true they got other medication apart from DES, but both groups got the same medication. They were comparable as much as could reasonably be made possible, except the one group had DES and one didn't. And I think that is a significant difference.

With respect to Justice White's point regarding the burden of the Commissioner to come forward, that issue was tried and challenged by PMA as to the validity of the regulations -- the Pharmaceutical Manufacturers Association, of which Hynson is a member -- and it was adjudicated in favor of the Commissioner.

Also the Ciba-Geigy case in the Second Circuit upheld the Commissioner's view on that position.

Thank you.

MR. CHIEF JUSTICE BURGER: Mr. Hoffman.

ORAL ARGUMENT OF JOEL E. HOFFMAN, ESQ.,

ON BEHALF OF USV PHARMACEUTICAL CORPORATION.

MR. HOFFMAN: Mr. Chief Justice, and may it please the Court:

The fifth and final case in these consolited proceedings is USV Pharmaceutical Corporation against Weinberger. This case is here on certiorari to the Court of Appeals for the Fourth Circuit and, like CIBA and Bentex, it arose as a civil action in the district court for a declaratory judgment, that the products involved are not new drugs as defined by the Act.

The issues in the USV case involve solely the interpretation of the grandfather clause in the 1962 amendments, Section 107(c)(4). The district court held that the products involved do enjoy grandfather status, and the Court of Appeals held that they do not.

Now, before proceeding to the specifics of this case, perhaps it would be helpful to step back for a moment and look at the over-all statutory scheme which we've been discussing, since ten o'clock this morning.

There has been some imprecise use of terms during the course of the arguments and, with the Court's permission, I should like to briefly restate some of the fundamental principles with which we are confronted.

There are only two relevant terms used in the statute of all those shorthand expressions that have been brought up today. As Mr. Justice Stewart pointed out, the term "old drug" does not appear in the statute. There are only two terms. The terms are "drug" and "new drug", both of

these are specifically defined in the Act. And for present purposes, we need not get into the details of the definition of "drug" generally.

We can just assume that this refers to what we normally think of as drugs.

But the term "new drug" is explicitly defined. A special class of drugs is carved out, as defined by Section 201(p) of the Act, and this has been so since 1938. So that the Act regulates all drugs. It regulates drugs generally in a certain manner, and it regulates new drugs in a very specific manner.

This scheme is described in the brief for the Proprietary Association, which is the thick, light green brief, at pages 4 to 9, and also in the PMA brief, which is the thick, dark green brief, at pages 28 to 29.

Rather than repeat what is said there, let me simply summarize:

In 1938, the basic Food and Drug Act, the Pure Food and Drug Act of 1906, was totally revamped to strengthen the authority of the Food and Drug Administration, to protect the public in the field of drugs. This obviously is true.

But the powers of the Food and Drug Administration were strengthened very largely by way of increasing their authority as an enforcement agency, a prosecutor, if you will, in the district courts. The basic statutory scheme, which

applies to the regulation of drugs contemplates that the substantive prohibitions of the Act will be enforced in civil or criminal actions brought in the name of the United States on the reference of the Food and Drug Administration in the district courts.

So that if the drug is misbranded, the remedy available to the government is a civil action to seize the product or for an injunction or criminal prosecution.

If the drug is adulterated, the same remedies are available: a civil action for seizure or for an injunction or a criminal prosecution.

The Food and Drug Administration has no direct authority,with an exception that I will refer to in a few moments, to directly enforce these prohibitions. As was pointed out in response to a question of Mr. Justice Rehnquist, the agency has no cease and desist order authority, this is not the Federal Trade Commission; this is an Executive Branch agency, which refers cases to the Department of Justice for prosecution or for the initiation of civil actions.

Nor, for that matter, does the agency have subpoena power in the proceedings it does conduct. This has been recently pointed out in a study by the Administrative Conference, which characterizes FDA as perhaps the most important agency in the government which does not have any subpoena power.

So the agency that Congress strengthened in 1938, just to repeat it once more, is essentially a policing agency with regard to drugs, except with regard to new drugs as specifically defined by the statute. And that is the class of drugs with which the narrow issues in this case are concerned.

Now, the definition of new drugs is set forth in 201(p), and the basic function of 201(p) is to act as a valve or a selecting gate to determine down which regulatory road a particular product will travel. If the drug is a new drug, as defined in the statute, then it is channeled into an administratively applied regulatory scheme conducted by the Food and Drug Administration, the Commissioner of Food and Drugs.

If, however, the product is not a new drug, as defined by the statute, then it is simply outside that administrative regulatory scheme. The drug is regulated in the civil actions and criminal prosecutions which I described a moment ago.

The standard of whether a product is a new drug is section 201(p), and this is printed at page 3 of our brief, which is the thick blue brief, and also at page 482 of the Joint Appendix. And it provides that a drug is a new drug if it is a drug "the composition of which is such that it is not generally recognized by qualified experts as safe and effective for its intended use."

Now, in 1938, when this statute was first enacted, the word "effective" did not appear. A drug was regarded as a new drug if it was not generally recognized as safe for its intended use, its effectiveness did not enter into the matter.

The determination, however, whether a product was generally recognized as safe is a factual determination and was then a factual determination as to the state of informed expert opinion on the product.

The question, in short, was not whether the drug was in fact safe, because it might in fact be safe but not be generally recognized as safe; the question was whether the consensuse of informed expert opinion was that the product was safe. And in the absence of such a consensus, the product would be classified as a new drug.

In 19- --

QUESTION: When you speak of this "informed expert opinion", this is that category that is generally the general reputation of the drug as distinguished from evidence coming from controlled tests; is that correct?

MR. HOFFMAN: That is correct, with a qualification, that I would like to state at this time.

There has been a great deal of discussion as to whether you have to have substantial evidence as defined in the statute in 1962, that is controlled clinical studies, to have general recognition, the government says that you do.

The companies in these cases argue, uniformly I believe, that you do not need to have it. But if the government is right, that an expert couldn't possibly come to a conclusion as to the safety of the product without controlled clinical studies or, for that matter, its effectiveness, then there won't be a consensus.

QUESTION: It isn't a question whether he can come to a conclusion, it's whether he can come to a correct conclusion, isn't that what this 1962 Act is all about?

MR. HOFFMAN: Well, the 1962 Act defines substantial evidence in terms of controlled clinical studies with regard to the application of the standards for approval or disapproval by FDA.

As Mr. Williams pointed out, this definition does not in terms apply to the question of general recognition for purposes of classifying the drug in the first instance. But the statute does not say that the experts' consensus has to be a correct one, viewed from the vantage point of FDA or anybody else. The test is whether there is a consensus.

Now, if the government is right, that substantial evidence, in the statutory sense, of effectiveness under the new statute, or under the old statute -- to which I'd like to return in a moment -- whether there is a consensus as to substantial evidence of safety, if that depends on whether there are controlled clinical studies, then there won't be a

consensus, because if the government is right the experts simply won't come to a conclusion, if they are really qualified experts. It may be that they will come to that conclusion notwithstanding the absence of studies.

Now, the presence of studies may be relevant to an expert in deciding that he does or he doesn't recognize the product as safe or as effective, and it may be that he won't recognize that it's safe or effective if there aren't studies. But the statute doesn't tell the expert on what basis he has to decide for the purpose of the consensus.

QUESTION: But he does have to make the controlled study?

MR. HOFFMAN: The statute requires a controlled study, Mr. Justice Marshall, --

QUESTION: Well, I --

MR. HOFFMAN: -- only if a product is a new drug, as defined by the statute, and is therefore required to get premarketing clearance. Because if the drug is not a new drug --

QUESTION: Well, I thought you said that you didn't agree with that. You do agree with that for a new drug?

MR. HOFFMAN: For a new drug only, Mr. Justice Marshall.

QUESTION: You agree to that?

MR. HOFFMAN: Yes, I do.

QUESTION: Now, what is your definition of a new drug, the statute's definition?

MR. HOFFMAN: The definition is the statute's definition, which is that a product -- in 1962 -- up until 1962, the definition of a new drug was a product which is not generally recognized by qualified experts as safe for its intended uses. Products which were generally recognize as safe did not require preclearance and did not have to go through the new drug procedure.

QUESTION: And after the '62 Act?

MR. HOFFMAN: After the '62 Act, if the product was generally recognized as safe, but not generally recognized as effective, then it was a new drug. What we're --

QUESTION: And subject to the controlled test?

MR. HOFFMAN: That's correct.

Now, the change in definition of new drug, so as to expand that category, to expand the scope of the administrative regulatory scheme, that amendment would, in the absence of some grandfather clause, have applied across the board to all products that were on the market in 1962.

Congress -- and that is what the original Kefauver goal would have done. Congress did not, however, enact the original Kefauver bill in that respect. It added transitional provisions, and it added a grandfather provision.

And the precise issue in this case is the scope of

the grandfather provision, so that it can be determined whether or not a pre-'62 product is to be classified as a new drug or not as a new drug, according to the new definition or the old definition.

Perhaps it would be helpful, just for a moment, to state the factual origins of the controversy presented in this particular case.

For many years, beginning in 1955, USV, the petitioner in this case, has marketed a line of products principally containing a substance called citrus flavonoid compound. This is a naturally occuring combination of substances, called bioflavonoids, which are derived from citrus fruits. And the recommended use of the products is the control of abnormal capillary permeability and fragility, which is a condition of the capillary wall sometimes found in conjunction with serious ailments involving bleeding.

This side condition results,when it is present, in excessively easy rupture of the tiny capillary blood vessels which lie near the surface of the skin or near internal surfaces, and USV's citrus flavonoid products are recommended to physicians only as an aid in strengthening the capillary wall. In that sense, they are a prescription product, they are promoted for this use to physicians only, although they are available without a prescription, if you went in and asked for CVP, for example, you could get it, but there would be

nothing on the box to tell you that this is what it was good for. The promotion is only to physicians.

The products in the line of products in question fall into two separate groups. The original products in the line were new drugs, as defined by the statute in 1955, when they were first introduced for this use, for abnormal capillary permeability and fragility. And USV therefore filed new drug applications for them under Section 505 of the Act.

Now, by new drug application, I also mean what has been referred to today as an NDA. Now, this acronym, there's another term that doesn't appear in the statute, and in response to Mr. Justice Stewart's question of this morning, I would say that the term "new drug application" -- NDA does mean new drug application, it does not mean new drug approval. It doesn't appear anywhere in the statute, this acronym. The statute talks about applications, applications under Section 505, it does not talk about NDA's.

I have not personally heard of any use of the acronym to refer to a new drug approval until the Court of Appeals opinion in the Bentex case. I think that most members of the Food and Drug bar would be surprised to learn that it refers to something else.

The common understanding of NDA is "new drug application". But the important point is that the statute doesn't talk about NDA's, whatever NDA means, it talks about

applications. So, at least for my purposes, when I use the abbreviation, I am referring to the application, the new drug application.

After the new drug applications filed by USV had become effective for the original products in this line, and the products covered by them had become generally recognized as safe for their recommended use, so that they. were no longer new drugs for that use, as defined by the statute, USV introduced two additional products of the same type. New additions of old drugs, such as these two, are usually called me-too products. That's another term that doesn't appear in the statute. It's a shorthand term. And it has some perjurative connotations that were perhaps intended by those who developed the term, but I think today it has no such connotation.

Me-too products are competing products, competitive products; they are brought out on the market after a so-called pioneer product has been on the market sufficiently long so that drugs of this type become generally recognized as safe.

These two products were never the subject of new drug applications. The manufacturer never filed an application for them. They were simply brought out as drugs not new drugs, or as old drugs, if you will. There was no new drug application filed for them, no new drug application became effective for them. They were never regulated as new drugs

by the Food and Drug Administration. They were on the market as old drugs, just like aspirin.

These products were generally recognized as safe for their recommended use, and that's the basis on which they were brought on the market.

QUESTION: What if they had no effectiveness at all?

MR. HOFFMAN: If they had no effectiveness --

QUESTION: How would the -- if the FDA concluded that they were totally ineffective, how, in your view, do they address themselves to that problem in the public interest?

MR. HOFFMAN: The FDA could recommend to the Department of Justice that a -- that the products be seized, that the manufacturer be enjoined from further distribution, or that the manufacturer be punished. It is a criminal offense under the Act to market a misbranded drug.

The Act defines misbranding to include the use of labeling which is false or misleading in any particular, and there is certainly no question that a fasle or misleading claim of effectiveness for a drug is a misbranding.

The government has never brought such an action against the products that are involved in this case.

That would be the remedy.

Now, this was the only remedy available to the Food and Drug Administration for any product on the market as of 1962, if it believed that the product was not effective for its

recommended uses.

However, when Congress amended the Act to provide a degree of premarketing control over products, it did not apply that premarketing control retrospectively to products then on the market without qualification; instead, it added a grandfather clause, and it's the scope of that grandfather clause which is the crux of the controversy between USV Pharmaceutical Corporation and the government.

The question, as I said, is which definition of new drug applies. The grandfather clause says that if a product is a new drug -- I beg your pardon. The grandfather clause says that if a product is a new drug under the new definition, it still may not be required to go through the preclearance requirement if three conditions are met.

Now, this Section 107(c)(4) is a technical and very precise statute, and it's not the sort of provision which can be read impressionistically. Congress spelled out its three criteria extremely carefully, and we think a broad-brush treatment of the complex language it employed would not do justice to the statute, which is printed --

QUESTION: Where is that in the Joint Appendix?

MR. HOFFMAN: Page 482, Mr. Chief Justice.

And also at page 3 of the petitioner's brief in 666.

Page 482 sets out Section 107(c)(4) of the Act, and this is the first non-indented paragraph, a little bit below

the middle of the page.

And the three criteria are: first, that the product has been marketed in the United States prior to the enactment of the 1962 amendments. There is no doubt that the products involved in this case were so marketed, and that the products in this case, therefore, meet the first criterion for grandfather protection.

The second requirement is that the product was not a new drug under the statute as it stood when the amendments were adopted. That is, that the product was then generally recognized by qualified experts as safe for its recommended uses.

And the district court found, and the Court of Appeals agreed, that in 1962 the products involved in this case were generally recognized as safe for their recommended uses; that the products therefore were not new drugs when the statute was amended. So that the second criterion for grandfather status is also met.

The third requirement for grandfather status is the one that brings us here today. That requirement is that the product was not covered by an effective application under Section 505 of the Act at the time the statute was amended. And the controversy today is over the proper construction of this third criterion.

Now, as I've said, USV never filed an application

under Section 505 for either of its two me-too products. This was because each was considered from the outset by USV to be generally recognized by qualified experts as safe for its intended uses, and therefore was not a new drug. New drug applications were not required for such products, and the marketing of each of these two me-too products was initiated and continued on the strength of general recognition of safety.

That was the basis on which the products were marketed, and it was the only basis.

The Court of Appeals held in this case that products such as these meet literally the criteria for exemption stated in the grandfather clause; and this is at page 470 of the Appendix, meet literally the criteria for exemption. We agree.

But the court went on to hold that USV's products in this category do not enjoy grandfather status, notwithstanding that they meet literally the requirements for exemption, because USV, as the manufacturer, was itself the applicant under the NDA's for earlier additions of the products which were first marketed under effective NDA's.

We petitioned for certiorari to review the decision insofar as it drew a distinction on the basis of the identity of the manufacturer in his role in marketing other products, the government agrees with us that no such distinction is

supportable. The government agrees, in other words, that if a product was a me-too version of an earlier product, it matters not who the original manufacturer was. And the government therefore agrees that our me-too products should be treated just like everybody else's.

But we differ as to what that treatment should be. The government argues for affirmance of the judgment as to USV's products by attacking the Court of Appeals ruling as to never NDA'd the me-too products in general. The government argues that notwithstanding the Court of Appeals conclusion that the products meet literally the criteria for exemption, that they don't really qualify, after all.

So the question before this Court as to the me-too products is the correction of the ruling below as modified in accordance with the government's concession, that Congress did confer grandfather status on never NDA'd products, even though they were later versions of earlier products.

QUESTION: Does it make a difference that you didn't take a -- no; strike it. I'm out of focus here. That's right.

QUESTION: Well, this exemption is a derivative exemption on the me-too product, isn't it?

MR. HOFFMAN: If I --

QUESTION: It derives from the parent drug, does it not?

MR. HOFFMAN: We think not, Mr. Chief Justice. If

the parent --

QUESTION: Well, why not?

MR. HOFFMAN: If the parent drug, the pioneer drug, were protected by the grandfather clause, which is the other issue in this case, but one which, for the shortne-s of time, I would prefer to put aside and leave on the briefs: if the pioneer products are protected by the grandfather clause, then, yes, the me-too's would follow along. Because the only basis for the government's argument that the me-too's aren't grandfather is that the pioneers aren't grandfather.

But, regardless of this Court's decision on the original products that were covered by effective applications under Section 505, the me-too products, in our view, independently meet the criteria for exemption, because these products never were covered by an effective application. They weren't covered in '62, they weren't covered in '58, they weren't covered in '55, they were never covered by an effective application.

QUESTION: Isn't that because they got a free ride, a piggyback?

MR. HOFFMAN: No, Mr. Chief Justice, --

QUESTION: What is it, then?

MR. HOFFMAN: -- they didn't get a piggyback because their marketing in no way depended on the fact that there was a new drug application effective for some other product. The

marketing depended solely on the fact that this product had become, that this type of product had become generally recognized as safe for its intended uses. If there had been no prior product, but there were a general recognition of safety under whatever standard applied, then these products would have come on the market.

QUESTION: So that the me-too, on its own merits, met the test of the '38 Act for a new drug?

MR. HOFFMAN: Exactly. The me-too met the test of the '38 Act; was not a new drug; was marketed as a drug other than a new drug. It did not depend for its lawful marketing authority --

QUESTION: Before 1962?

MR. HOFFMAN: Before 1962. Or, for that matter, today.

The me-too product came on the market because it was generally recognized as safe, and therefore not a new drug under the '38 Act. It continues on the market today, in USV's view, because, while it would not meet the amended definition, so that it would require preclearance by FDA, if the amended definition applied, our view is that the grandfather clause withholds the amended definition from this product that was on the market prior to 1962.

The correctness of the decision below as to these me-too products is shown, we think, by three principal con-

siderations, which are gone into in our brief; and if I may briefly summarize them:

First is the literal language of clause (C) of Section 107(c)(4), construed in accordance with Congress' demonstrated understanding of that language and of the concepts it incorporates. That concept is the concept of an effective application under 505.

Now, the government says 505 is irrelevant in construing the grandfather clause. But it's not irrelevant. How can it be irrelevant if clause (C) says that one of the criteria for grandfather protection is whether the product was covered by an effective application under Section 505?

So the critical question, in terms of statutory language, we think, is: what did Congress think it meant when it used the words "effective application under Section 505"?

Now, we think Congress was pretty clear as to what that meant. Our brief explains that it was explicitly called to the attention of Congress by Secretary Ribicoff, that an effective application under Section 505 was a one-trip ticket only, it was good for the manufacturer who filed the product and it was good only for the product for which that application was filed, not for anybody else's product and not for any other product of the same manufacturer.

Congress reflected its understanding of this concept

in other provisions of the statute, which are discussed in our brief. And while it did not address the subject of me-too products directly at any time, as the government points out, that is only to show simply that Congress may not have been aware that the statute it did enact would protect me-too's.

But whether Congress was aware of it or not, this is the statute they enacted, and our position is that when Congress set up, as a criterion for grandfather protection, that the product not be covered by an effective application under Section 505, that the case has to be decided on the basis of what Congress thought was covered by an effective application under Section 505.

The second consideration that we think militates in favor of the Court of Appeals ruling on me-too products in general is that the only available evidence of Congress' purpose in amending the definition of new drug in the first place shows a very limited purpose. Remember, the grandfather provision controls the applicability of the amendment to the Section 201(p) definition of new drug.

So, we believe it's relevant to inquire: what was Congress' purpose in amending the definition?

The government has stated in its brief that they agree that there is only a limited evidence of purpose in the legislative history, and that purpose was to clear up some confusion that was prevalent in the Senate at the time that

the new drug definition was amended.

The purpose of the amendment was to insure that new claims for old products would be covered by the new definition, so that if aspirin were to be newly recommended for acne, for example, to use the example that's been used here this morning, then a new drug application would have to be filed for aspirin insofar as it was being recommended for the new use.

That was the purpose, that was the only purpose that is evidenced in the legislative history; and we think that because me-too products obviously have nothing to do with that purpose, that the statute should not be distorted so as to deny these products the grandfather status which Congress literally and explicitly conferred on them.

If the Court has no further questions, I prefer to save the balance of my time for rebuttal.

MR. CHIEF JUSTICE BURGER: Very well.

Mr. Frey.

ORAL ARGUMENT OF ANDREW L. FREY, ESQ.,

ON BEHALF OF THE GOVERNMENT IN RE USV.

MR. FREY: The Court of Appeals characterized its holding in this case that me-too drugs are exempted as compelled by the literal language of the statute. And as I listened to Mr. Hoffman, he's urging you to feel compelled by the same literal language of the statute, regardless of how absurd the

results, let the whole house of cards that Congress erected fall down around our heads, the literal language of the statute requires it.

We submit that the language of Section 107(c)(4) in no way compels an exemption of me-too's. And, indeed, that the only sensible way you can read the provision does not exempt me-too products; it treats them in the same way as the products that were named in the new drug application.

QUESTION: What language of the statute, precisely of section (4), do you rely on to bring me-too drugs?

MR. FREY: Well, I think it's very significant, if you'll turn to the statute, I rely not on the statute that Mr. Hoffman read to you, in which he inserted the word "product" in place of "drug". I rely on Section 107(c)(4).

Now, in Section 107(c)(4) --

QUESTION: That's on page 482?

MR. FREY: Page 482. -- it does not say "In the case of any product which was not covered by an effective application", it says "In the case of any drug".

Now, the drug here is bioflavonoids, the product is Bivam. Now, there isn't anything here on this page, in this statute, that compels you to read that to say Bivam instead of bioflavonoids. And if you read it in the generic sense that we urge in our brief, everything falls in place, and you have a coherent and sensible statutory --

QUESTION: Except in a colloquy with Mr. Friedman this morning, I understood that the government's definition of me-too drug was not just different trade names for precisely the same generic product, but similar products as well as identical products.

MR. FREY: Well, because -- it depends on the degree of similarity of the product. You can have, and in many cases you have a product that is identical in everything but the brand name. And under the Court of Appeals reading, that product would be the me-too.

QUESTION: That's the easy case for you under the grandfather clause.

MR. FREY: Now, there is an issue in some cases, as there is in the Bentex case, for instance, as to whether you may really be dealing with a different drug that is not the same drug that was covered by the new drug application. But the position of the agency, and it has been explained in its drug efficacy study, Implementation Regulations of October 1972, which we've cited in our brief, it's basically that identical, similar, or related products, and this is defined by chemical composition and therapeutic use. It's a scientific concept which has parameters which I can't really get into today, and there can be factual issues as to whether a particular product is in the same generic family with the drug that's covered by the NDA.

Now, if Section 107(c)(4) is construed in the way USV urges, in an individual product sense, the results are irrational, they're discriminatory among manufacturers, they're completely destructive of the congressional purpose in requiring that drugs be shown to be effective for their claimed uses.

Now, let me give you a scenario of what would happen. Sometime between 1938 and 1962 a manufacturer decides that a certain compound is useful for the treatment of a certain disease or condition. He does studies regarding the safety of that compound, and he files an application with FDA, which reviews his application and allows it to go into effect. He then starts manufacturing that product.

Now, two or three or five other manufacturers may decide that they also want to market the same product, and if it's not patented they're free to do so, except they have to file their own applications until such time as the drug comes to be generally recognized as safe, which it comes to be because there have been NDA'd products out on the market that are generically the same. And at that point any manufacturer can market his product without going through the regulatory procedure, and that includes the NDA holder, who can put it out under different brand names or anything else.

Now, the ratio of these me-too products to the products that are named in the application is quite high. FDA

has found that as high as 13 to 1. In the Bentex case we have 23 manufacturers of me-too products, and only two manufacturers who held NDA's.

Now, under the '62 amendments, Congress said, review these NDA's, determine the efficacy of these drugs. And the agency does it. And the agency finds under the standards that Congress has established that the drugs are ineffective, or that they lack substantial evidence of effectiveness, which is somewhat different. And it withdraws approval of the NDA's, and it takes the pioneer drugs off the market. And here are twenty other manufacturers still on the market with the identical product sitting on the drug store shelves.

Nothing has been accomplished for the consumer; nothing has been accomplished but a completely irrational discrimination between identically situated people that does not correspond to any regulatory purpose that Congress had.

Now, nothing in the legislative history indicates that this was Congress' intent. Mr. Hoffman relies on something in Part 2 of the Senate Report, when he says that they were concerned with new claims. He omits in his brief, and he omitted to mention in his argument, the closing sentence of that paragraph, which says: the effect of this amendment on drugs already on the market is discussed below under transitional provisions.

So that the paragraph on which he relies has nothing

to do with the effect of the amendment of Section 201 on drugs already on the market in 1962.

Now, he says, well, let's rely -- and the industry says, let's rely on the power of FDA as a prosecutor with the aid of the Department of Justice, to go chasing these people in the courts with these very serious remedies. And in our reply brief we've tried to point out to the Court some of the practical problems that exist.

But what I would like to point out to the Court now is that Congress, when they passed the 1962 amendments, expressed a concern with the inadequacy of the judicial remedies. They said, "Evan where the effectiveness" -- and this, I am quoting from the House Report, H. R. 2464, page 3, which we have cited in our brief.

"Even where the effectiveness of a new drug enters into determining its safety, the Food and Drug Administration cannot, if it finds the drug safe, refuse clearance because the claim of effectiveness is exaggerated." That's under the old statute. "Rather, the Administration would have to stultify itself by allowing clearance and then causing court action to be brought for misbranding."

The committee goes on to note: "As a result, good medical practice is hampered and the consumer is misled until perhaps years later the government has gathered the necessary evidence to sustain the burden of proving the violation in the

courts."

That is what Congress was concerned about when it sought to bring these drugs under the regulatory scheme for evaluation of drug efficacy.

QUESTION: The burden of proof there, of course, would be the conventional criminal burden of proof, wouldn't it?

MR. FREY: Yes, and it's --

QUESTION: What's the burden of proof in --

MR. FREY: In an administrative proceeding, the burden is clearly on the manufacturer. He must demonstrate that there exists substantial evidence of effectiveness. And I think that's the only way it could be. There is no practical way for the Commissioner to demonstrate the non-existence of such evidence. I don't know how he would go about it.

QUESTION: The burden in a civil injunctive action, I take it, would be the normal preponderance of the evidence test that you have in civil proceedings?

MR. FREY: I think that's correct.

And that's a significant difference, in terms of discrimination between the pioneer and the me-too. The pioneer is being made to show to the agency's satisfaction that there exists substantial evidence of effectiveness, and the me-too, if the FDA could ever chase after and collar

all of them all over the country, in these thousands of individual suits, the burden would be on FDA to establish their ineffectiveness in a misbranding action.

Now, the structure of the '62 amendments, of 107(c)(4), clearly supports our position. 107(c)(4) talks about the applicability of the revised definition of new drug in 201(p). Nobody has told you, and nobody will tell you, that the definition in 201(p) is in an individual product sense. It's generic, and plain common sense tells us to interpret section 107(c)(4) generically also.

I see my time is up.

MR. CHIEF JUSTICE BURGER: All right, Mr. Frey. You have a few minutes left, I think, Mr. Hoffman.

REBUTTAL ARGUMENT OF JOEL E. HOFFMAN, ESQ.,
ON BEHALF OF USV PHARMACEUTICAL CORPORATION

MR. HOFFMAN: I'll try not to use them all, Mr. Chief Justice. We are grateful for the expansion of the time.

MR. CHIEF JUSTICE BURGER: I think it's about seven minutes.

MR. HOFFMAN: Mr. Frey has said, quite correctly, that Section 107(c)(4), on page 482, refers to a drug rather than to a product.

But that doesn't advance the ball any, in our opinion. He says that 201(p) is generic, and therefore 107(c)(4) must be generic. But, again, we stress that, as the

government did in its brief, it just ignores the fact that in carving out an exemption from the applicability of the amended definition, which is generic, Congress made that exemption turn on a highly personal and particularized factor; namely, was the drug -- and I'll use Mr. Frey's and the statute's word -- was the drug covered by an effective application?

Now, if Mr. Frey is right, and a drug is covered by an effective application, if any member of its generic class is covered, then once the first NDA is approved, nobody else need file a new drug application. Because Section 505(a), the basic statutory requirement, and this is on page 477, 505(a) says "No person shall introduce or deliver ... any new drug, unless an approval of an application filed pursuant to subsection (b) is effective with respect to such drug."

Now, if the word "drug" is generic, then it's generic. If it's personal, it's personal.

We pointed out in our reply brief that what makes the 201(p) definition generic is the rather awkward phrasing that a new drug is any drug the composition of which is such that a -- that it is not generally recognized by experts.

Now, that's not found anywhere in the statute. Except 201(p). The grandfather clause doesn't say that a product is disqualified from grandfathered status if it's a product which, the composition of which is such that it's

covered by a new drug application. And so we, therefore, rest on the proposition that Congress enacted a statute, Mr. Frey is not testifying before a legislative committee, he's here before this Court asking it to interpret what Congress wrote.

QUESTION: Mr. Hoffman, if your position, as I understand it, is that this regulatory scheme depends largely, if not entirely, on criminal sanctions in the district court where the burden of proof is on the government beyond a reasonable doubt; now, is there any other regulatory scheme of this general character in which that burden is placed on the regulatory agency?

MR. HOFFMAN: We think there are no regulatory schemes that are precisely like this in the respect to which Your Honor refers. I am not a Securities lawyer. My understanding, however, is that, for example, if a person violates the Securities Act by failing to comply with registration requirements and the like, the principal remedy -- and I am just not certain if it's the only one -- but the principal remedy is an action in the district court.

And the action, I might add, need not be criminal. The government has civil remedies available. It can seize the products, it can enjoin, with a civil burden -- preponderance of evidence burden. And as far as the necessity of bringing thousands of suits is concerned, we think the

history of the regulatory statute in question shows that where a point is established, if it has relevance to other cases, it need not be litigated thousands of times.

MR. CHIEF JUSTICE BURGER: Thank you, Mr. Hoffman.

QUESTION: Mr. Hoffman, I take it you have no response to the anomaly Mr. Frey points out, in a withdrawal situation where the pioneer bears the entire burden and the me-too's go scot-free?

MR. HOFFMAN: I do have an answer, Mr. Justice Blackmun, if I may state it just briefly.

The Congress continued in force, we believe, as to products that were on the market in 1962, whatever regulatory scheme was then in force as to that product. If the product was being regulated as a new drug, actively regulated, then it would continue to be so regulated under the amended scheme. If it wasn't being regulated under the administrative new drug scheme, which is the position of the me-too's, then it continued not to be.

Now, this may be seen as unfair, and the Pharmaceutical Manufacturers Association have suggested that in fact NDA'd products which had become no longer new are not subject to the amended definition of new drug, either. That issue is present in our case with a refinement. We are in the position of, as the district court found, having withdrawn the application from FDA. But that is an entirely separate issue,

which there simply hasn't been time to discuss.

We think, in other words, this is not anomalous any more than any grandfather clause is anomalous that distinguishes between products in various regulatory statuses, when the statute is amended. But if there is an anomaly, it's for Congress and not for this Court to change.

MR. CHIEF JUSTICE BURGER: Thank you, gentlemen.

The case is submitted.

[Whereupon, at 2:36 o'clock, p.m., the case in the above-entitled matters was submitted.]