ORIGINAL

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PROCEEDINGS BEFORE

SUPREME COURT OF THE UNITED STATES

DKT/CASE NO. 81-1222

TITLE UNITED STATES, Petitioner
v.
GENERIX DRUG CORPORATION ET AL.

PLACE Washington, D. C.

DATE November 3, 1982

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IN THE SUPREME COURT OF THE UNITED STATES

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GENERIX DRUG CORPORATION ET AL. :

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Washington, D.C.

Wednesday, November 3, 1982

The above-entitled matter came on for oral argument before the Supreme Court of the United States at 1:01 p.m.

APPEARANCES:

JERROLD J. GANZFRIED, ESQ., Office of the Solicitor General, Department of Justice, Washington, D.C.; on behalf of Petitioner.

MRS. ROBYN GREENE, ESQ., Miami, Florida; on behalf of Respondent.

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CHIEF JUSTICE BURGER: Mr. Ganzfried, you may proceed whenever you're ready.

ORAL ARGUMENT OF JERROLD J. GANZFRIED, ESQ.,

ON BEHALF OF THE PETITIONER

MR. WASSERSTROM: Thank you. Mr. Chief Justice and may it please the Court:

This case presents an important question under the federal Food, Drug and Cosmetic Act that will have a profound effect on the public health. The Court of Appeals' decision permits the sale without FDA approval of a large category of prescription medicines known as generic drugs. Such products purport to be interchangeable with preexisting or pioneer drugs for treating serious and life-threatening diseases, but they are not identical to the pioneers and they may in fact be unsafe and ineffective.

By way of background, I should explain that drugs are composed active ingredients, which are intended to have a therapeutic effect on the patient, and inactive ingredients, which are not intended to have a therapeutic effect. The inactive ingredients, however, play an important role. They may comprise 90 to 99 percent of a product and they often have a significant impact on how the active ingredient does its

job.

For example, the inactive ingredients influence how much active ingredient reaches the bloodstream and how quickly this occurs. So even if two drugs have the same active ingredient, we cannot assume that they will have the same results. The inactive ingredients may slow down or block the action of the active ingredient altogether, so it's as if the patient took no medication at all. For a patient who's taking a drug to control high blood pressure, such as most of the drugs involved in this case were, this means he runs the risk of heart attach or stroke.

On the other hand, the inactive ingredients can speed up or increase the effect of the active ingredient, and this is perhaps most apparent in time release drugs, where the result can be a dumping of active ingredients too quickly into the bloodstream, causing toxicity, overdose and other adverse side effects. It's as if in that case the patient has taken two or three or ten times the appropriate dosage.

By the same token, different manufacturing methods can also affect how the drug works. If the drug is packed too densely or too loosely into the tablet, the patient may suffer from wholly unintended reactions.

These differences are vitally important for generic drugs. These drugs are offered as substitutes for preexisting products whose effects and proper dosages are well known. But unless the generic actually performs the same way the pioneer does, the substitution may be dangerous.

Because the generic company does not know the full composition or manufacturing methods of the pioneer, the only way to be assured that the copy and the pioneer will in fact work the same way is by testing one against the other. If they perform in a similar way, they are considered to be bioequivalent and substitution will not affect the patient. But if they do not work the same way, then substitution poses a real danger.

In this case, the district court found that the products Respondent sold were not tested and were not generally recognized by experts as safe and effective for their intended uses, and that was all the Government needed to show for Respondents to be enjoined.

But the Eleventh Circuit held that these untested drugs could be sold with no scrutiny whatsoever. The court wrongly concluded that the Act's use of the term "drug" refers only to active ingredients

and not to the real life drugs that doctors prescribe, pharmacists dispense, and patients ingest, that is drugs as products.

As a result, the court has discarded the carefully crafted statutory scheme that assures that all drugs available for consumption by the public are in advance determined by experts to be safe and effective. And this holding creates a mammoth exception that would allow untested prescription drugs to reach the public simply because a manufacturer wants to sell them.

QUESTION: May I ask two questions. First, you don't adopt the position of the district court, do you?

MR. GANZFRIED: As to what the Government needed to show?

QUESTION: Yes.

MR. GANZFRIED: No.

QUESTION: They were wrong, too?

MR. GANZFRIED: That's correct. The district court tried to adopt a middle ground.

QUESTION: Your position is, even if there's no evidence of dangerousness, that the statute still applies?

MR. GANZFRIED: In essence, that's right.

QUESTION: And also, your position, if you

read the statute literally, would apply to over the counter drugs, too?

MR. GANZFRIED: Our position would apply to over the counter drugs, and the FDA treats over the counter drugs in a manner that's consistent with the statute.

QUESTION: Well, but it doesn't require a new drug application every time you put a different coating on a piece of aspirin.

MR. GANZFRIED: Well, two things as to over the counter drugs. First of all, none of the drugs involved in this case are over the counter drugs.

Second, what the FDA has done in the over the counter drug monograph system is to determine practical working definitions in advance of general recognition.

QUESTION: They just don't read the statute literally. They just say they don't really have to enforce it?

MR. GANZFRIED: They read it literally, but they understand that in looking at what an expert would need as the requisite evidence of safety for an over the counter drug, which, keep in mind, is not as potent, not as toxic, and has a much wider range in which it can be used effectively before you reach overdose situations.

QUESTION: Well, some of them can be pretty

dangerous, I think, over the counter drugs; can't they?

MR. GANZFRIED: They can be, and in fact the FDA does have regulations relating to inactive ingredients of certain over the counter drugs. The important thing is that in both cases, the prescription and over the counter drugs, the FDA looks at products, and it is the product that must meet the standards, not simply the active ingredient.

QUESTION: Mr. Ganzfried, isn't what the FDA does with over the counter drugs, though, somewhat similar to the test that the district court would have employed, where it said if there is no reasonable possibility that the differences between the excipients will make the product less safe and effective than the recognized product, it would be approved?

MR. GANZFRIED: Well, I think they --

QUESTION: As a practical matter, is that what the FDA --

MR. GANZFRIED: I'm trying to think that through. It's possible that the results may be the same, but I think what has happened is very different. First of all, we are dealing in this case with prescription drugs. And although the district court did apply the wrong standard, it did find that the Government had shown that there was a reasonable

likelihood that Respondent's drugs were unsafe and ineffective, and that they presented no evidence to rebut that.

QUESTION: Right. But I take it both the Government and the Respondents do not support the district court test for the prescription drugs?

MR. GANZFRIED: The Government does not. My understanding is that the Respondents do not, either.

QUESTION: What is the definitional line between prescription drugs and over the counter drugs?

MR. GANZFRIED: The definitional line is that if the finding is made by the Food and Drug Administration that a particular drug product has sufficient risks or side effects attendant to it that it cannot be sold without a doctor's prescription and under a doctor's care, those drugs require prescriptions. For drug products that are ordinarily used for minor and self-limiting illnesses, where there is a very broad range in which a product can be used effectively before you reach any dangerous levels --

QUESTION: Do you mean aspirin and bufferin and so forth?

MR. GANZFRIED: Those are over the counter drugs.

QUESTION: Well, supposing I decided I'm going

to go ahead and manufacture something called "Ufferin," which is just like aspirin only it's buffered a little bit differently than bufferin is. Is there some way I can tell whether I have to apply for a new drug application?

MR. GANZFRIED: Well, if it complies with an over the counter drug monograph -- and I'm assuming in that case that you're describing some kind of an analgesic -- you would have to check the over the counter drug monograph which defines in advance what the general expert recognition would be, tells you what active products must be in it, what suitable inactive products must be in it, and what dosages are allowable. And if you satisfy that standard, then it could be marketed as an over the counter drug.

Now, my understanding is that at the present time the analgesic monograph has not yet been completed. But that is in the works as part of the overall over the counter drug review system.

QUESTION: Does the statute draw a distinction between over the counter drugs and prescription drugs?

MR. GANZFRIED: In the definition of drug it does not. In other provisions of the statute it does, where it imposes certain restrictions on drugs that can be sold only by prescription.

QUESTION: On some drugs that can be purchased over the counter there is a printed disclaimer or warning, "Not to be used except under the direction of a physician." Now, is that just a case where the manufacturer is being ultracautious, or is that required?

MR. GANZFRIED: Well, I don't know about the specific case, but ordinarily in the over the counter drug situation the understanding is that information can be provided to the patient that will be understood by a layman. So that if you do have the sort of package insert that you've described along with an over the counter drug, then presumably it either conforms to what the monograph describes as what the packet insert should be for the over the counter drug or it --

QUESTION: But that warning is not something that is required by the FDA, is that right?

MR. GANZFRIED: Some warnings are, and some a manufacturer would add, I assume as a matter of prudence in particular cases.

I'd like to explain why the decision below should be reversed, by touching on the statutory language and the legislative history, and then turning to the strong public policy arguments that also mandate reversal.

The Court of Appeals went astray from the very first step of its analysis by ignoring crucial portions of the definition of the word "drug." Section 321(g)(1) has a four-part definition. If you satisfy any one part, you have a drug.

Now let me draw your attention to subsection (B), which defines a drug as "an article intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease."

QUESTION: Counsel, Respondents say that the word "article" as used in the definition is a word of art and refers only to items that are the subject of monographs, and would you deal with that in your discussion?

MR. GANZFRIED: In a word, it's nonsense. As this Court said in Bacto-Unidisk, the statute is to be read as broadly as its literal language indicates and not narrowly to accord with any particular medical or scientific definition. So in terms of the way this Court has read the statute, that argument is not correct.

QUESTION: And what about the legislative history?

MR. GANZFRIED: In terms of the legislative history and the use of the word "article" in these

formularies that are the reference point, the formularies in fact have monographs of drug products, dosage forms, and finished products. So the argument is not correct.

It would also not make any sense --

QUESTION: Does it mean something different in the different subsections, in your view?

MR. GANZFRIED: No, it doesn't. In any of the subsections, an "article" can refer to an active ingredient, but never to an active ingredient alone. It can refer to active ingredient and the final drug product.

QUESTION: In your view who has the burden of proof in determining whether a drug product is a new drug?

MR. GANZFRIED: As these cases have come along, the Government has assumed the burden, in an injunction action such as this, of proving that a drug is not generally recognized by experts as safe and effective.

QUESTION: Are you willing to adhere to that position?

MR. GANZFRIED: Excuse me?

QUESTION: Are you willing to adhere to that position, or should the burden be on the manufacturer?

MR. GANZFRIED: I think there are good arguments as to why the burden should be on the manufacturer, because the statute puts it on the manufacturer in the first instance by requiring him to get the NDA. But as a matter of history and practice, the Food and Drug Administration has sought to meet that burden in the cases. We're not asking anything different from this Court.

QUESTION: I take it the Administration has not been consistent over the years in its position?

MR. GANZFRIED: Well, the fact of the matter is that the Food and Drug Administration has been consistent on the critical issue that's involved in this case, and that is whether the FDA has regarded the words "drug" and "new drug" as referring to products. From the very first regulations that the FDA issued under the statute in 1938, it said that differences in inactive ingredients may cause a drug to be a new drug, and that regulation has remained substantially unchanged to the present.

Respondents point to certain practices, some of which are no longer in effect --

QUESTION: But for 30 years it issued these "no new drug" letters.

MR. GANZFRIED: "Not new drug" letters, that's

correct.

QUESTION: And you think that's consistent with --

MR. GANZFRIED: It stopped in 1968.

It is consistent in the sense that, first of all, it provided notice to the FDA that a drug was proposed to be marketed, and such notice is not going to take place under the Court of Appeals' decision.

Second, it was clear that the FDA, even in issuing these advisory opinions, was looking at products because on occasion it rejected the sale of so-called generic products that were copies of the active ingredients of products already on the market.

And third, that practice, which as I said was terminated in 1968 when all the "not new drug" letters were revoked, was in place at a time when the burgeoning generic drug industry was significantly smaller than it is today. Through the 1960's most of the states had anti-substitution laws, so that if a brand name drug was prescribed it had to be dispensed. You could not substitute a generic.

Around the end of the 1960's and into the 1970's, the states had shifted their position, in large part because the 1962 amendments to the Act that we're concerned with here called for effectiveness to be

demonstrated before a drug could be sold. And in reliance on that, in reliance on the fact that the Food and Drug Administration was going to be reviewing in advance products that were going to be on the market, the states have moved to the current regime of drug substitution where generics can be substituted when the brand name has been indicated but the doctor allows substitution.

And that points up one of the major problems in this case. Unless the generics are subject to FDA scrutiny, the doctor is not going to know what product his patient is actually getting. He's not going to know how the inactive ingredients may differ, he's not going to know how the manufacturing methods may differ. The patient may end up with results that are altogether different from what the doctor intended. And because the doctor doesn't what drug --

QUESTION: Well, if he doesn't know why shouldn't he write his prescription for the pioneer drug?

MR. GANZFRIED: The fact of the matter is, he will. And that was what the testimony in this case was, that doctors, as they had experience with generic drugs that simply failed to do what they purported to do and found that when they shifted their patients back to the

brand name drugs that the situations were remedied -- and that is exactly what is going to happen. The generic drug industry is going, and the demand for generic drugs is, as the amicus briefs indicate, going to evaporate if there can be no assurance for doctors, pharmacists and patients that they're actually getting the drugs that they think they're getting.

The other difficulty is that the doctor may never know that there was a problem with the drug, in the case of a progressive disease --

QUESTION: Well, isn't it up to him to know? He certainly assumes that risk with a prescription drug.

MR. GANZFRIED: He should know, but he often will not know.

QUESTION: Well, he can prescribe and on the prescription write "no substitution."

MR. GANZFRIED: He can do that.

QUESTION: And they often do.

MR. GANZFRIED: And they often do, and they are doing it more and more as the problems with generic drugs are becoming more apparent.

QUESTION: What is left of the exemption provision if your view prevails? Certainly when the statute was written it appeared as though Congress

thought that certain articles that would be drugs, which were widely accepted in the field as being equivalent, would not require the NDA's. And under your view that kind of an exemption would just disappear, would it not?

MR. GANZFRIED: No, it wouldn't. It wouldn't for the reasons that this Court described in Hynson. A drug would come on the market, to take one example, subject to an approved NDA, new drug application. At some point after there has been significant experience with that drug and enough published in the literature so that that drug comes to have general recognition, it will no longer be actively regulated as a new drug.

And perhaps I should say something here that addresses a problem in the Court of Appeals' opinion. I think there was the assumption in the Court of Appeals that once FDA approves an application the drug is no longer a new drug. In fact, the drug is a new drug and is actively regulated as a new drug, including requirements that the manufacturer report to the FDA subsequent evidence of adverse reactions.

Now, once there has been material usage and material time and enough expert recognition to have general recognition of the drug, it will no longer be in a category of new drugs.

QUESTION: But it takes what, 13 years to reach that stage?

MR. GANZFRIED: No, no, no. I think the 13 years figure that you use is something that Respondents argue as the time it takes from the first concoction of a drug in the laboratory up through the time that you get approval from the Food and Drug Administration. That's not the time period that would be involved for generic drugs, because the FDA has implemented procedures to expedite and simplify the process of getting approval.

In fact, there have been recent regulations by the FDA in the Federal Register of October 11th, and the Food and Drug Administration is making great progress towards simplifying the process so that it will be a much quicker one. As I recall, the evidence in terms of those regulations is that it may take approximately two years for an application to be approved from the time it is submitted and filed with the FDA to the time that it is approved. But the active regulation as a new drug would continue thereafter.

Now, the portion of the statutory definition of the word "drug" that I referred to, subsection (B), is something that the Court of Appeals ignored altogether, and its finding that only the active

ingredients are covered finds no support in the statutory language.

The Court of Appeals' error is even clearer when viewed in the full context of the Act. Congress passed this Act in 1938 in the wake of the Elixir Sulfanilamide tragedy, in which more than 100 people were killed by an unsafe inactive ingredient in a drug that had the same active ingredient as another product that had been used safely for years. The Act was passed to ensure that such incidents never be repeated.

The Congress went about this task with great care. It established a statutory scheme that we've discussed in some detail already. Under this scheme all drugs would be subject to expert scrutiny before they could be sold. And the cornerstone of this legislation is the NDA process.

Now, I should add that in the statute Congress specifically identified the information that was to be supplied in an NDA, and that included, in addition to evidence of testing to establish a drug's safety, all the ingredients in the drug must be listed and the precise methods of manufacture supplied. So it's clear that from the very start Congress expressed its concern for inactive ingredients and manufacturing methods, as well it should have after the Elixir Sulfanilamide

situation.

Now, Congress amended the Act in 1962 following the Thalidomide tragedy in Europe. At that time it expressed its approval of FDA's efforts in keeping Thalidomide off the market, and it expanded the Act's protection of the public by adding the standard of drug effectiveness, so that now a manufacturer must demonstrate by substantial evidence that its product is both safe and effective for its intended use before it can be sold. And there was no indication in 1962, or 1938 for that matter, of any Congressional intent to weaken FDA's power to keep unapproved drugs off the market.

Aside from the preclearance program, the Act also provides other means for ensuring that drugs, once on the market, perform as they are supposed to. While these misbranding and adulteration provisions are important enforcement tools, they address only products already being sold and are not a substitute for premarket review, nor were they intended to be such a substitute, as again the Elixir Sulfanilamide history shows.

That drug was in fact seized as misbranded, but the experience led Congress to conclude that such after the fact remedies alone were not enough.

Now, in totally exempting the generic drugs from the NDA process the Court of Appeals said that they may be sold even though they're not tested, as was the case with the drugs in this case. And under the decision below, because there will not be an approved NDA for these products, they are also exempt from other safeguards.

Among these is the requirement I mentioned before, that the NDA holder report subsequent evidence of adverse reactions under Section 355(j). When circumstances warrant, the agency may withdraw its approval and in that event the drug may no longer be sold.

This exemption that the Court of Appeals created was unintended by Congress, and in reaching the conclusion it did the Court of Appeals acted in a manner that was contrary to the way this Court has consistently interpreted the Act. Dotterweich, Bacto-Unidisk, Rutherford, Hynson, and the Park case in 1975 teach us that the Act is to be read broadly and its exceptions narrowly, in order to give full effect to Congress' effort to protect the public.

I mentioned also the FDA experience of 40 years, the question I had before as to whether we've changed our mind. We explained in our brief why on the

critical issue in this case we haven't changed our mind.

If Respondents contention is right that there has been some agency vacillation, what we are doing now is returning to where we were in 1938. We are not coming up with something new. And we are recognizing that the Congressional intent to incorporate ongoing medical and scientific research, which today leaves no doubt and is undisputed that differences in inactive ingredients and manufacturing methods often can cause differences in the way the products react -- taking all of this into consideration, the fact is that we're consistent on the main issue, and if in fact we've changed our mind, then as this Court said in the 1978 NLRB versus Iron Workers case, the agency is certainly entitled to change its mind and its interpretation should still stand so long as it's a defensible interpretation of the statute, as this one certainly is.

QUESTION: May I ask one other question. What is the FDA's position with respect to a pioneer drug that changes an inactive ingredient? Say they change from the pill from green to blue or something.

MR. GANZFRIED: An approved pioneer drug --

QUESTION: Must it file an NDA?

MR. GANZFRIED: It must file. It could be a supplement, depending on how drastic the change might be. It could be a supplement, it could be an amendment.

QUESTION: Say they just change the coating on it.

MR. GANZFRIED: But the fact is that the manufacturer is making a change in the product that's been approved.

QUESTION: And he must file a new drug application?

MR. GANZFRIED: Or an amendment or a supplement.

QUESTION: Well, it wouldn't be an amendment. It would be a new drug if you change it from blue to green.

MR. GANZFRIED: It could be.

QUESTION: Well, it could be or would be, under your view?

MR. GANZFRIED: If you change the inactive ingredient --

QUESTION: Yes.

MR. GANZFRIED: -- he has a new drug.

QUESTION: And so he would be required, the pioneer drug company, would be required to file an NDA?

MR. GANZFRIED: It could be an ANDA or one of the other.

QUESTION: But at least he has to --

MR. GANZFRIED: He would have to file something to notify the FDA, because he's no longer manufacturing the product that had been approved.

QUESTION: No matter now minor the change in the inactive ingredient might be?

MR. GANZFRIED: That's correct.

QUESTION: Counsel, if the generic is a bioequivalent of an approved pioneer, is the situation any different?

QUESTION: The legal situation is not, but that is something for the FDA to determine after there have been tests and a submission made. It is not something that the manufacturers are in a position to determine absent conducting bioequivalence tests. And all we're saying is that if they -- basically what we're saying in this case is that they should be -- we're asking them to do what they hold themselves out as doing.

If in fact the drugs are bioequivalent, they're going to be approved and they're going to be on the market. But if they're not, then that's where the problem exists, and those are the drugs that Congress

intended should not be on the market. FDA is the only agency Congress created for this purpose and is the only central clearing house for this information that can possibly make those conclusions.

QUESTION: It's the only agency Congress has created, but are there not some state agencies that on occasion are even more careful in their administration than the FDA? I'm thinking of over the counter drugs. In some states, some that are not bothered by the FDA are prohibited by state law.

MR. GANZFRIED: If I can eliminate the word "careful" from the question, there certainly are state regulatory authorities and in some cases they may have limitations that FDA does not. But the fact is that the states do not have any premarket clearance system.

QUESTION: After all, though, aspirin is not harmless.

MR. GANZFRIED: When used properly, it should not be. That's the problem. None of these drugs are harmless. They have to be used properly and their effects have to be known, and they have to be known in advance.

I'd like to reserve my remaining time for rebuttal.

CHIEF JUSTICE BURGER: You may lower the

lectern if you'd like, Mrs. Greene. You had a tall predecessor.

Mrs. Greene.

ORAL ARGUMENT OF ROBYN GREENE, ESQ.

ON BEHALF OF RESPONDENTS

MRS. GREENE: Mr. Chief Justice, may it please the Court:

This case does not involve the issue of whether premarket approval of generic products would make those products safer. The issue is whether generic drug products, both prescription and nonprescription, which contain active ingredients which are generally recognized as safe and effective are new drugs requiring premarket clearance from the FDA before they're sold.

The issue of prescription-nonprescription drugs is very important here, and it wasn't until this case got into this Court that the Government suddenly took the position that only prescription drugs were involved. In the complaint which was filed against my client, the Government sought to enjoin the distribution of all unapproved drugs. When the case was argued in front of the Court of Appeals, the issue of over the counter drugs was raised and discussed before the court.

It was only when the Government filed its

petition in this case that it suddenly claimed that the issue was only prescription drugs, and it was joined by amicus curiae, The Proprietary Association, which represents the various groups which make over the counter products.

The Government's reason for trying to narrow this case is obvious. As this Court has recognized in its prior decisions, there are in excess of half a million over the counter products currently on the market. It is simply impossible for the FDA to approve new drug applications for every over the counter drug, and in fact FDA does not require over the counter products to have new drug approvals, although the statute in question does not distinguish between over the counter and prescription drugs.

In this case both the language of the statute and the very, very clear legislative history show conclusively that Congress has never intended that each and every prescription and nonprescription drug product obtain premarket approval from the FDA before it is sold. Congress has rejected licensing of products on at least three separate occasions, beginning in the 1930's.

The original Food and Drug Act was passed in 1906 and during the early 1930's Congress began to

re-examine it. Very few of the early drafts of bills before Congress contained any language about premarket clearance. However, there was one such bill and that was submitted by Representative Coffee, who seemed to be kind of a Ralph Nader of his time. He was a very liberal man.

His bill was called the Consumer Union Bill. He believed it was in the interest of consumers to have product by product licensing. And his bill specifically provided -- he used very specific language -- each product must get a license. Congress didn't want to hear from Representative Coffee at that time and his bill died.

The Elixir Sulfanilamide incident occurred, and at that point there was a great hue and cry to have some form of premarket clearance. The Government has argued in this case that simply because premarket clearance came after the Elixir Sulfanilamide incident, that therefore the premarket clearance that was passed must have been product by product licensing.

It's a non sequitur and it's simply belied by the legislative history, which we cited extensively in our brief. Representative Coffee and other people got up repeatedly in the legislative history and said, the bill that we have before us that is going to be passed

is not a product licensing provision, we are rejecting product licensing. And it's just clear that the type of bill that Representative Coffee wanted, product by product licensing, was decisively rejected by Congress.

The Government has claimed that we have cited snippets of the legislative history in our brief. We have devoted at least five full pages to going through portions of the Congressional Record, and it is much more than a snippet that we rely on.

The second time the issue came up in front of Congress was in the 1960's. In the 1960's Senator Kefauver wanted product by product licensing. He submitted a bill which provided "that there would be licenses for the maintenance of establishments for the propagation or manufacture or preparation of products described in subsection (a) of this section." And the products for which a license is desired must meet standards designed to ensure the continued chemical structure, strength, quality, purity, safety and efficacy of such products.

Senator Kefauver presented this bill to Congress and it eventually passed, but in a much modified form. The factory licensing provisions which were contained in the bill originally remained. The product licensing provisions were taken out. And this

was in the 1960's.

Now, the Court I think is correct in saying that the FDA's position has been anything but consistent. For at least 30 years it said that what my client was doing, namely selling unapproved generics, which they are not doing any more, as we have pointed out in our suggestion of mootness -- they took the position that it was perfectly proper. And when the FDA last came to this Court in a case involving a similar issue involving generic drugs in the 1970's, it argued before this Court that when it withdrew an approval, a new drug approval for a pioneer drug, that that would automatically require that all unapproved generic drugs be removed from the market.

In the 1970's, this Court recognized in the Hynson decision and other decisions that all of the generics it was talking about had never received approval from the FDA. It's stated in the opinions.

The Government never argued that these products were not legally on the market because they did not have new drug approvals. Instead, it argued that the withdrawal of the new drug approval for the pioneer automatically resulted in a determination that the generics could not be sold.

So the FDA's position that it has been

consistent is simply incorrect, and the FDA's actual change in position came about some time in the mid-70's. After the FDA had changed its position approximately in the mid-1970's, the Third Circuit decided the first of the cases which involves the issue here, the Lannett case.

QUESTION: Mrs. Greene, was the FDA's change of position which you described as having taken place in the mid-70's evidenced by any decision or statement, or was it simply something that those in the industry could tell was happening?

MRS. GREENE: Well, I think the Government is correct in saying that they always had the regulation on the book, but I think it reflected more in the agency's practice than in anything that was said or done. They started to file injunction actions and sue people trying to get the generics off the market.

QUESTION: Whereas previous to 1975 they had never done that?

MRS. GREENE: Not to the best of my knowledge, not in a reported decision. Maybe a little bit earlier, there may have been several cases that may not have reached the appellate court level earlier to that, but I'm not aware of earlier decisions involving the generic issue.

QUESTION: But apart from the time, the year, you say that there was a noticeable and sharp change in policy some time in the late 1960's or 1970's?

MRS. GREENE: I think probably the change occurred between 1968 when the FDA stopped issuing the "not new drug" opinion letters and the mid-1970's. The stopping of the issuance of the "not new drug" letters was an official policy that could be pointed to.

But the Lannett case is the first case of an appellate court that reflected the FDA's new position in terms of generics. After Lannett was decided, the FDA went to Congress again in the late 1970's and it told Congress, it said, the Third Circuit has decided that generics do not need premarket approval and we think the Lannett decision is wrong.

And the FDA at that point put before Congress several bills, among them Senate Bill 1075, which would have legitimized every single thing that FDA was doing. It would have done away with the new drug provisions. It would have adopted an over the counter monograph system. It would have legitimized the abbreviated new drug approval process.

QUESTION: Is it possible that Congress didn't act because they thought it wasn't necessary to act?

MRS. GREENE: That is a possibility. But I

think that the rejection of Senate Bill 1075, viewed together with Congress' specific rejection of premarket licensing in 1938 and 1962, shows that Congress just didn't want premarket licensing. That rejection of the statute alone in 1979 I agree would not be determinative. But I think if it's viewed in the historical context from the thirties through the sixties to the late seventies, it shows a definite pattern on the part of Congress.

QUESTION: What do you call the requirement to have a clearance on new drugs? Is that some kind of a premarket licensing system? There are some kind of drugs, I suppose, that need preclearance, don't they?

MRS. GREENE: New drugs.

QUESTION: Yes. What do you call that?

MRS. GREENE: Well, I think that what Congress had in mind when it passed the statute --

QUESTION: What is that? Is that a limited premarket, market licensing system, drug licensing system, product licensing system?

MRS. GREENE: It is not a product licensing system. What Congress had in mind is that, for example, a manufacturer will develop a brand-new chemical entity. It will go out, it will test it, it will perform investigations.

QUESTION: And then --

MRS. GREENE: And then it will --

QUESTION: Perhaps approve it for marketing.

MRS. GREENE: Then it will decide whether the product is a good product to sell, and if it thinks it's effective and safe and useful and the company can make money it will then go to the FDA and it will seek a new drug approval for that particular product.

QUESTION: Well, isn't that a kind of licensing?

MRS. GREENE: Well, it is not really a license. It is an approval to sell.

QUESTION: Well, what was it you think the Congress was rejecting in the legislative history that you referred to?

MRS. GREENE: Well, I think what Congress was rejecting was the idea that each and every product had to go for an NDA, because after the product gets on the market in terms of an NDA 99 percent of all products, both in the 1930's and today, are patented. The company which has the original patent is permitted to put the product on the market for a period of 17 years. It may issue licenses to several other manufacturers to distribute that product, but the product stays on the market for 17 years in more or less of a monopoly

situation.

At the end of 17 years when the patent expires, other companies then are free to come in and duplicate the product. After the 17 years some products, some active ingredients that have been sold, are then generally recognized as safe and effective and can be sold without premarket clearance.

Other products, for example a product like Oraflex, which was on the market for a year, even though it had FDA approval certainly no one would recognize it as being particularly safe today, and in fact it has been taken off the market.

So the 17-year patent period is a period of time during which the community of experts can formulate opinions about whether the active ingredient that is being sold is generally recognized as safe and effective. And I think that if the statutory scheme is viewed in that way it makes a tremendous amount of sense.

The bioavailability and bioequivalence concerns that the Government raises were dealt with by Congress very specifically in the statute that exists through the adulteration requirements. It is -- under the Act as it has existed since the 1930's, a manufacturer is not allowed to sell a product if its

strength, quality or purity falls below compendial standards as recognized in the United States Pharmacopoeia or the National Formulary, both of which are expressly mentioned as guidelines in the statute.

If one opens the United States Pharmacopoeia and the National Formulary, one finds mainly definitions of drug substances, and the drug substances are listed and underneath it will give the percentage of the active ingredient that should be found in the product that is sold, and there are disintegration requirements.

The Formulary and the Pharmacopoeia both in the 1930's and in the 1980's would not tell a neighborhood pharmacist or a manufacturer exactly how to fabricate a product. Rather, they would set standards, tolerances within which the products had to be made in order to comply with compendial standards.

QUESTION: Mrs. Greene, your opponent says -- I haven't looked, of course, at the original documents -- but says that these compendia do also contain some drug products as well as active ingredients. Is that correct?

MRS. GREENE: The compendia do not contain any drug products at all.

QUESTION: Not by trade name, but is everything in there limited to active ingredients,

according to your submission?

MRS. GREENE: What they do contain -- if you go back to the 1935 Pharmacopoeia which Congress had before it, most of the items that are listed in the Pharmacopoeia are drug substances.

QUESTION: Well, but "most" seems to imply that there are some that are not.

MRS. GREENE: Well, I was getting to that. The second thing that the Pharmacopoeia in the 1930's had, they had items called official preparations. And the Pharmacopoeia was more or less at that point like a cookbook for the neighborhood pharmacist for how he would fabricate --

QUESTION: Well, would some of those preparations include inactive ingredients?

MRS. GREENE: The recipe that is in the Pharmacopoeia would include inactive ingredients. But at the beginning of the 1935 Pharmacopoeia, in the portion we've cited in our brief, it said that pharmacists could substitute a suitable diluant or excipient for the inactive ingredients which were mentioned in the recipe that was put in the Pharmacopoeia.

QUESTION: Is there anything similar to the Pharmacopoeia, any other book similar to that?

MRS. GREENE: Well, the two works referred to in the statute are the United States Pharmacopoeia and the National Formulary, both of which are similar.

QUESTION: They're two separate?

MRS. GREENE: They used to be. In the 1930's they were separate competitors. In the seventies USP bought the National Formulary and changed its function slightly.

But in no event is any item listed in the Pharmacopoeia or the National Formulary a drug product. Instead --

QUESTION: Well, but you said they did list some recipes that the pharmacist might use, which would include both active and inactive ingredients.

MRS. GREENE: With the provision that they could substitute --

QUESTION: That you can substitute the equivalent. But the mere fact that they are listed in there seems to me to be contrary to your basic argument.

MRS. GREENE: Well, I don't think it's contrary. I think that in terms of the use of the word "articles" in the statute, Congress defined a drug as an article, articles are things listed in the Pharmacopoeia. And for example, the National Formulary,

which is mentioned in the statute today, only lists drug substances.

Obviously there's a kind of dynamism involved, because the Pharmacopoeia and the Formulary referred to in the statute have changed over a number of years. But the one thing that is definitely not mentioned is drug products, and that's why I think it's important, to the extent that there is an ambiguity in the word "articles," to look at the legislative history in determining exactly what Congress meant when it used the term "articles."

QUESTION: Mrs. Greene, in Code Section 321(g)(1)(D) it also says that "drug" means "articles intended for use as a component of any article specified in clauses (A), (B) or (C) of the paragraph. Doesn't that indicate that all of these excipients are covered?

MRS. GREENE: Well, I think -- but the statute still uses the word "article," and the Government has claimed that "article" should be used in its broad generic sense and not in any way related to its use in the Pharmacopoeia and the Formulary. If in fact "article" means items in the Pharmacopoeia or the Formulary, it should mean the same thing all the way through the statute, and it shouldn't be changed in that part of the statute.

There are various items recognized in the Pharmacopoeia which are combinations of active ingredients and are specifically listed as combinations in the Pharmacopoeia.

I think that at a minimum the Government has tried to take the position partially that the statute is unambiguous and that this Court should not look at the legislative history. It's our position in our brief that the statute at best is ambiguous and that any ambiguities in terms of the word "articles" should be resolved by reference to the legislative history.

I think in resolving the issue of what the word "articles" means, one useful thing that I did, I went through the entire statute and I looked at the word "drug," and every time it said "drug" I substituted "active ingredient" versus "product" in order to determine which interpretation made more sense. 90 percent of the time it didn't make any difference at all.

But in a couple of situations it did make a very large difference, and if I can just find the one place where it was absolutely most erratic, Section 502(i) of the Act says: "A drug or device shall be deemed to be misbranded if it is an imitation of another drug."

Now, if we take the word "product," which is what the Government says "drug" means, and substitute it into the Act, that portion of the Act would then mean a product shall be deemed to be misbranded if it is an imitation of another product. Well, of course all generic drugs are imitations of other drugs, and if you use the word "product" in this part of the Act it would effectively outlaw the entire generic drug industry.

And by substituting in other parts of the statute it's clear that Congress could not have intended the word "drug" to be "product," but rather it meant the active ingredient or combination of active ingredients in the product. And I think again and again in going through the legislative history, Congress has stated that it is relying on the adulteration provisions and adherence to compendial standards to bring -- I'm sorry.

QUESTION: Mrs. Greene, in the section that requires a new drug application to be filed, doesn't it require that they list the inactive ingredients of the drug?

MRS. GREENE: Yes, it does.

QUESTION: So doesn't that have to be broader than the active ingredients, in that section at least?

QUESTION: In that section of the Act. I

think when you are dealing with the original pioneer drug that is first going on the market, that the testing and the items that are required are definitely more extensive than what is required after a product has been on the market for 17 years and achieved a certain amount of general recognition. I think before the FDA wants something that is brand new on the market it wants to take every possible precaution to make sure that a disaster will not happen, although even the FDA's efforts do not prevent disasters from happening in all instances.

I think that --

QUESTION: Do I detect that you are about through, Mrs. Greene?

MRS. GREENE: Just about, but --

QUESTION: Well, I have a -- I thought I would just ask you if you thought the Court was quite wrong in rejecting your suggestion of mootness.

MRS. GREENE: Yes, I did.

QUESTION: And do you think it is even more moot today than before, if that's possible?

MRS. GREENE: Well, the government and I are debating on how moot it is, because there was a warehouse full of drugs in Miami, most of which should have been destroyed, but the marshal can't destroy the drugs because he can't burn them, because it would pollute the air, and he can't bury them because it violates the Toxic Waste Disposal Act.

(General laughter.)

QUESTION: You know that if we had accepted your suggestion, you would have lost your favorable judgment. We would have vacated it.

MRS. GREENE: Yes. We pointed that our in our --

QUESTION: Exactly. You did.

MRS. GREENE: What basically happened, and the

government has ascribed all manner of bad motives to us, when this issue came to the public forefront, in the media, there were some very unfavorable reports on national television. As a practical matter, it became almost impossible for someone like my client to sell unapproved generic drug products, and my client was not necessarily interested in the legal issue. My client was interested in his business.

So, he just stopped selling unapproved drugs. We told the government we would consent to the entry of an injunction against us to prevent us from selling unapproved drugs, since we weren't doing it any more, and we didn't plan to do it in the future.

QUESTION: Are you still of that persuasion?

MRS. GREENE: Yes, and really the only difference that the government pointed out, it suggested that we had to recall everything that we had sold in the past. In our suggestion of mootness, we pointed out that under the cases, most of the cases that exist today, the FDA did not have the power to recall.

QUESTION: And haven't all the drugs that had been distributed expired in there?

MRS. GREENE: We believe that most of them have expired.

QUESTION: Most of them.

MRS. GREENE: We thought that all of them had. It is possible -- there are a lot involved. The government claims that there are perhaps three bottles in Oklahoma that have not expired. We haven't really resolved that issue, but we still do believe the case is moot, and that any problems along those lines would best be resolved by the trial judge on some type of a remand.

In fact, I checked with my client last night. They are not selling unapproved drugs as of today, and do not intend to.

QUESTION: Does this mean that the position of your client and perhaps a substantial segment of the industry is that the approval by the government actually enhances the marketability of the generic drug?

MRS. GREENE: There is no question about it, and I think that is reflected in the transcript in this case. The government witness, Dr. Palmer, was asked whether certain drugs were generally recognized as safe and effective, and he said they were, and when asked why, he said, because they have FDA approval. He said, whenever anything has FDA approval, I recognize it as being safe and effective. If it is not approved by the FDA, I do not recognize it as being safe and effective.

And I think that the government is correct in a way in saying that a lot of doctors do not have

intricate knowledge of pharmacology. They look at the FDA approval as a stamp of approval.

QUESTION: So your client isn't out of the generic drug business. It is just that your client will present them for approval.

MRS. GREENE: Well, my client will not. My client is merely a distributor of products manufactured by other people, and there are a great many manufacturers on the market who make approved products, and in light of the adverse publicity and the difficulty of selling the products, and the potential exposure under products liability laws, there is simply no reason to continue in the practice.

Now, the government wanted us to confess error, which we will not do, because we think that the Fifth Circuit was absolutely correct, but what is correct legally and what is correct from a business point of view --

QUESTION: Is two different things.

MRS. GREENE: Correct.

QUESTION: Apart from the particular articles in dispute in this case, your client no longer has a financial interest in winning this case.

MRS. GREENE: No. The last remaining vestige of financial interest was --

QUESTION: Is your lawyer's fee.

(General laughter.)

QUESTION: You won't collect that from the government, though.

MRS. GREENE: -- were the drugs that were in the warehouse. The injunction case was never consolidated with the seizure case, and we received an order requiring the government to allow us to take the drugs out of the warehouse in Miami, and this Court stayed that order requiring the return of the property, and during the passage of time, at least 90 and probably 100 percent of the shelf lives of the products have expired. That was our last remaining financial interest. And we really have none today. But my client said, why do I have to come to this Court, and I said, as long as I am your lawyer, you are not going to not file a brief, you have to come to this Court.

We think the Fifth Circuit was absolutely correct from a legal point of view, and the government may be entirely right in saying that the scheme that they have now with the monograph system and the abbreviated new drug applications is an ideal statutory scheme, but unfortunately, it is not the statutory scheme that Congress passed in 1938 and amended in 1962.

It is a statutory scheme which Congress

expressly rejected in 1979, and as good as it may be, perhaps if I were the legislature, I would have passed Senate Bill 1075. It did get through the Senate, and it was rejected by the House. It is not the statutory scheme that we have today.

We think that the Fifth Circuit was right for the reasons stated in our brief, and that its decision should be affirmed.

CHIEF JUSTICE BURGER: Do you have anything further, Mr. Ganzfried?

ORAL ARGUMENT OF JERROLD J. GANZFRIED, ESQ.,

ON BEHALF OF THE PETITIONER - REBUTTAL

MR. GANZFRIED: Yes, just briefly.

QUESTION: Could you address the distinction, if there is one, under the Act between over the counter and prescription drugs?

MR. GANZFRIED: Yes, there is a statutory provision that does provide the distinction. It is 21 USC 535(b)(1), that describes the situations in which a drug would have to be sold only under a doctor's prescription. Basically, as I said earlier, prescription drugs are used for --

QUESTION: Well, does this case involve only prescription drugs?

MR. GANZFRIED: It certainly does. The only

drugs that were at issue --

QUESTION: Is that the position of the government all through the case?

MR. GANZFRIED: That is absolutely correct. The only drugs referred to in the complaint and the request for preliminary injunction were prescription drugs. The only drugs discussed at the hearing on the preliminary injunction were prescription drugs.

QUESTION: So you think there is a statutory basis for treating the two categories differently?

MR. GANZFRIED: There is a statutory basis for treating them differently.

QUESTION: But the definition is the same, is it not?

MR. GANZFRIED: The definition is the same, that's correct.

QUESTION: In the statute.

MR. GANZFRIED: That's correct, but there is this other provision in Section 353 that does set out a basis for recognizing that prescription drugs used for serious and life-threatening diseases are something other than drugs that can be sold over the counter and used by laymen.

QUESTION: But just recognizing there is a difference is all. If your position is vindicated as a

statutory matter, there would be nothing to prevent the FDA from tomorrow adopting a regulation saying, we are going to require premarket clearancing of all new over the counter drugs.

QUESTION: As a matter of fact, I would think that would be -- somebody could easily argue that they would have to.

MR. GANZFRIED: Well, if that were the case, and I disagree with it, it would be something that we would have to take up at that time. It is not this case, and it never has been this case.

QUESTION: Well, but it might be the consequence of this case, if we read the statute the way you do.

MR. GANZFRIED: I don't agree, but if there will be another case, then so be it.

QUESTION: May I ask this? Supposing we did conclude that the case was moot on the basis of what has been said, and we vacated the judgment of the court of appeals. What adverse consequence to the government, if any, would follow from that?

MR. GANZFRIED: The adverse consequences is that this industry of unapproved generic drugs is in large part a creature of dictum in the Linette decision. It was cited and discussed broadly in the

merchandising materials that Respondents put out, and that are in the record in this case. It spawned an industry. It was dictum from which the Third Circuit has arguably withdrawn in its review in the Pharmadyne case.

The fact is that without the FDA there to review these drugs before they reach the market, they are going to reach the market. We have the situation, and I refer you to Paragraph 15 of --

QUESTION: You can still -- you could just get after somebody else.

MR. GANZFRIED: Well, we may not know about them

QUESTION: Well, how did you find out about this one?

MR. GANZFRIED: Well, one of the reasons we found out is that there had to be a recall of the pherocemyde that was being distributed.

QUESTION: Well, how will you ever be? I mean, even if you win, you won't know any more.

MR. GANZFRIED: If people -- If there is compliance, we are going to know more --

QUESTION: Well, I know, but there won't be if there isn't.

MR. GANZFRIED: -- and if there is not

compliance, we have a remedy for going after them.

QUESTION: If there isn't compliance.

MR. GANZFRIED: Well, they referred to the adulteration provisions as a substitute for premarket clearancing. I suggest that if we --

QUESTION: I don't blame you for wanting to get off the books a decision you don't want to -- that you think is wrong.

MR. GANZFRIED: Well, the holding in the Linette case had nothing to do with the issue in this case. It had to do with a hearing.

QUESTION: Well, I know, but you would like to get this particular decision off the books that you think was wrong in this case.

MR. GANZFRIED: In this case, that's one of the reasons why the case is not moot.

QUESTION: You want it reversed.

MR. GANZFRIED: The other reason it is not moot is because they did not agree to a recall. They also did not agree to an injunction as broad as the one that we had sought. Now, the suggestion that we had from them is that the named Respondents would be willing to agree to an injunction. What we asked for was something that would be broader than that, and we indicated in our brief in response to the suggestion of

mootness that one of the problems it that they have shrouded the corporate relationships of the company in some mystery.

Now, they continue to do so to this date, despite Rule 28.1 of this Court.

QUESTION: Perhaps instead of rejecting the suggestion we should have just vacated and remanded it to the lower courts to consider.

MR. GANZFRIED: Well, or reversed would have been the preferable course.

QUESTION: Not if it's moot.

MR. GANZFRIED: Not if it's moot, but they haven't established the strong burden that they have of showing mootness, for the reasons that we described in our brief addressed to that subject.

I was going to talk about the adulteration provisions in which they say that's a substitute for premarket review. You could get at these drugs after the fact. I commend to your attention the Secretary of Agriculture's report on elixir selphenilamide in 1937. It demonstrates beyond any doubt that Congress was concerned with the kinds of issues that this case presents. The arguments that they have presented in support of their selling their generic copies of other drugs with the same active ingredient was precisely the

defense that was made by the manufacture of elixir selphenilamide. So I commend that Secretary's report to your review.

Thank you.

CHIEF JUSTICE BURGER: Thank you, counsel. The case is submitted.

(Whereupon, at 2:01 o'clock p.m., the case in the above-entitled matter was submitted.)

CERTIFICATION

Alderson Reporting Company, Inc., hereby certifies that the attached pages represent an accurate transcription of electronic sound recording of the oral argument before the Supreme Court of the United States in the Matter of:

No. 81-1222

United States, Petitioner v. Generix Drug Corp., Et Al.

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BY _____

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