

PUBLIC HEARING

before

ASSEMBLY COMMERCE, INDUSTRY AND PROFESSIONS COMMITTEE

on

ASSEMBLY BILL NO. 1257
(Generic Drug Substitution)

Held:
June 28, 1974
Assembly Chamber
State House
Trenton, New Jersey

MEMBER OF COMMITTEE PRESENT:

Assemblyman Martin A. Herman (Acting
Chairman)

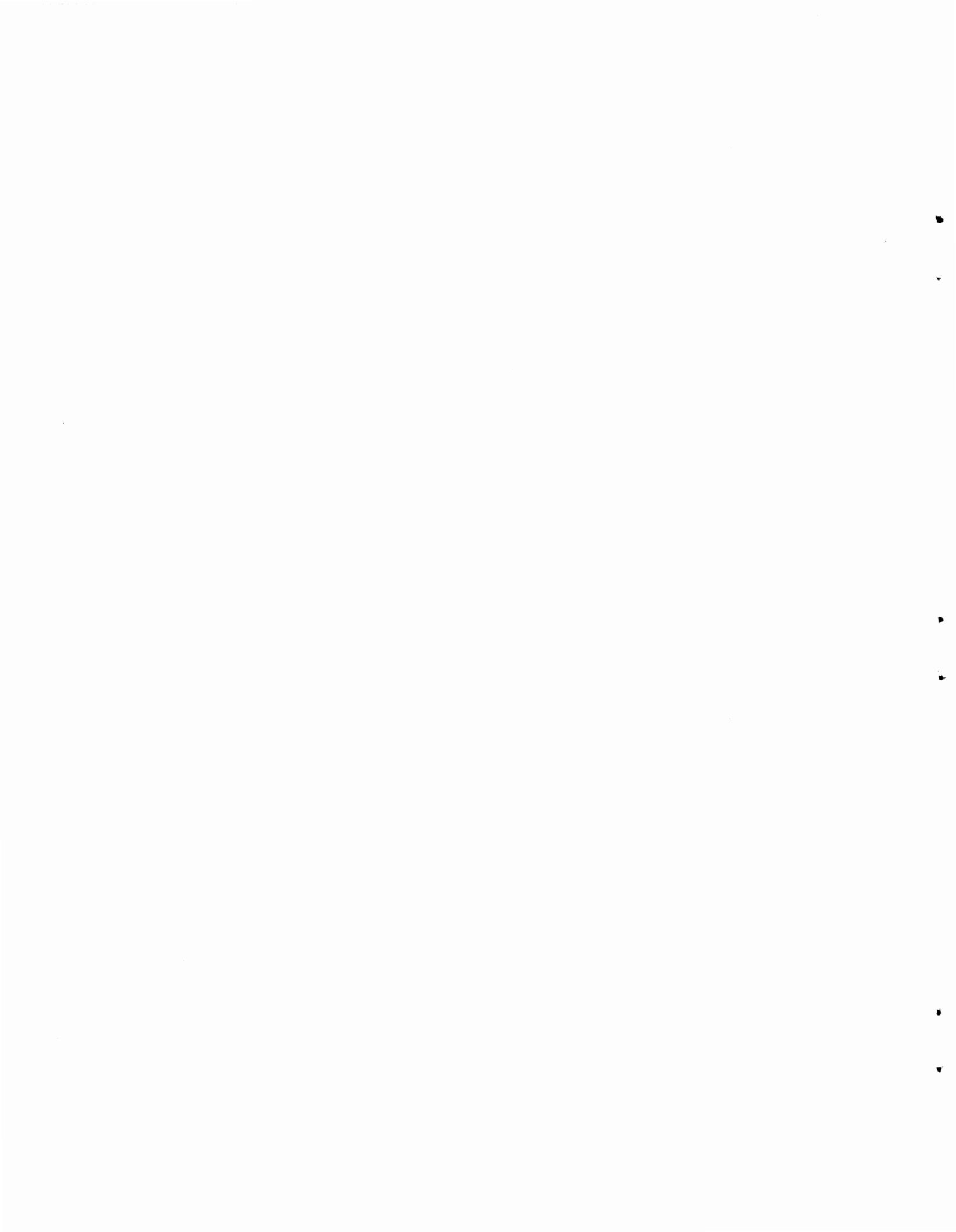
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I N D E X

	<u>Page</u>
Dr. Arthur Flanagan Vice President Warner-Chilcott Laboratories Warner Lambert Company	2
Dr. Murray Weinstock Licensed Pharmacist and Physician	14 & 49A
Gerald G. Hunt President Knoll Pharmaceutical Company	29 & 64A
Verne M. Willaman President Ortho Pharmaceutical Corporation	46
Dr. George Braun Vice President Ortho Pharmaceutical Corporation	48
Frank L. Bate Attorney for Merck and Company	57, 71A and 72A
Dr. Frank J. Malta Practicing Physician Toms River, New Jersey	68
William R. Jones Executive Director, Control Division McNeil Laboratories	82
Donald J. Foley Chief of Drug Control New Jersey Department of Health	1A & 40A
Dr. Garth K. Graham Manager, Medical Affairs Smith Kline and French	2A & 44A
Marvin R. Friedman Pharmacist	15A
Dr. Mary Hall Allergist	27A

- - - - -

(See next page)



Index (Continued)

LETTERS AND STATEMENTS RECEIVED FROM THE FOLLOWING:	<u>Page</u>
Dr. Albert J. Salzman Member, Council of Medical Staffs for South Jersey	79A
Sandra Helton Montville, New Jersey	81A
Edward Kross President, Rahway Local No. 8-575 Oil, Chemical and Atomic Workers International Union, AFL-CIO	84A
William M. Weinstein Registered Practicing Pharmacist Livingston, New Jersey	86A
Sidney H. Willig Director, Food Drug Cosmetic Unit Temple Law School	89A
Dr. Chary Tan Sy Director, Internship Training Program Christ Hospital Jersey City, New Jersey	93A

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ASSEMBLYMAN MARTIN A. HERMAN (Acting Chairman):
For the record, this is a continuation of the public hearing on Assembly Bill 1257.

We have a long list of witnesses and we will try to stick to the time schedule as closely as we can.

My name is Martin Herman. I am the Vice Chairman of the Committee and the only member of this Committee here today. I am also sponsor of this bill, along with 27 other Assemblypersons.

Before we begin the formal testimony, I would like to make a comment or two for the record. As those of you who have been here at the previous hearing are aware, because of the large number of persons who have asked to be heard and who have been heard, I basically waive my sponsor's prerogative to present an initial, detailed and thorough evaluation of this bill, because most of you already know my position, although you may not agree with it.

I would like, however, to make a general observation in regard to the manner in which some firms in the pharmaceutical industry are approaching their opposition to this bill. As many of you who are acquainted with me know, I am blunt spoken and outspoken and do not hide my feelings.

I believe if certain pharmaceutical manufacturers desire to go to the doctors and various other medical people within my given district and ask them to express opposition to the bill, which is certainly your privilege and, certainly, that's what it is all about, to have a full and complete expression of both sides of an issue -- I would believe it would be incumbent upon you to fully express an accurate detail of what this bill does. I don't believe it is fair to say, as some doctors have called me - it is funny how these things get back to you - and said that they were told that this would completely take away the doctor's prerogative and other such things. I am not going to go into a detailed litany of what has

and hasn't been said to them.

However, I am going to read one letter from a doctor in Salem County, dated June 17, 1974. I am going to not mention his name for reasons which I think will soon become obvious. It is addressed to me.

(Reading)

"Dear Sir.

"It is my understanding that you are sponsoring Bill No. A-1257. As a practicing physician since 1946 in New Jersey, I wish to express my displeasure. I am sending you this note to voice my opinion and also for several physicians in my area. We all object to being dictated to when private practice and patients are involved. Please send me a copy of your proposed bill.

"Very truly yours,"

Now I would trust that both pharmaceutical manufacturer and physician alike would engage in the same degree of empiricism that they do in the preparation of their product as well as in the diagnosis of their respective patients before making an evaluation on proposed legislation. I would trust if you are going to ask physicians in my area or in any other area in the State of New Jersey, which is certainly your right, to oppose this bill, be so kind as to ask them to read the bill first before they make a diagnosis on the legislative patient.

With that, I see we have our first witness present, Dr. Arthur Flanagan of Warner-Chilcott. Is that correct?

D R. A R T H U R F L A N A G A N: That's right.

ASSEMBLYMAN HERMAN: For the record, I believe that I have asked Mr. Raven on behalf of Warner-Chilcott previously to answer certain questions that were put to him at the last hearing. I believe that those answers are still unavailable.

For the record, I will repeat them. The first question

was in regard to a quote in the brochure from Warner Lambert: "These amounts exclude promotional sales price reductions which have become a more important part of our marketing effort in recent years." I believe the question was put as to what was the price tag on the promotional sales price reductions as they applied to physician orientation and education. That answer has not been supplied, also the actual net promotional costs, excluding costs of the other products, such as the Certs and whatever other medical products for which there are bioequivalent substitutes today, and a critique of the Ontario par-cost law.

I might add - and I don't say this disrespectfully - that I believe it has been three or four weeks since the last hearing; and for an industry that has cried for more time for preparation, I believe that the answer to these simple questions which could be supplied, should have been supplied. And I only ask one question which may be rhetorical, why haven't these answers been supplied? I get the gut reaction that the answers may not be to the liking of this pharmaceutical manufacturer. But, if we have to, we will go to the Assembly and ask for subpoena power and maybe we will just take the subject a bit farther.

Thank you for your patience, Dr. Flanagan. If you would kindly present your testimony, I would appreciate it.

DR. FLANAGAN: Thank you, Mr. Vice Chairman, and I appreciate the opportunity of coming today and appearing before you.

For the record, I would want to identify that I am Vice President for Medical Affairs, for the Warner-Chilcott Laboratories, Division of Warner Lambert Company.

My background deals with sciences and medicine. I have a Bachelor's degree from the University of New Hampshire

and a Master's degree from Harvard University and a Medical degree from Tufts University.

Since 1960, I have been associated in one form or another with the pharmaceutical industry, and all but two years of that period with Warner Lambert in the Warner-Chilcott Division.

I have come today really to talk with you about the question of efficacy and good manufacturing practices, because I think that is the essence of the problem I have with paragraph 4 of the matter pending here today.

One might assume that any chemical substance, if it were put together with appropriate ingredients, would become equivalent to any other. I think that there are a couple of good examples which disprove that assumption. I can refer to one which may be nebulous to some because one doesn't usually think of thyroid diseases as being a problem in treatment. But people who do have an insufficiency of thyroid hormone must depend upon an outside source of thyroid hormone for their maintenance. For many years, the only source of this was glands from animals which were treated and tableted to have a potency which could be predicted and could then be duplicated day after day in these patients, because everyone doesn't need the same amount of thyroid hormone every day. It ranges over a fairly broad range.

Originally, thyroid hormones prepared from animal glands were assayed by measuring the amount of iodine present in the mix and then being sure that each batch had an equivalent amount of iodine before tableting. It was with some surprise when biological tests of that material demonstrated that the iodine assay was not very reliable - it was accurate, but not reliable - in predicting the potency of tablets produced from a given lot. So additional tests have been made of thyroid products by some manufacturers; others do not.

So while one meets the compendial specifications of

the iodine concentration of a given lot of thyroid USP, it may not have the biological potency that that chemical equivalent should have.

A second chemical inequivalence which was even more startling occurred about two years ago when some doctors at Columbia decided to investigate why certain people reacted differently to the same lot of digoxin, a drug used in the treatment of heart failure. And it was a great surprise to find that even in a given lot of digoxin, there was tablet to tablet variation of the active ingredient. This led to a full-scale investigation by the Food and Drug Administration and the resulting action on the part of the agency was to decree that all digitalis or digitoxin preparations now must have batch certification by the FDA.

These are two simple examples of two medications which are life-supporting, which may have great variability from lot to lot were it not that there is testing specifically designed now, but which was not designed a few years ago, to elucidate the potencies of various batches from various manufacturers.

In addition to chemical equivalency, I would like to mention biological equivalency and perhaps a single example will do, and that concerns a drug used in the prevention and treatment of asthma attacks. This drug is known as Tedral from the brand name point of view or TEP from the generic point of view. Three years ago, the pharmacy department at the University of Iowa wondered why their generic product, which they made themselves for use in the Iowa University complex, failed to produce the results that were expected, and certainly didn't mimic the results produced by Tedral tablets. So the Director of that division, Dr. Lark, undertook some studies to ascertain what was wrong, and was quite surprised to find

that there was a physical-chemical complexing between two of the ingredients of that tablet that they were making, namely, between phenobarbital and between theophylline. Technically theophylline is important in the product because it inhibits an enzyme which would destroy another enzyme which is responsible for the relief of bronchospasm in asthma. Taking those tablets and making the complexes and then testing the complexed material by administering it to volunteers demonstrated that there was a delay in the onset of any action of these tablets for over two hours and there was less than an ideal clinical result from the amount finally absorbed.

So in this instance a generic-type product made under the best of conditions, if you will, failed just because there was some technology not known, but which affected the ultimate availability of the drug once it was ingested by a patient.

There is a third kind of equivalency question and that is clinical equivalency. Rather than going into any further detail, I would just refer back to the Tedral versus TEP and its effects on a patient. The doctor assumes when he prescribes the drug that there is an adequate amount of active drug present, but, if it is bound to an inert or another active and thus reduces its availability, it will not produce the result desired.

There is a final concern which I would just mention in passing and, that is, that it does not really deal with equivalency so much as it deals with good manufacturing practice. And I will just mention one example since the time is short. My colleague who was the Director of the Chest Service of the San Francisco General Hospital gave me the details of a situation which occurred a few years ago on the Chest Service there. Surprisingly, there still is a TB ward for children in San Francisco General. There isoniazid, which is one of the two drugs used for treatment of tuberculosis in children, was purchased on bid from a

generic manufacturer. Shortly after it was introduced into the wards, four little girls in the ward began to have menstrual bleeding. This was a concern and it was felt that it was probably not due to the simultaneous occurrence of tumors in four children. So they went and looked at the isoniazid and determined that it was contaminated with DES, diethylstilbestrol, and that was a cogent reason for discontinuing that particular source of the product and locating a different one.

I have said quite a few things in a very short period of time, and I would go back now to try to sum up in a few statements the concerns that I have about paragraph 4.

In 1962, the late Senator Kefauver and his colleagues in passing the drug amendments of '62, introduced into the law the requirement that the Food and Drug Administration pass on the efficacy of products, as well as their safety. Prior to that time, efficacy was determined on the basis of implied efficacy because, if a drug was safe, it had to be efficacious. There were no regulations really which imposed a positive test of efficacy on those products.

Since that time, new drugs are required to positively demonstrate efficacy and old drugs have been evaluated and those which don't have sufficient of that documented evidence must supply some within a given time frame.

To provide efficacy of a drug, one must also assure there is good manufacturing practices and that a product is consistent from lot to lot. I don't consider, at least certainly at Warner-Chilcott, that we never make bad batches of drugs. But we do quality control at various times on a scheduled basis throughout the manufacture of any given drug product. And when we fail to comply with our own specifications for that product, we throw that batch away. We don't go ahead and make some adjustment in our specifications so that we can distribute it.

It is generally considered that all laboratories who produce any drug product are inspected by the Food and Drug Administration on a regular basis and, therefore, there is great comfort in buying any drug from any source because it has been produced under conditions that have satisfied the requirements of good manufacturing practices and have been investigated or inspected by the Food and Drug Administration. That is not true. It is probably one of the most common misunderstandings or misconceptions about the way in which the industry is regulated. Certainly the large companies enjoy frequent inspections by the Food and Drug Administration, but certain others don't. The one example I would cite to kind of give the extreme, if you will, was that one of the companies that was cited by Senator Kefauver in his hearings, prior to the passage of the '62 amendments, as being the example of a generic house which was a good one was, I believe, Primol Laboratories. This group apparently resisted, one way or another, any inspection by the Food and Drug Administration until last year. Finally, when it was inspected, the Food and Drug Administration went to court and closed it down for not complying with good manufacturing practices.

So, in conclusion, I would simply like to say that it is not a question in my mind of whether a drug from one source or another can provide equivalence. But I think it is incumbent upon the manufacturer of a product to demonstrate equivalence. In that light, I attended a meeting of the Advisory Council of the Food and Drug Administration on Pulmonary Disease in May of this year, and was surprised to find that in the largest area of bronchodilated therapy, there are not data which tell what the blood levels and what the effects of chronic administration of xanthine are, with the exception of data provided by our company.

I think it is incumbent upon anyone who does produce a product to demonstrate its efficacy. While it may sound trite, I would quote what someone else has said: In terms of drug costs, the most expensive drug is the one that doesn't work.

I thank you very much.

ASSEMBLYMAN HERMAN: Thank you. I have a couple of questions based on your testimony.

This concept of inspection - I would gather from your testimony that you feel that it is not widespread enough, that the Food and Drug Administration inspections are not frequent enough?

DR. FLANAGAN: It either is a matter of frequency or at all. My understanding is that there are many companies which produce drugs for intrastate use, which do not come under the ICC regulations and, therefore, are not inspected by the Food and Drug Administration.

ASSEMBLYMAN HERMAN: I gather from your testimony that you feel that this is certainly an area that should be upgraded.

DR. FLANAGAN: I don't know whether I would answer the question that it should be upgraded or rather that, in the absence of inspection, one has to find some other means of assuring himself.

ASSEMBLYMAN HERMAN: The point is that I assume you consider the quality of drugs at all levels you have testified to, to be a very important matter to the public.

DR. FLANAGAN: Absolutely.

ASSEMBLYMAN HERMAN: And one in which government should concern itself in order to assure that throughout the entire industry, the best possible product of any company is put on the market.

DR. FLANAGAN: I agree.

ASSEMBLYMAN HERMAN: Are you aware of what the U.S. Government does in the meat industry, for interstate commerce, as far as having inspectors on premises?

DR. FLANAGAN: Yes, I am acquainted with that.

ASSEMBLYMAN HERMAN: Would you object to that type of legislation, whether it be Federal or State, which would guarantee that for those drug houses doing business in interstate commerce that there be quality inspectors, using that term in its broadest sense, on premises?

DR. FLANAGAN: Yes. You know, in fact, when you produce for the military, you must produce only when there is a government inspector present in the plant.

ASSEMBLYMAN HERMAN: Is this perhaps the reason why the military has so few drugs on their list recalled?

DR. FLANAGAN: I believe so. You may have had access to the article by the head of that branch, citing the list of horrors that he has witnessed in his experience. If not, I would be glad to provide you with copies.

ASSEMBLYMAN HERMAN: That would be very kind. With no barb meant, I hope it would be a little more expeditious than the other material.

DR. FLANAGAN: I know where that one is.

ASSEMBLYMAN HERMAN: One or two other questions: I assume that you are aware that present New Jersey law allows doctors to prescribe generically.

DR. FLANAGAN: Correct.

ASSEMBLYMAN HERMAN: Then it would be up to the pharmacist to pick out the particular brand of that generic drug which he would give the patient.

DR. FLANAGAN: That is correct.

ASSEMBLYMAN HERMAN: Are you advocating that we repeal that law?

DR. FLANAGAN: No, I am not. I think my concern for the present status of that law is that it puts the burden of selection on the pharmacist who may not have available to him sufficient information about that particular product and, therefore, he is relying on what I presume is the superior authority of the state which permits a company to

be in business.

ASSEMBLYMAN HERMAN: Let's just take that for a moment a bit further. The law presently is that a pharmacist can fill a generic prescription with the brand that he sees fit if the doctor prescribes that way.

DR. FLANAGAN: Correct.

ASSEMBLYMAN HERMAN: Based on your experience in the trade, what problems have arisen because of that law?

DR. FLANAGAN: Let me cite you an example where I have facts and I am not speculating. You know in California there is a statute by which it is mandatory for anyone receiving Medicaid to get the generic product that is on the MAIC list that is put out by the Director of the Department of Health in California.

Going back again to the tederal versus the generic products, the MAIC was not awarded to tederal, but to a less expensive generic product produced by Town, Paulson and Company. We analyzed a number of generic TEP products which were available from California pharmacies, including two lots of Town-Paulson TEP. Neither of those lots complied with the compendial specifications. I can't say whether any patients were damaged or whether they failed to get the effect that was desired by the physician who prescribed the product to those patients. But I can say that they did not meet the compendial specifications for the product.

ASSEMBLYMAN HERMAN: Let me put it more specifically, if I can, by way of example. We are all aware, are we not, that percentagewise there is an increase of generic prescriptions by physicians throughout the United States, correct?

DR. FLANAGAN: I don't know, but I take your word for it.

ASSEMBLYMAN HERMAN: I want to use a drug that I used in the prior hearing for the sake of consistency,

ampicillin, produced by Squibb, Wyeth, Parke-Davis, Pfizer, Bristol, Upjohn, etc. Based on your knowledge of the trade and these companies, do you see any problem with any pharmacist prescribing any one of those brand names for ampicillin if the doctor says, "ampicillin"?

DR. FLANAGAN: I have no knowledge that would make me say that there was any problem. But I would point out every batch of ampicillin that is produced and distributed is certified by the Food and Drug Administration in their own laboratories.

This is my whole point. If every drug that were available met the same specifications as each one of those brands of ampicillin did, we wouldn't be discussing this here today.

ASSEMBLYMAN HERMAN: Fine, although I might philosophically differ with you.

DR. FLANAGAN: Let me amplify that statement, sir, because I don't know if you realize what the percent of cost of a drug product is that is related to quality control. If every manufacturer had to meet the same standards and, therefore, had to meet the same amount of expense for quality control operations within his plant, we wouldn't have these discrepancies in prices.

ASSEMBLYMAN HERMAN: Let me ask you this then, if you are using that fact as a universal: Can you tell me why then the New Jersey institutional list that is published on a bid basis -- I'll see if I can find that document. I think it is rather important. You raised an interesting question, why there should be such a wide discrepancy in pricing between products that are sold to the State of New Jersey -- and I am not talking now on a quantity basis, I am talking on an average basis that any pharmaceutical manufacturer would sell to the retail druggist, retail pharmacist -- Could you tell us, for instance, what the reason would be as far as the quality control argument is concerned?

I am now referring to Multiple Decavitamin capsules, produced by Squibb, standard packing is a thousand, price to the State of New Jersey is \$3.80. The price to the pharmacist is \$7.74. If you would like, I can go down the list, without reading brand names. This is a State contract document. Following are other items sold to the State: For instance, for one the difference per thousand is \$45.78 - \$75.89 to retail pharmacists; Bristol - sodium oxacillin, sold to the State for \$118.35, sold to the retail pharmacist for more; penicillin phenoxymethyl tablets, by Abbott, sold to the State as described here in packaging at \$2.35, sold to the retail pharmacist at \$17.50. I don't want to encumber the record with hundreds of items contained on this list and give you an item for item discrepancy. But can you tell me what that price differential would have to do with quality control?

DR. FLANAGAN: I am not an economist or businessman. But I guess in my own kind of innocent lay sense with respect to business operations that it is probably the same reason that the State gets a car sold to it at about half the retail price that you or I would pay for it, or why indigent patients don't pay as much as other patients, etc. It is not in my sense related -- at least, I don't have the facts to give you an answer other than what my intuition is.

ASSEMBLYMAN HERMAN: Doctor, I just have a gut reaction that those people in those firms that sell to the State don't do so philanthropically, that they do it with a sense of making a profit.

Thank you very much, Doctor.

DR. FLANAGAN: You're welcome. Thank you for the opportunity.

ASSEMBLYMAN HERMAN: Dr. Murray Weinstock.

D R. M U R R A Y W E I N S T O C K: I brought a few samples.

ASSEMBLYMAN HERMAN: I would ask, for the record, we note that as an exhibit of Dr. Murray Weinstock. Will you give us for the record a brief description of the packet of information that you have given us.

DR. WEINSTOCK: They are xeroxed copies of various articles concerning the things I would like to talk about today. Many of them are from different articles and only single pages. I think my discussion will make the exhibits obvious.

(Exhibits submitted by Dr. Weinstock can be found beginning on page 49A.)

ASSEMBLYMAN HERMAN: I am going to ask because of the number of witnesses that we have - and I should have announced this previously - that I would appreciate that direct testimony be kept in the area of 10 to 15 minutes at the maximum since we are running on the basis of 20 to 25 minutes per witness.

DR. WEINSTOCK: My name is Dr. Murray Weinstock. I am a graduate of Rutgers College of Pharmacy. I am a licensed pharmacist in New Jersey. I am also a physician. I practice internal medicine and cardiology. I am also Assistant Chief of Cardiology at the Bronx Veterans' Hospital. I came here because the bill was called to my attention by one of the pharmaceutical companies.

ASSEMBLYMAN HERMAN: Which one?

DR. WEINSTOCK: Warner-Chilcott.

I came at my own volition. I was not offered any money to come here nor have I asked for any money. I cancelled patients out of the office to come down today because I feel as a pharmacist and a physician quite strongly about this bill.

Perhaps the best way to proceed would be to go

into a personal experience that I had with generic drugs. About four years ago, I had a patient come into the office who had a condition of the heart called atrial fibrillation where the heart beats very quickly. There is only one drug available for this, and that is digoxin. And the more digoxin you give, the more you slow the patient's heart down. He was taking two digoxin tablets a day, which is a little unusual. Most patients take one. In spite of that, the patient's heart was going at about 140 beats per minute.

That is quite unusual. I went through the usual tests to see if there were other extenuating circumstances and there weren't. Finally, I asked the patient to bring his tablets in. It was obvious that the tablets were not Burroughs Wellcome, which are readily identifiable. I had the patient stop his own digoxin tablets and prescribed Burroughs Wellcome and when he came back to the office his pulse had dropped from 140 to about 60.

In the last two pages of the material I gave you are his two cardiograms. You don't have to be a doctor to interpret them. The next to the last one is his first cardiogram and every deviation off the base line is a heart beat. On the second page is the electrocardiogram after giving him the Burroughs Wellcome. You can see the number of blips is much less. His heart has considerably slowed down.

I had occasion to mention this to a friend of mine who is a pharmacist and he sent me the sheet that is the second sheet of what you have here. That is out of one of the pharmaceutical journals. It is called, "FDA Drug Recalls." On the lower lefthand corner, at the bottom, are a couple of batches of digoxin that were recalled from small companies, interestingly enough, here in New Jersey. The reason for their recall is given in

the last column on the right, which is content uniformity. It says reason number 4. In the middle of the second column are the reasons and you see that number 4 says, "Samples of product indicated potency ranges of from 21.2 to 242.2 per cent of declared (amount)." That is a very, very significant deviation in the amount of digoxin that is supposed to be in the tablet. 242 per cent of the amount that is stated on the label is maybe enough to kill a patient when given over a period of time.

On the next page is a reputable publication, "The Medical Letter," and you will see the next to the last paragraph says - and, by the way, this came out quite a bit after I had observed this in my own patient: "Many cardiologists now recommend Burroughs Wellcome's Lanoxin brand of digoxin, especially for patients. . . ." On the next page is the note my friend sent me from the pharmacy saying that 50 per cent of digoxin in the area was made or distributed by these small companies.

I am not here to say that every small company is a crook and a cheat and a liar. But the problem is that it is very, very hard to know which are the reliable companies and which are not. A lot of these companies are very, very small. They don't do the testing themselves. Some of them may not do it at all. Some of the companies are not subject to inspections. Some of them are purely operated as a one-man outfit. A lot of them have been closed down.

I brought some tablets along from some of these small outfits if you would like to see them. Some of the tablets are discolored. I have some where two tablets in a bottle are different sizes, decomposed and broken down.

This is the problem with generic drugs, that once you prescribe generically, you don't know what the patient

is going to get. You just don't know the company - you don't know what is going on. They may have been inspected by the FDA or someone else a year ago and things may have changed markedly since that time. You just can't take a chance on these drugs.

I know the financial problems of patients. I know they don't have money. But this is very, very serious business and I think you are making a very, very great mistake to pass this because you are opening up a Pandora's box.

Getting down to the bill here, it says in paragraph 4 that a different brand name shall be dispensed if it reflects a lower cost to the consumer. Such action by the pharmacist ---

ASSEMBLYMAN HERMAN: Read the whole paragraph.

DR. WEINSTOCK: "Notwithstanding any other law, unless the physician or other authorized prescriber explicitly states otherwise when transmitting an oral prescription or in the case of a written prescription, indicates in his own writing or by initialing an appropriate, imprinted statement, a different brand name or nonbrand name drug product of the same established name shall be dispensed by a pharmacist if such different brand name or nonbrand name drug product shall reflect a lower cost to the consumer and is contained in the latest list of approved drug products published by the council, provided, however, that such action by the pharmacist shall be authorized only if in each case the pharmacist indicates on the prescription and immediately transmits notice, either orally or by written notice to be mailed no later than the end of the business day, to the prescriber specifying the drug product actually dispensed and the name of the manufacturer thereof."

ASSEMBLYMAN HERMAN: The only reason I stopped you is because you left out the sentence or the phrase "and is contained in the latest list of approved drug products."

DR. WEINSTOCK: I don't think I left that out.

ASSEMBLYMAN HERMAN: All right. Go ahead.

DR. WEINSTOCK: First of all, I wouldn't want a brand name for myself. I have a feeling that deep down you probably want the best drug for yourself and for your family too. I think the patients are entitled to the same thing.

Now it says that a written notice shall be mailed no later than the end of the business day. The way the mail goes now, it may be a week before the physician finds out that the patient has gotten a different brand than what he had wanted for the patient. A week may be a very long time if the patient has some kind of serious infection.

Another thing - I don't want to cast disparaging remarks on pharmacists. I am a pharmacist myself and I know a lot of them. They are good friends of mine. And, by and large, they are honest people. But there are dishonest people in all professions. I think Watergate proves that. Who is going to police this? If a pharmacist writes on the back of a prescription, "Called doctor - doctor said O.K. to give cheaper brand," who is going to go around to the pharmacy and see if that is what actually happened and if the doctor actually was called? It is certainly not going to be the Board of Pharmacy because in the four years that I practiced pharmacy, I never saw an inspector in any of the stores in which I worked. I think they used to have two inspectors for the entire State. There is no way of actually checking whether the pharmacist actually did call the doctor and check on it.

A lot of the prescriptions written in the State are written by residents and internes in hospitals who are foreigners. Six months or a year later, they go back to their own country. How are you even going to check and see if they approved that change? Sometimes you can't

read the name of the doctor on the prescription and the prescription just says "Hackensack Hospital" or some other hospital. Sometimes the doctor's name is Batell; we have three Batell's at our hospital. Batell in India is like Smith in the United States. There is no way that you can be certain that in every case the pharmacist did actually contact the doctor or did notify him. There may be a long delay before the time a doctor is contacted. Sometimes the doctor may be on vacation or something else. The doctor may be dead. How are you going to check and see if the pharmacist did call the doctor?

Similarly, paragraph 6 says, "The pharmacist shall include on the label of any drug product dispensed pursuant to a prescription the brand name of such drug product, or the established name and the name of the manufacturer if a nonbrand name drug product is dispensed, except where the prescriber indicates to the contrary on the prescription." With these generic drugs, there is no way of checking that. The label can say that it is one brand of drug and it may be a brand not on the approved list. When you are dealing with a product from a large company like Squibb, each tablet has the Squibb imprint on it, the Squibb stamp. I can hold up the tablets and know that this is a Squibb product or a Lilly product or an Abbott product. When you get to the generic tablets, they have no imprint on them and there is no way of knowing when it has company X on the label, that it is not going to be company D on the inside. There is just no way of checking that.

This is the problem - there are too many loopholes in this bill, too many places where an unscrupulous person can substitute an inferior drug without the person knowing it and without the doctor knowing it. And the saving to the patient in most cases is probably not going to be a

heck of a lot and you are jeopardizing people's lives.

Digoxin, the most well-known brand of digitalis tablets, costs the average patient about three cents a day. Now why should anyone even buy a cheaper brand than that? It costs only three cents a day and yet cheaper brands are bought and used in place of digoxin. This is the problem with the whole bill here.

The worse one of all, I think, is paragraph 5. That is what sent my blood pressure up.

ASSEMBLYMAN HERMAN: What are you using for it?

DR. WEINSTOCK: I am using a generic drug. (Laughter.)

(Reading) "Notwithstanding any other law, where a different brand name or nonbrand name drug product of the same established name shall reflect a lower cost to the consumer but is not included in the latest list of approved drug products published by the council, or where in the professional judgment of the pharmacist there is no valid proof of efficacy for the drug product prescribed, or the pharmacist's patient profile record discloses drug sensitivity, allergies or adverse reactions to the drug product prescribed, or there exist a more appropriate drug product than the drug product prescribed, a different brand name or nonbrand name drug product shall be dispensed by the pharmacist. . ."

Now, according to that, if the doctor writes for penicillin and the pharmacist thinks that Carter's little liver pills is more appropriate, he can give the patient Carter's little liver pills, "provided, however, that such action by a pharmacist shall be authorized only if in each case the pharmacist notified the prescriber of the drug product to be dispensed and the name of the manufacturer thereof, and receives the approval of the prescriber to substitute such drug product for the drug product prescribed. The pharmacist shall be required to indicate on the prescription the date and time of the prescriber's

approval and whether the approval was communicated orally or in writing."

Again there is the same problem, that there is nothing in this law to provide for policing this. You can't go around and call every doctor and say, "Did you approve this or did not not approve it?" I think there is going to be a certain amount of cheating on this and substituting one brand or one completely different drug for another, and it is going to be to the detriment of the patient. I think the costs involved are only secondary here. I think the health of the patients is most important and I think that has to be the main consideration.

I think all of us in this room want the very best drug for ourselves, regardless of the fact that it costs a couple of cents more. I think all you can do is act on the patient's behalf and say, all right, the patient will have to pay a little more and it will be a little harder for them, but at least I know what they are getting and it is going to be effective for them.

ASSEMBLYMAN HERMAN: Thank you.

I have a question or two for you. First of all, for the record, you talk about dishonest pharmacists and I think it ought to be made clear, as you said, that there are many dishonest people in all trades. Is that correct?

DR. WEINSTOCK: Yes.

ASSEMBLYMAN HERMAN: If we use your argument as a comparable, I would assume we would have to be more worried about the question of the dishonest physician rather than the dishonest pharmacist if we use the Medicare fraud indictments and convictions. I think there has been only one pharmacist indicted and I don't know how many doctors have been indicted and convicted under Medicare abuses.

DR. WEINSTOCK: I don't know how many either. I think percentagewise probably not very many. I think that is really not ---

ASSEMBLYMAN HERMAN: If I were to tell you, Doctor, that to my knowledge there has only been one pharmacist indicted for Medicare abuse and a number of physicians indicted and convicted, would you change your mind and say that we need better policing of our physicians? Are you recommending that, Doctor?

DR. WEINSTOCK: No. Wait a minute. You are not being fair. The records of the Board of Pharmacy are public records. You can go through them and see how many pharmacists are cited or fined each year for substituting drugs or for other violations of the pharmacy laws. Percentagewise, again, it is not a lot. But they are there. And this is what the public has to be protected against.

ASSEMBLYMAN HERMAN: We can see how many doctors have been convicted of Medicare fraud too because that is a public record.

DR. WEINSTOCK: All right - fine. That does not change my argument.

ASSEMBLYMAN HERMAN: O.K. If you are trying to cite an example, then perhaps what we need is better policing of both the pharmacists and the doctors, right?

DR. WEINSTOCK: All right. I'll go along with that.

ASSEMBLYMAN HERMAN: Let me ask you a couple of other questions, if I may. Let's start with paragraph 5 of this particular bill. What stops a pharmacist today if he wants to cheat and substitute a cheaper drug from doing it anyway?

DR. WEINSTOCK: First of all, it is much more difficult to do it today for the reason I gave, that the name-brand drugs have their imprints stamped on them and they are easy to identify. The generic drugs - the drugs by small companies don't have that imprint. They may be completely identical in every way, except they don't have the stamp of the company on them.

ASSEMBLYMAN HERMAN: I am talking now about paragraph 5 of the bill and I would appreciate it if you would take a look at that. What stops a pharmacist today from substituting another drug if he wants to cheat, without the doctor knowing?

DR. WEINSTOCK: I am trying to explain to you why it is not easy for the pharmacist to do it. First of all, a lot of the medications that people take are taken on a chronic basis. They are taken for a long period of time. The patients know what the medication looks like and they know it has a funny little "W" on it or funny little "M" or some number on it. Once there is a substitution which does not have that on it, the patient knows he is getting something different.

Another thing, a lot of doctors like myself have elderly patients that are taking a number of medications. They are all white pills. One is once a day, another is twice a day, and yet another is three times a day. I periodically have my patients bring their medications into the office to make sure they are taking what I think they are taking. When they bring them in, I have a chance to look over the tablets. If I see that one of them is not what I have prescribed, I have called pharmacists.

ASSEMBLYMAN HERMAN: Doctor, would you say what you do with reference to the medicines is actually standard in your profession?

DR. WEINSTOCK: I think so.

ASSEMBLYMAN HERMAN: Do you think most of the doctors do that, honestly, Doctor?

DR. WEINSTOCK: I think so.

ASSEMBLYMAN HERMAN: Let me ask you this: Are you aware of what the present New Jersey law is as far as the ability of a pharmacist to call a doctor today when he thinks there should be a different prescription or there is a change called in? How about when the doctor calls

the pharmacist and says, "Change this prescription and make a notation on it"? That's the law. A doctor can do that today, can't he?

DR. WEINSTOCK: Yes.

ASSEMBLYMAN HERMAN: How is that done?

DR. WEINSTOCK: I just call the pharmacy and tell them I want the label changed to read four times a day or three times a day.

ASSEMBLYMAN HERMAN: How do you know he makes that notation on the prescription?

DR. WEINSTOCK: Well, why shouldn't he make it? I asked him to do it.

ASSEMBLYMAN HERMAN: Do you know if you go out of the state or go to practice somewhere else --- Let's reverse that cycle that you are talking about, Doctor, about the ability of the physician to find out what the pharmacist did. Let's talk about the pharmacist's ability to find out what the physician did. Where is the guarantee that we will be able to meet the reverse of the situation which you described in your testimony, which is presently the law today?

DR. WEINSTOCK: What specifically do you mean?

ASSEMBLYMAN HERMAN: -- namely, that the pharmacist can call the doctor and the doctor can call the pharmacist and make a notation on the prescription. Isn't that the law?

DR. WEINSTOCK: Of course the pharmacist can call the doctor.

ASSEMBLYMAN HERMAN: Do you disagree with that law, Doctor?

DR. WEINSTOCK: No, I don't disagree with the law.

ASSEMBLYMAN HERMAN: Then how can you disagree with paragraph 5? Doesn't that basically expand the present law?

DR. WEINSTOCK: Well, no -- It expands the present law, but I think to a much greater degree than it should

be expanded.

ASSEMBLYMAN HERMAN: Let's take them. There are only four identities, Doctor. Let's go over each of them and let's establish which ones you think shouldn't be expanded.

Number one is where a different brand name or nonbrand name drug product of the same established name shall reflect a lower cost to the consumer. Do you see anything wrong with the pharmacist taking the time to call the doctor and, if the doctor says, all right, give that to the patient - it's a good drug - it's lower cost - let's give the patient a break, dispensing that drug? Do you see anything wrong with that, Doctor?

DR. WEINSTOCK: Let me try to explain?

ASSEMBLYMAN HERMAN: No, I would like an answer to the question. Do you see anything wrong with that when the doctor says, yes?

DR. WEINSTOCK: No.

ASSEMBLYMAN HERMAN: Let me go to the second one - "where in the professional judgment of the pharmacist there is no valid proof of efficacy for the drug product prescribed." Wouldn't you as a doctor in good conscience if you prescribed a drug for which there might not be any valid proof of efficacy -- wouldn't you like the pharmacist to call you and at least have the opportunity to say, "no, leave the prescription the way it is" or "yes, I agree with you"? Do you see anything wrong with that, Doctor?

DR. WEINSTOCK: No, I don't see anything wrong.

ASSEMBLYMAN HERMAN: Let's go to the third one - "or the pharmacist's patient profile record discloses drug sensitivity, allergies or adverse reactions to the drug product prescribed." You don't see anything wrong with the pharmacist calling you in that case either?

DR. WEINSTOCK: No.

ASSEMBLYMAN HERMAN: Because it is a known fact that patients may treat with different doctors and may be taking different medicines at the same time and the patients may not communicate that fact to you. Isn't that correct? And you would want the pharmacist to call you. Is that correct? I assume by your nod, you mean, yes.

DR. WEINSTOCK: Yes.

ASSEMBLYMAN HERMAN: Let's take the fourth situation - "or there exist a more appropriate drug product than the drug product prescribed." If the pharmacist felt in his professional judgment that there was a better product around for what the patient was being treated for, you would want him to call you, wouldn't you?

DR. WEINSTOCK: Yes.

ASSEMBLYMAN HERMAN: They are the four circumstances contained in this bill in this particular paragraph. Let me carry this one step further because we have the benefit of you being both a pharmacist and a doctor. Would you tell us, Doctor, what the primary difference is in the training that a pharmacist gets in drug utilization and drug prescribing versus what a doctor gets in the normal course of going to medical school? In other words, why five years of training for a pharmacist?

DR. WEINSTOCK: That question has been debated in pharmaceutical circles for many years now. But the pharmacist is really not taught in great detail about disease.

ASSEMBLYMAN HERMAN: I want to know what the pharmacist is taught in five years? What is his function?

DR. WEINSTOCK: Well, the pharmacist's function -- he is taught how drugs work. He is taught how to prepare drugs that have to be mixed together. He is taught chemistry to a good extent. He is taught about how stable drugs are and what can be mixed with what, how stable they are

on the shelf, and a whole host of other related subjects.

ASSEMBLYMAN HERMAN: In reference to drugs and the utilization of drugs, how does the training of a pharmacist and a doctor differ?

DR. WEINSTOCK: Well, that is not a fair question.

ASSEMBLYMAN HERMAN: I know. There are a lot of unfair questions. But if you could perhaps answer it, I would appreciate it.

DR. WEINSTOCK: The difference is that the pharmacist is trained in the areas that I mentioned to you. The pharmacist knows nothing about the specific patient. The pharmacist for the rest of his life is more or less dispensing prepared preparations, whereas the physician, every hour of the day is prescribing medication and observing how that medication works on the patient and making the appropriate changes.

In other words, the physician in essence is involved the whole day in seeing how drugs work and evaluating their efficacies and studying the patients and the patients' interaction with the drugs. The pharmacist the whole day is involved more or less in preparing prescriptions for the patients' use, but is not involved in studying the effects on the patients or really evaluating the efficacy of the drugs. The pharmacist doesn't do that.

ASSEMBLYMAN HERMAN: How many drugs or medicines does an average pharmacy carry?

DR. WEINSTOCK: I would roughly estimate 20,000.

ASSEMBLYMAN HERMAN: And that pharmacist has to be familiar with those 20,000?

DR. WEINSTOCK: No, he doesn't have to be familiar with them.

ASSEMBLYMAN HERMAN: But he would have to be familiar with a great many.

DR. WEINSTOCK: No.

ASSEMBLYMAN HERMAN: Would you say that a pharmacist is basically more aware of drugs as they come out on the market than a doctor would be?

DR. WEINSTOCK: Yes.

ASSEMBLYMAN HERMAN: And isn't there a real need ---

DR. WEINSTOCK: Wait a minute. Let me take that back, that "yes." Do you mean the pharmacist knows which drugs are on the market and which are not or does he know more about what each new drug is used for and what it shouldn't be used for?

The answer to the first question is "yes." The pharmacist knows probably more than the doctor every new tablet that comes out on the market and who it is made by. As to the uses and the indications and contraindications and the reports and the literature on the drug, the physician by far has knowledge over the pharmacist in that field.

ASSEMBLYMAN HERMAN: Just personally, Doctor, because you may be the exception -- how many hours a week do you spend reviewing new drug literature?

DR. WEINSTOCK: In reviewing literature, I would say probably about six or seven hours.

ASSEMBLYMAN HERMAN: Do you think the average doctor spends that much time?

DR. WEINSTOCK: Yes, I think so.

ASSEMBLYMAN HERMAN: I hope so.

How many pharmaceutical representatives do you basically deal with - how many companies?

DR. WEINSTOCK: I don't deal with any of them.

ASSEMBLYMAN HERMAN: You don't deal with any of them?

DR. WEINSTOCK: No.

ASSEMBLYMAN HERMAN: They send the literature through the mail and you make an evaluation?

DR. WEINSTOCK: I don't make it through their literature.

ASSEMBLYMAN HERMAN: A number of doctors do though.

DR. WEINSTOCK: Some may. I can't speak for other doctors.

ASSEMBLYMAN HERMAN: But it is not an unusual practice, is it?

DR. WEINSTOCK: No, I would say it is probably not unusual.

ASSEMBLYMAN HERMAN: And most doctors will wind up primarily dealing with a few what they consider to be reputable drug houses?

DR. WEINSTOCK: Yes.

ASSEMBLYMAN HERMAN: One or two last questions: It would appear that there is a need for more inspection of drug products. Would you agree?

DR. WEINSTOCK: Very definitely.

ASSEMBLYMAN HERMAN: And the greater degree of inspections we have, certainly the greater degree of equivalencies we will have.

DR. WEINSTOCK: Well, it depends on whether or not the inspection is a cursory one and is done just ---

ASSEMBLYMAN HERMAN: Assume they are done appropriately and in accordance with good scientific practice.

DR. WEINSTOCK: If they are so done, yes.

ASSEMBLYMAN HERMAN: All right, Doctor. Thank you very much. I certainly appreciate your taking time out from your busy schedule.

Is Gerard G. Hunt here?

MR. HUNT: Could I for the sake of the figures I am going to talk about set up an easel?

ASSEMBLYMAN HERMAN: Sure. Take a few moments. Our stenographer won't mind.

G E R A R D G. H U N T: My name is Gerard G. Hunt. I am President of the Knoll Pharmaceutical Company.

We are located in Whippany, New Jersey. My firm celebrates its 70th anniversary of doing business in the United States this year and since 1923 we have been operating in New Jersey. I would like to make it clear to the Vice Chairman that I am not a professional witness, and I will probably demonstrate that. This is the first time that I have appeared before any committee like this.

ASSEMBLYMAN HERMAN: I will promise I won't bite.

MR. HUNT: Like you, I am interested in what is best for the health care system in our state. I'm proud to be in a state so heavily involved in the supply and development of medicinals which have had such a positive influence on the reduction of illness and pain throughout the world. Therefore, I am somewhat awed by your group because if anyone in the world knows the drug industry, it should be the legislators in the State of New Jersey. I don't know of any other area in the world where there is such a concentration of pharmaceutical companies. Naturally, legislation developed in New Jersey will therefore be looked upon as being perhaps the model which may be adapted in other areas.

In view of your knowledge and concern for one of the largest businesses in the state, I am going to attempt to present some ideas which hopefully will give you some new thoughts on the proposed legislation A 1257. I wish to refer specifically to comments made at the June 3, 1974 hearing which referred to the savings the public would gain in the event the A 1257 bill on substitution became law. More specifically, I am going to address myself to some remarks which were made by Mr. Joseph G. D'Amico, President of the New Jersey Pharmaceutical Association.

As you can see, I am no artist. (Mr. Hunt is referring to his charts.)

ASSEMBLYMAN HERMAN: What we will do is include the graphs in the record. We will mark them or perhaps if

you would be so kind as to take them with you and reduce them to regular-size paper, we will append them to the record.

MR. HUNT: I will be glad to do that.

Mr. D'Amico stated that the prescription market in New Jersey averages about \$300,000,000 per year of which 12% is now written generically. I would like to comment on both of these figures because apples and pears are being mixed.

When one quickly thinks of this statement one may conclude that 12% of \$300,000,000 or \$36,000,000 represents the size of the generic prescription market in New Jersey. It does not. The 12% refers to the percentage of new prescriptions which Mr. D'Amico claims are written for generics in New Jersey. According to the April 1974 issue of Pharmacy Times, the national average is 10.6% of new prescriptions are accounted for by generics.

Furthermore, when you analyze new and refilled prescriptions the percentage drops to 9.2%. There is a big difference between 9.2% and 12.0%. I suggest that these figures have been overstated by as much as 30%. Now let us take a look at the size of the

market as stated by Mr. D'Amico, \$300,000,000. In terms of new and refilled prescriptions, this would amount to about 67,415,000 or an average of 9.1 Rx's for each resident of our state. The national average is closer to 7.3 per person. Therefore, we must have a very sick population because we are running 25% above the national average. I believe that this information further substantiates my premise that you have been given inflated data. Let me take it one step further. The 1973 Survey of Buying Power which is put out by Sales Management Magazine lists the total sales of drug stores for all commodities in New Jersey to be \$464,954,000. If \$300,000,000 of this total is supposed to be for new and refilled prescriptions, this is 64.5% of their sales. The national average is 45.78%. Why is New Jersey so much higher than the national average? If we use a national average figure, our market size is more in the range of \$212,855,000 not \$300,000,000. Actually according to the buying guide the per capita sales in New Jersey drug stores is \$63.00 per person versus \$70.00 for the U.S. average. On a per household basis,

it is \$195.000 versus a U.S. average of \$217.00. So we actually spend less in drug stores than the national average. I believe then that we must work with more realistic figures if we are to accurately assess the saving impact on New Jersey which it is said will result if A 1257 becomes law.

Where will these savings come from? In order to determine this, let's look at how the total market is constructed. I will use Mr. D'Amico's figures to illustrate this.

The prescription market in New Jersey is \$300 million. Now the average markup - and these are from statistics that came out of Drug Topics - is 45 percent for the retail pharmacist. So of that \$300 million, \$135 million has to be taken off for the part that the pharmacist demands for his services. In addition we have to take 9.2 percent off because this is what the wholesaler gets in supplying the drugs. So we take off another \$27 million. So, in effect, of the \$300 million, \$138 million represents what the manufacturers get out of the total prescription market.

Mr. D'Amico further claims that the potential is 40 percent of the prescription market. Therefore, the branded products would have 60 percent of the \$138 million or \$82.8 million and the generics would be 40 percent or \$55.2 million. He also stated that the savings could be as much as \$15 million. Now these products are going to replace the so-called higher priced branded products. So the economics would be as follows:

If you have a savings of \$15 million and your total market is \$55.2 million, you are carving out 27 percent of that

as savings. We also note from the PMA that the average return that a pharmaceutical company gets on its pharmaceutical products is 9.5 percent. So in effect the savings here are three times the return that a pharmaceutical company gets. I just don't believe there is that much in there in the way of profit to support a \$15 million type of saving. We are using here the maximum figure that he said, 40 percent generic. Suppose it is 30 percent. Then this total goes down to about \$41 million. If it were 20 percent, it is only \$27 million. Therefore, the saving even looks that much more ridiculous when you look at the \$15 million total.

If we take the real size of our market, which is closer to \$212 million, here is what it looks like:

I have made the same appropriate deductions for the retail markup and for the wholesale markup, which gives us a manufacturers' total of \$97 million. The non generic total would be \$58 million and the generic market \$38 million. Therefore, this now represents 38.6 percent, assuming you get total potential out of that market. And if you reduce it to 30 percent of the market, the dollar figure drops to \$29,128,800, at 20 percent it is \$19,419,200 and at 15 percent it is \$14,564,400. A saving of this amount certainly is not realistic when you are working with total market sizes like this.

I have attempted to use the figures which you have been working with and now I would like to give you some additional facts on the current size of the generic market.

In dollars in drug stores, it represented 4.3 percent of their purchases of prescription drugs in 1973. This is a statistic from a national auditing firm that has about 800 stores in its sample. The significant part of this is that vitamins and Nutrients make up 35%, with antibiotics and laxatives being the next two most important categories at 6.5% each. I suspect that this is the reason the average generic Rx prices are quoted somewhat lower than branded because of the influence of the lower priced vitamins and nutrients. I would also ask you to study the savings which can be documented in those places where such substitution laws exist. During the past year, I have made frequent business trips to Canada. Each province has its own program. The cost of prescriptions show a 10% increase each year despite the fact that in Ontario about 25% of the market is generics and in Quebec, 20% is generic. These two provinces account for over 60% of the Canadian prescription market. In the Maritime provinces which are considered the poorer area of Canada the government is really doing everything to try

to make the program work, including setting up a central purchasing group. Despite this the average Rx price in the Maritime area is over 3% higher than the Canadian national average.

You have also indicated that a sum of \$7,500 would be appropriated to establish a Drug Utilization Review Council consisting of eight members appointed by the Governor. The Council shall be entitled to employ such technical and clerical personnel as it deems necessary within the limits of any appropriations made available therefor. Gentlemen, you are planning, through this Council, to establish drug equivalency.

The U.S. Government has not been able to do that as is evidenced by the fact that they, through the OTA (Office of Technical Assessment) have awarded a \$150,000 contract to a private health care consulting group to study the issue of drug product interchangeability. They are asking the same question you are, "Whether present day technology can determine that two drugs with the same chemical composition, but produced under different manufacturing processes will produce the same

therapeutic results." I can envision a research staff requiring an appropriation of at least one-half a million dollars annually to perform these tests most of which have not been developed yet.

I leave further comments on equivalency to the scientific community. In addition to the research costs you would have to add substantial enforcement personnel.

In closing I would like to state that the savings which you believe A 1257 will produce have been overstated and the cost of operating such a plan has been underestimated.

Keep this in mind when you think about our industry. We are competitors. You can see industry representatives here shaking hands and smiling at one another. When we hit that street outside, we are competitors and this is why our industry is no different than other major ones from the standpoint of built-in controls. My company wants to get as large a share of our markets as we can. But I have competition and this keeps us both on our toes and since equivalency of products remains

in a state of flux the present system seems to protect the consumer most adequately. Currently the New Jersey law provides for substitution if the physician has given his prior approval. This procedure has worked and the consumer, namely the patient, has been protected. What evidence has been presented to show that this system doesn't work?

I thank you very much, Mr. Vice Chairman, for letting me give these comments.

(The exhibits submitted by Mr. Hunt can be found beginning on page 64A.)

ASSEMBLYMAN HERMAN: Thank you.

Just one comment, there has been a re-evaluation of costs involved. That will be appended to the statement. It will be substantially upward, as perhaps you indicate.

Let me just ask you a couple questions if I may. You say the present New Jersey law provides for substitution and there are no problems, right?

MR. HUNT: I say that the system is working and, to my knowledge, I don't know of any problems.

ASSEMBLYMAN HERMAN: I assume, your being familiar with the industry, that if there were problems, you would be aware of them. Do you think that is a fair statement?

MR. HUNT: If they were big enough to be made known to the public, I probably would hear about them.

ASSEMBLYMAN HERMAN: Today a doctor could prescribe tetracycline generically and the pharmacist could fill it, right?

MR. HUNT: Providing the doctor indicated that the generic drug could be used.

ASSEMBLYMAN HERMAN: You don't see anything wrong with that?

MR. HUNT: No.

ASSEMBLYMAN HERMAN: O.K. Now you talk about competition. Your firm is a public company?

MR. HUNT: No.

ASSEMBLYMAN HERMAN: Your firm has pharmaceutical reps on the street --

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: (Continuing) -- servicing the entire state?

MR. HUNT: Yes. We cover the entire United States. We are not just limited to New Jersey.

ASSEMBLYMAN HERMAN: How many reps would there be, for instance, in the State of New Jersey?

MR. HUNT: I have about six.

ASSEMBLYMAN HERMAN: They cover the entire state?

MR. HUNT: Right.

ASSEMBLYMAN HERMAN: And I assume there is doctor orientation and education programs continuously conducted by your company to keep them abreast of your products?

MR. HUNT: Yes, not only of our products, but also to keep them up on their own basic medical knowledge.

ASSEMBLYMAN HERMAN: And I assume you send doctors samples or leave them samples from time to time?

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: With reference to the education and the sampling and what we might call the encouraging of doctors to be familiar with your products and, of course, encouraging their use, I would assume, what does your company spend per doctor per year?

MR. HUNT: On what?

ASSEMBLYMAN HERMAN: On education of doctors.

MR. HUNT: I wonder how you mean that. Do you mean what is our total promotional budget?

ASSEMBLYMAN HERMAN: Well, start there, yes.

MR. HUNT: I would say at this point we are running in the neighborhood of two and one-half million dollars. This is out of a seven million dollar volume.

ASSEMBLYMAN HERMAN: Out of seven million dollars gross sales?

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: And you spend two and one-half million dollars on promotion?

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: How much does your company spend on basic research?

MR. HUNT: We spend about a million and a half dollars.

ASSEMBLYMAN HERMAN: So you actually spend a million dollars more for promotion than you spend for research.

MR. HUNT: Yes. Research though, you know, is a factor of the number of products that you have to work with. If I had the products where I needed two and one-half million dollars, I am sure I could get it from my stockholders to spend that kind of money on research. Right now we only have so many products that demand that kind of a research budget.

ASSEMBLYMAN HERMAN: But it would certainly indicate that if you had more research money, you would have more gross sales too.

MR. HUNT: No, that doesn't follow. If you are lucky, it does. You know, you make that big breakthrough - you make that discovery - but so much of this stuff just goes down the drain. It is nonproductive, but you can't anticipate it.

ASSEMBLYMAN HERMAN: But you do it for a particular reason. You do it because you hope to be able to patent a product which will give you a marketing advantage over your competitors.

MR. HUNT: I think that is one of the reasons why we try to develop a product. I think we also try to develop a product to come out with something better than is already on the market.

ASSEMBLYMAN HERMAN: That also would give you a marketing advantage over your competitors.

MR. HUNT: Hopefully.

ASSEMBLYMAN HERMAN: -- especially if you have a

patent on it.

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: Because then one of two things will happen with the patent - either you will manufacture that product solely, correct?

MR. HUNT: Right.

ASSEMBLYMAN HERMAN: -- and then you will have the total market, or, two, you will be able to license that patent to other companies for manufacture, correct?

MR. HUNT: Right.

ASSEMBLYMAN HERMAN: -- which is also not a nonprofit venture. You hope to make a profit out of licensing.

MR. HUNT: Exactly.

ASSEMBLYMAN HERMAN: Where is your company located at the present time?

MR. HUNT: We are in Whippany, New Jersey.

ASSEMBLYMAN HERMAN: And you engage in the preparation, sale and distribution of generic products?

MR. HUNT: We have some. These are in the parenteral narcotic area.

ASSEMBLYMAN HERMAN: Would you be so kind as to name a few and name a few of your competitors' products which are in the market in competition with those?

MR. HUNT: Well, we make injectable morphine, injectable codeine, which are made by a number of companies. There is no one branded product there. We make meperidine, which is sold by the trade name or brand name of demerol. We also have our own trade name dilaudid, which is our narcotic preparation.

ASSEMBLYMAN HERMAN: The demerol - do you do that on that basis of licensing from another company?

MR. HUNT: No. In order to be able to manufacture that product because there is no longer any patent coverage on that, we had to submit an abbreviated new drug application

to the Food and Drug Administration before we were permitted to manufacture that. So, in effect, we had to show we had the same product that the branded product was.

ASSEMBLYMAN HERMAN: The Federal Food and Drug Administration was satisfied with that?

MR. HUNT: They passed on the application.

ASSEMBLYMAN HERMAN: Favorably, I assume.

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: Do you see anything wrong with taking your company as well as others who have likewise been approved by the Federal Food and Drug Administration for such products and saying to the pharmacist, "here are seven companies who have been approved by the Federal Food and Drug Administration for this particular drug product; you can use any one of these"?

MR. HUNT: So long as the equivalency has been demonstrated.

ASSEMBLYMAN HERMAN: Assuming that, you would have no objection?

MR. HUNT: No.

ASSEMBLYMAN HERMAN: In regard to the injectable morphine that you mentioned, how does a doctor prescribe that?

MR. HUNT: He doesn't. It is primarily a hospital item.

ASSEMBLYMAN HERMAN: And there are plenty of hospitals around.

MR. HUNT: But I want to make this clear - I don't want to bring in hospitals to your bill because I think your bill pertains to drugstores.

ASSEMBLYMAN HERMAN: Maybe my bill should be expanded. We are here for an educational process and let's get all the education we can with your expertise, if we may. This injectable morphine, how does the hospital buy it?

On what basis do they buy one product over another?

MR. HUNT: Well, they have a certain set of specifications, particularly in the case of morphine. They have certain strengths that they want, certain sizes that they want it in. They want it packaged perhaps in a certain way.

ASSEMBLYMAN HERMAN: But there are a number of companies that make equivalent products, right?

MR. HUNT: Right.

ASSEMBLYMAN HERMAN: And hospitals could be readily assured if they bought one brand versus another, that they would be getting a safe product?

MR. HUNT: Right.

ASSEMBLYMAN HERMAN: In your figures that we are dealing with, you mentioned the percentage of the market of the wholesaler?

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: And you took that across the board of the total drug sales.

MR. HUNT: Right.

ASSEMBLYMAN HERMAN: Do all drug products that flow from the manufacturing process to the retail pharmacist go through a wholesaler?

MR. HUNT: No. Some of them go direct.

ASSEMBLYMAN HERMAN: What percentage of the dollar market goes through a wholesaler to a retailer and what percentage goes directly to the retailer?

MR. HUNT: I don't know.

ASSEMBLYMAN HERMAN: Then your figures can't be accurate.

MR. HUNT: Oh, no. My figures can be accurate because the pharmacist takes that additional markup. In other words, whether it goes through the wholesaler or not, somebody gets it. If the wholesaler isn't there, then the pharmacist gets the advantage of the additional markup.

ASSEMBLYMAN HERMAN: Do you sell to the State of New Jersey?

MR. HUNT: We probably have for some of the institutions that you have here. We probably sell to them.

ASSEMBLYMAN HERMAN: Is your price different to the institutions of the State of New Jersey?

MR. HUNT: We have one price. Whether it is a private institution, one that is operated for profit-making, or whether it is a state institution, we have the same price list.

ASSEMBLYMAN HERMAN: Don't you bid for state business?

MR. HUNT: Yes, but I do the same thing with a private institution too - I bid.

ASSEMBLYMAN HERMAN: You sell to the pharmacists, don't you?

MR. HUNT: No, we only through wholesalers.

ASSEMBLYMAN HERMAN: Let me ask you this then: Is the price that eventually reaches Institutions and Agencies of the State of New Jersey from your company different than the wholesale price that eventually reaches the pharmacists?

MR. HUNT: Not on the items that we sell on bids that are branded products.

ASSEMBLYMAN HERMAN: What items are different?

MR. HUNT: The generic products are different because we don't sell those to the wholesalers. In other words, the wholesalers are not carrying my brand of morphine, etc., because these are hospital items. I have no experience in selling generics to the retail pharmacy.

ASSEMBLYMAN HERMAN: Or through the wholesaler?

MR. HUNT: Or through the wholesaler. Well, there is one case where a wholesaler in the southwest covers some hospitals, but I consider that to be hospital business.

ASSEMBLYMAN HERMAN: So you do sell branded products

though to the State of New Jersey?

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: And the price that you sell the branded product to Institutions and Agencies doesn't differ from the price to the wholesaler?

MR. HUNT: No.

ASSEMBLYMAN HERMAN: But it would differ when the wholesaler adds his markup on when it gets to the retail pharmacist?

MR. HUNT: Yes.

ASSEMBLYMAN HERMAN: So the eventual consumer will pay a substantially different price than the State of New Jersey?

MR. HUNT: Well, the point is - how are you going to get distribution? If you don't go through the wholesaler, where do I go as a small company? How do I get my product from my warehouse to the pharmacy if I don't go through a wholesaler?

ASSEMBLYMAN HERMAN: Isn't it true that most large pharmaceutical manufacturers deal directly on a retail business?

MR. HUNT: I don't know. That is your statement. I have to say that I can't do that. I have to go through the wholesaler. I would say - and I am giving you a guess - that a majority of the business that is done by retail pharmacies is done through the wholesaler.

ASSEMBLYMAN HERMAN: O.K. Thank you very much. We appreciate it.

We will now have a five-minute break.

(Short Recess)

ASSEMBLYMAN HERMAN: I would like to call the hearing back to order.

The next witness will be V. N. Willaman from Ortho Pharmaceutical Corporation.

V E R N E M . W I L L A M A N :

My name is Verne M. Willaman. I am President of Ortho Pharmaceutical Corporation, a subsidiary of Johnson & Johnson. Accompanying me at the witness table is Dr. George Braun, Vice President of Research at Ortho. We would like to thank the Committee for inviting us to testify on this important bill. Ortho is in the prescription drug business, primarily in the field of birth control. We employ over 1,000 people at our Raritan, New Jersey, facilities.

I accepted the invitation to testify here today because I agree with one of the objectives of A.1257, that being to reduce the cost of health care for the people of New Jersey. If this can be accomplished without reducing the effectiveness and/or safety of drug products, it is a worthy goal.

The issue of substitution is very complex. It involves almost all segments of the health care industry, including the physician, the pharmacist, the State medical and pharmaceutical associations and, more important than all of these combined, the patient. Let me briefly mention some of the possible problem areas.

There are questions of liability of the pharmacist, of the physician, of the possible involvement of several manufacturers in one adverse drug reaction, of the State, of the members of the Drug Utilization Review Council.

Elaborate and costly mechanisms , which have not been identified , to ensure compliance would have to be established.

It has not been demonstrated with reliability that savings to the patient will result. Implementation of such a bill should guarantee that the patient will not be harmed by substitution of a product less effective or with more side effects than the one prescribed.

There are important issues of quality control that need to be considered. A drug manufactured so poorly that it will not produce the desired effects is not only worthless , but under some circumstances could be a health hazard.

The conditions under which a medicine is made are more important than how it is named. Neither generic nor trademarked products are any better than the reliability of the company that makes them. The reputation of a quality conscious manufacturer depends on the integrity of the prescription drugs bearing that company's name.

The successful implementation of this bill rests totally on the capability of the State to prove therapeutic equivalency of drugs. It is entirely impractical, if not impossible, for New Jersey to guarantee its residents therapeutic equivalency without doing clinical evaluation in humans or without establishing large and expensive testing laboratories staffed by highly trained scientists. To our knowledge, no estimates have been made as to how much it would cost to provide the

testing programs which would be necessary to properly implement this bill.

The complex issue of therapeutic equivalency is being studied today by top medical and scientific people in the country. Recently the Congressional Office of Technology Assessment was assigned the responsibility to study drug equivalency and to attempt to resolve this very difficult issue. This group has not yet made its report.

Since therapeutic equivalency cannot be assured, except as described above, legislation which, on the basis of price alone, forces the pharmacist to substitute a drug product prescribed by a physician is not only illogical, but could cause patients to be victims of ineffective and possibly unsafe medications.

Possibly the most important issue on which this bill depends is that of therapeutic equivalency. I would like to ask Dr. Braun, Vice President of Research at Ortho, to comment briefly on this complex issue and to answer any questions you may have.

D R. G E O R G E B R A U N:

Therapeutic equivalence simply means that two different dosage forms with the same active ingredient(s) will have the same effect in terms of time of onset, duration of action, effectiveness and side effects. Therapeutic equivalence for the same active ingredient(s)

made by different companies can be established with certainty only by studying the clinical effects of the two dosage forms in patients suffering from the disease to be treated.

Neither chemical assay nor the measurement of tablet disintegration and/or release rate are sufficient to predict the potential therapeutic equivalence of two dosage forms. These tests do not measure the complex and varied factors involved in drug absorption and elimination such as gastric acidity, gastric emptying time, and intestinal alkalinity. They do not measure the biochemical events that are responsible for drug absorption, metabolism and elimination. They do not measure any possible interaction between inactive ingredients and active drug which may alter cellular availability of the drug.

The procedure which allows the most critical evaluation, short of therapeutic measurements, involves studying the metabolic profile of the two dosage forms in man. Unfortunately, methods do not exist for many, if not most, drugs which are sufficiently specific and sensitive to detect the quantity of unchanged drug in blood or urine.

Furthermore, there are few tests more difficult to carry out than those required to establish standards for therapeutic equivalence based on absorption and elimination rates of the drug. What standards will be applied to assay equivalence when a drug is to be used in treating psychotic patients over long periods of time? In this case, it

is most probably not important if one dosage form yields peak blood levels of drug in half an hour as opposed to a second dosage form which may produce peak blood levels in an hour. However, if the drug is a potent analgesic to be used for the rapid relief of intense pain, then a 15 minute lag in the time in which peak blood levels are reached may not be acceptable.

If the test drug can be shown to have a blood level profile in man essentially identical to that of the standard, one would have a high degree of confidence that the drug would be therapeutically equivalent. That confidence is lost when the profiles differ.

When they differ, and they will, we must then ask, "what tolerances are acceptable?" Blood levels within plus or minus 5% of the reference compound; within 20% of the reference compound? In most cases it is not known precisely what minimum blood level is required to produce efficacy. Most probably a standard of plus or minus 5% of the reference drug would result in efficacious blood levels. However, one's confidence drops considerably as the allowable tolerance becomes larger. The risk attendant on the low side would be potential for decreased efficacy and, on the high side, potential for increased side effects and possible overt toxicity.

In summary, short of an actual determination using clinical measurements, there is no technique presently in existence which can be em-

ployed to predict, with a high degree of confidence in a wide variety of drug products, the potential for therapeutic equivalence of the same drug in two dosage forms. The World Health Organization, in a report issued this year,¹ put it this way, "...changes in bioavailability may have important repercussions on the therapeutic and adverse effects of the drug. At present there is no satisfactory method of predicting bioavailability in man from in vitro measurements or animal studies..."

¹ BIOAVAILABILITY OF DRUGS: PRINCIPLES AND PROBLEMS

World Health Organization Techn. Rep. Ser., 1974, No. 536

Thank you.

MR. WILLAMAN:

Whether it's possible to write a bill that would resolve all of the problems mentioned, in my view, is doubtful. Even if it were possible, there are some fundamental questions that remain.

We should look very carefully at the impact this or any similar bill will have on the well-being and rights of the patient. A patient with an illness makes a free choice and selects a physician. The physician makes a diagnosis and writes a prescription for a particular medication. The physician's selection of a medication is based on his experience with that particular medication. He has confidence in it and knows what to expect in terms of effectiveness and side effects. In other words, because of his professional competence and experience, he is familiar with the patient and the product he prescribes. A pre-

scription is a written direction to the pharmacist to dispense a specific medication for the patient. While the pharmacist is knowledgeable and well trained in drug usage, drug interaction and pharmacology, he does not share the physician's intimate knowledge of the patient. In our judgment, it makes no sense for the State to intervene in this situation and enact legislation that directs the pharmacist to override the physician's judgment. What about the rights of the patient? Does the patient have nothing to say about whether his prescription is substituted? The patient, who is ill and who will be taking the medication, is now forced to take a medication different to that prescribed by his freely selected physician. And the patient has nothing to say about it.

The fact is, the physician is free today to write a generic prescription if he so chooses. And he writes generic prescriptions, leaving the choice up to the pharmacist, for those drug categories that he feels are appropriate.

In summary, for the reasons stated, we believe that A.1257 will not accomplish its stated objectives and, in fact, might create new problems for the citizens of New Jersey.

ASSEMBLYMAN HERMAN: Just a question or two, if I may.

MR. WILLAMAN: Surely.

ASSEMBLYMAN HERMAN: In reference to this doctor's professional competence and experience and ability to write - I am quoting now - "a written direction to the pharmacist,

to dispense a specific medication..." What specific written direction does he give to the pharmacist when he prescribes ampicillin or tetracycline?

MR. WILLAMAN: Well, the written direction is how to dispense the medication.

ASSEMBLYMAN HERMAN: What does that have to do with the brand of that medication?

MR. WILLAMAN: It has nothing to do with the brand. He allows the pharmacist the freedom to select the brand in that particular case.

ASSEMBLYMAN HERMAN: He trusts the pharmacist with that choice.

MR. WILLAMAN: That is correct.

ASSEMBLYMAN HERMAN: And whether a prescription is generic or by brand name, the doctor in any event will give the direction as to how it is to be used, so that is a variable that never changes whether you had a generic drug law or you didn't have one.

MR. WILLAMAN: That is correct.

ASSEMBLYMAN HERMAN: It really has nothing to do with drug substitution. Whatever the proper dosage for taking ampicillin or tetracycline may be, such as one so many times a day, what does that have to do with prescribing ampicillin or tetracycline?

MR. WILLAMAN: Well, you ask what the specific directions were that the physician gave when he prescribed the ampicillin. And in that particular case, he is instructing the pharmacist to dispense the ampicillin - he is instructing him to provide the dosage form and the frequency of tablet intake.

In the case of another type prescription where the physician specifically directs the pharmacist to dispense a brand name, then that is the other ingredient, the other element, that is added to the specific instructions.

ASSEMBLYMAN HERMAN: O.K., But let's stick with the ampicillin and tetracycline. Using the doctor's experience and professional expertise, wherein is the written specific direction to the pharmacist as far as the utilization of the best possible brand for that particular patient which you say that physician knows best?

MR. WILLAMAN: I believe the answer to that question is obvious from the fact that the physician in that particular case in his prescription allows the pharmacist to make the brand selection.

ASSEMBLYMAN HERMAN: You see nothing wrong with the physician doing that, making brand selections?

MR. WILLAMAN: In all of those cases where in the physician's judgment -- I can see absolutely nothing wrong with it.

ASSEMBLYMAN HERMAN: Now in reference to the emphasis on reliable and respectable companies in the trade, I don't think that we will deny that respectable and reliable companies have been sued for their products successfully on occasion. In other words, major drug companies have been defendants in law suits.

MR. WILLAMAN: Is that a question?

ASSEMBLYMAN HERMAN: Yes, that is a question.

MR. WILLAMAN: Yes, that is true.

ASSEMBLYMAN HERMAN: And major drug companies have been sued successfully on occasion for the "reputable product" which they have put on the market.

MR. WILLAMAN: That is true.

ASSEMBLYMAN HERMAN: Especially, I would believe, in the area of birth control there have been a number of law suits against reputable companies, successful law suits.

MR. WILLAMAN: That is true.

ASSEMBLYMAN HERMAN: In fact, there are a number of class action suits against these reputable companies in the birth control area.

MR. WILLAMAN: I am not aware of class action suits.

ASSEMBLYMAN HERMAN: Nevertheless, there has been a large amount of litigation as a result of which people have collected a substantial sum of money.

MR. WILLAMAN: Those are all true statements. I don't see how they apply to the issue of A 1257.

ASSEMBLYMAN HERMAN: Well, the point is very directly, sir, is it not, that notwithstanding the question of whether we try to throw a blanket around those who are "reputable" or "non reputable," any product is susceptible to fault or bioavailability insufficiency; isn't that correct, whether it is made by a reputable company or not?

MR. WILLAMAN: I'm sorry.

ASSEMBLYMAN HERMAN: Let me repeat the question.

MR. WILLAMAN: I don't get the pertinence.

ASSEMBLYMAN HERMAN: Notwithstanding whether you get the pertinence of the question, let me ask you the question and see whether we can get an answer to it if you understand it. Many reputable companies do have products which may not cut the mustard, so to speak, and have been recalled.

MR. WILLAMAN: I can't accept that question. Would you describe "cut the mustard"? What do you mean specifically?

ASSEMBLYMAN HERMAN: Those that have been determined to be scientifically insufficient, have not come up to standards of the trade or what has been acceptable by Federal standard.

MR. WILLAMAN: Yes, there have been product recalls, I guess, of all kinds of companies.

ASSEMBLYMAN HERMAN: That can happen to any company?

MR. WILLAMAN: That is correct.

ASSEMBLYMAN HERMAN: And that can happen to brand-name products?

MR. WILLAMAN: That is correct.

ASSEMBLYMAN HERMAN: Where is the guarantee to the physician for a brand-name product that a particular new product is not going to be subject to those same problems?

MR. WILLAMAN: There is no guarantee to a physician at all in any of these situations. We are not talking, I don't believe, an issue of a guarantee by a manufacturer; we are talking an issue of requiring a pharmacist to override a physician's judgment when the physician selects a particular product for his particular patient.

ASSEMBLYMAN HERMAN: -- according to your understanding of this particular bill.

MR. WILLAMAN: Well, in certain circumstances.

ASSEMBLYMAN HERMAN: But assuming we can overcome the physician's prerogative, then you would not see that as a problem, right?

MR. WILLAMAN: If we could overcome the physician's ---

ASSEMBLYMAN HERMAN: The question of "trying to take away the physician's prerogative".

MR. WILLAMAN: If the physician's judgment is not overridden by some regulation, then, no, I don't see anything wrong with it.

ASSEMBLYMAN HERMAN: Just a few more questions, if I may: Your company, you said was primarily engaged in the manufacture of drugs and medication for birth control.

MR. WILLAMAN: Primarily, yes.

ASSEMBLYMAN HERMAN: A national distribution?

MR. WILLAMAN: Yes.

ASSEMBLYMAN HERMAN: Just as a matter of my education, your company has employed throughout the country pharmaceutical reps who go from doctor to doctor?

MR. WILLAMAN: Yes.

ASSEMBLYMAN HERMAN: How many pharmaceutical reps does your company have in the State of New Jersey?

MR. WILLAMAN: Well, their territories are overlapping. I can't give you a precise number. I'll say approximately ten.

ASSEMBLYMAN HERMAN: To service how many doctors?

MR. WILLAMAN: I don't know the number of physicians.

ASSEMBLYMAN HERMAN: Could you tell us - this is basically the same question I asked the other gentleman because I am interested in knowing - what the gross sales of your company are and what the promotional budget and research budgets are for your company?

MR. WILLAMAN: No, sir, I can't give you that information. We do consider that proprietary information. We believe that putting information of that nature out at a public hearing would place us in an unfair competitive situation.

ASSEMBLYMAN HERMAN: Let me ask you this, if I can, without trying to infringe on your proprietary interests: Do you spend more for promotion than you do for basic research?

MR. WILLAMAN: There is no end to that line of questioning and I'm sorry but ---

ASSEMBLYMAN HERMAN: I think the answer is obvious because I don't think that that would affect your proprietary interests whatsoever.

Thank you very much. I appreciate your coming down. Thank you too, Doctor.

I understand Mr. Vickery is not here.

Our next witness will be Frank Bate.

F R A N K L. B A T E: Good morning. I have a short biographical sketch.

ASSEMBLYMAN HERMAN: We will make that part of the record. (See page 71A.)

MR. BATE: I do want to make it clear that I am here as an attorney for Merck. I am not an operating officer or familiar with the operations of that company.

I am here to make some observations concerning what I believe is in your field too, the question of liability and responsibility that is involved in this bill.

Initially, I might comment that the American system in my opinion has been built in many respects by the individual's pride in the product he produces and his willingness to put his name on that product as evidence of that pride and his responsibility for the product. That name is an assurance that the manufacturer stands behind and is responsible for its quality. This morning, I had a very fine breakfast of bacon and I have often gone to the supermarket to purchase bacon. I happen to eat Shop-Rite bacon which is about half as expensive, I think, as Swift or Armour bacon. But, nonetheless, I am amazed to find that Swift and Armour bacon remain on the supermarket shelves. Somebody must want to buy them and they must have a reason in their own minds for buying the Swift or Armour bacon rather than the Shop-Rite bacon. And I would personally hate to see a country or a system where that choice was denied to the housewife or myself. I believe the difference is their own opinion of the quality of the product. That is what makes them pay more for some products than for others.

But pharmaceutical products are not as simple as bacon, and it is not the housewife but the physician who makes the judgment. Active ingredients in most capsules and tablets which cause the so-called therapeutic equivalence or bioavailability of the product referred to in the present legislation constitute a minute fraction of the total ingredients of a capsule or tablet, most of which ingredients are the inert carriers of the drug. I have been through plants and seen how capsules and tablets are made. It is rather complex. The chemical is mixed and formulated in very intricate machinery, which may or may

not mix it thoroughly. There are various degrees of mixers. I am also familiar somewhat with that aspect of things since I represented on one occasion a person who manufactured mixers, and I know there are various qualities of mixers, for example. They are formulated, mixed together, encapsulated or tableted, packaged and marketed in quantity in a widely varying degree of meticulousness or lack thereof, and have a widely varying degree of quality control, all supervised, I concede, by our Federal government, but nonetheless the Federal agents are not there at every step of the manufacturing process in every case.

A physician may have confidence that a particular brand name, therefore, represents in his mind quality and hence he prescribes a drug by that name. If, however, under the proposed legislation he slips up and fails to put the nonsubstitution legend on the prescription in his own handwriting, the druggist must under Section 4 of the present Bill, substitute another drug and not even on the basis of his professional judgment but on the basis that it is cheaper.

Hence, for example, if the druggist in his judgment were to agree that the initially prescribed drug were of the highest quality, the druggist would have to substitute a cheaper, different drug. And this is not the end. As I read the final paragraph of Paragraph 5 of the Bill, even if the physician were to decide that the next to cheapest drug on the whole list of "therapeutically equivalent drugs" were the appropriate one for the patient and neglected to put the

handwritten legend on the prescription the druggist would have to substitute the very cheapest product omitting any option to substitute any of the higher cost items again without regard to his own or the physician's judgment as to quality.

In view of the nature of what we are talking about, i.e. life saving or life destroying agents, it would seem that this should be the last area where the sole criteria that should be applied is that of cost.

Secondly, this Bill would create a council that would make judgments concerning the therapeutic equivalency of various products. I will pass over for the moment the question of how effective \$7,500 which is appropriated for the expenses of this council will go in making the complex, including double-blind, clinical studies on each and every one of thousands of drugs available on the market today.

ASSEMBLYMAN HERMAN: You can eliminate that. That has been revised.

MR. BATE: I would think it would be revised many, many times, sic.

Let us assume, however, that this council like every other governmental (or non-governmental) agency, being human, might make an error on this subject and that a consumer/patient suffers because of this, possibly even fatally. Who is responsible? Hitherto the physician has been the pivotal point of responsibility or liability under

the law. But this physician has attempted to discharge his responsibility by prescribing a drug which he thought was well made, of high quality and of appropriate therapeutic effectiveness. The council, however, has made a judgment that other drugs are of similar effectiveness and, under my hypothesis, may be wrong. It seems to me probable that the physician has no liability any longer if the mistake was the council's, unless it would be negligence, per se, for the physician to omit the appropriate legend. However, I think in view of the fact that a governmental agency has made a decision, it might be assumed that he would be able to take protection under the fact that the duly-authorized governmental agency has made a decision that is contrary to his own judgment.

Also, if the physician-- and here is where I would recommend that the physician omit that legend, because by putting on the legend, he, himself, takes the sole responsibility for the drug that he prescribes. By omitting the legend, he spreads the responsibility between himself and the council.

ASSEMBLYMAN HERMAN: In view of the cost of malpractice insurance, maybe that is the better thing to do. Go ahead.

MR. BATE: I think you might advise a physician that this would be the wiser course - I don't know.

If he put the legend, however, on every prescription, there is no reason for this legislation at all. If that is the safest thing to do, then this legislation is meaningless because in every case the doctor will put that legend on. He would

feel he would have to write the legend if it was negligence to omit it. He would feel he would have to write the legend in order to protect himself. This would, as I say, render the present legislation meaningless.

The more likely result then would be that the physician and druggist are entitled to rely upon the findings of the council and that, hence, to fail to put the legend on a prescription is not even evidence of negligence. So the physician, hypothetically, escapes liability.

The druggist, similarly, is bound by the statute and bound by the finding of the council and he might well have no liability because he has only done what the statute required him to do, i.e. substitute a cheaper product, possibly even against his personal judgment that the original prescription was more appropriate.

The manufacturer of the substituted product, on the other hand, simply warranted that the product was what he represented the product to be and if he put appropriate warnings in his package insert, which he is required to do under the Food and Drug Administration laws, he probably escapes liability.

Of course, if one could prove that the particular drug was negligently manufactured, which I think might be difficult, this might create liability on the part of the drug manufacturer, but it would seem to me, as I say, very difficult to prove. The probabilities are that the drug was simply manufactured in a different way. It might have a different

inert ingredient than the prescribed drug.

This would leave us with the council itself for liability. But I think you are familiar with the New Jersey Tort Claims Act, where either the council or the public entity is exercising a judgment or discretion, it too escapes liability, and that goes to the individual members of the council and it goes to the public entity itself. I am sure you are also familiar with the fact that the statute of limitations, if it can be called a statute of limitations in a question of the Tort Claims Act -- as I understand it, the statute of limitations in a private action merely stops you from being able to sue on an existing action. The Sovereign State of New Jersey, however, is not subject to suit, except as it consents to be sued. And if you don't sue it in accordance with the provisions of the act, it escapes liability too.

I call your attention to something I am sure you are familiar with, the 90-day provision rather than the 2-year provision for the giving of the notice. And in the area of product liability, medical malpractice, we are all familiar with how difficult it is for the patient or the courts to determine exactly at what point a cause of action accrues. I think you may have read a recent most difficult case in the Advance Sheet in the Appellate Division, that of Seaberg v. Baldwin, which states how the courts in a private action applied equitable principles to determine when the

cause of action arose, when it should be sued upon, whereas I think under the State Tort Claims Act - I don't think it is equitable principles - the question is, did you meet the conditions of the statute by which the sovereign consented to be sued?

So I think this piece of consumer legislation may very well turn out to be an anti-consumer piece of legislation because it forecloses or greatly impedes in some instances, in my opinion, the ability of a patient who has been injured to recover.

In conclusion, not only does this Act by emphasizing cheapness over quality in this delicate field increase the hazards to the patient, but in addition it severely limits the recovery that the patient may have against anyone should a mistake be made. For this reason, I strongly urge that this committee give much further study to this matter and, I am sure, that after such study the committee will realize that this bill should not be reported out favorably.

ASSEMBLYMAN HERMAN: Mr. Bate, are you house counsel for Merck?

MP BATE: No, sir. I am an outside attorney. I am with the firm of Shanley and Fisher.

ASSEMBLYMAN HERMAN: Just a few questions, if I may: In regard to drug suits, there are many instances in which

the law is being liberalized today? Excuse me, not drug suits, the question of the ability to sue government. I assume that one of your criticisms is that you feel that in this area, if legislation such as this does come to be, that the ability to join the state should be liberalized?

MR. BATE: I would certainly assume so. I think it should go hand in hand, but there is no guarantee that it would.

ASSEMBLYMAN HERMAN: I am just asking for your comment in that respect. I assume that that is one of your comments, that it should be liberalized.

MR. BATE: Yes.

ASSEMBLYMAN HERMAN: Secondly, in reference to drug litigation in and of itself, isn't it true that when the pharmaceutical manufacturer is made successfully a party defendant, usually we talk about two areas of potential liability, one, that the drug doesn't do what the manufacturer says it will do, the doctor prescribed it and the patient took it relying on what the manufacturer said -- Correct?

MR. BATE: That is a possible cause of action if the facts warrant it.

ASSEMBLYMAN HERMAN: I am assuming the general area or theory of liability under which one would sue a pharmaceutical manufacturer is, one, that the product did not do what it was said it would do, and, conversely, that it had a bad result for the patient, the eventual user; and, two, ---

MR. BATE: Let me quickly state that, of course, there are many bad results of some drugs which are in the package insert - you know that is a potential hazard of using the drug.

ASSEMBLYMAN HERMAN: No. I am talking about those that are not disclosed and those where there is a representation made ---

MR. BATE: -- where there is a potential of liability hypothetically.

ASSEMBLYMAN HERMAN: And the other potential area of liability is that in which the manufacturing process itself may be deficient, which may create a harmful result for which liability would accrue.

MR. BATE: That is also a potential cause of action.

ASSEMBLYMAN HERMAN: So basically, as far as I understand the law, they are the two instances in which a manufacturer would be sued.

MR. BATE: I am not sure there aren't others, but at least those are two.

ASSEMBLYMAN HERMAN: Primarily. But, of course, as far as the physician is concerned in the dispensing or the prescribing of medications, we again talk about the physician's judgment as to whether he has prescribed the proper medication for that patient's ills.

MR. BATE: That's correct.

ASSEMBLYMAN HERMAN: We are talking about the usual areas of suing a doctor now for misprescription or negligence or medical malpractice in the prescribing of a drug. That is essentially where the doctor's responsibility would lie. In other words, did he prescribe the right drug for the patient?

MR. BATE: Yes.

ASSEMBLYMAN HERMAN: Under today's law, where a doctor prescribes ampicillin, for instance, which is manufactured by Squibb, Wyeth, Parke-Davis, Pfizer, Bristol, Upjohn, and others, not limiting the number of reputable companies - and let's assume that all those various companies would be on the State approved list as appropriate substitutes - if there were a bad result from the ampicillin under those standards, where would the standards of liability change?

MR. BATE: Well, there wouldn't -- in that particular instance, if in the physician's judgment he prescribed generically, then he is saying that is my opinion, I stand behind that, it is perfectly all right.

ASSEMBLYMAN HERMAN: The point is that the physician

has the right in the State of New Jersey today to prescribe generically.

MR. BATE: Right - and the right to prescribe non-generically.

ASSEMBLYMAN HERMAN: In essence, the cornerstone of most drug litigation really goes to, one, whether the physician has prescribed the right drug for the right patient - whether it matches up - correct?

MR. BATE: Right, or again, the other side of that, that it was a poorly manufactured drug.

ASSEMBLYMAN HERMAN: Based on your knowledge of litigation in this area, aren't most of the cases against the manufacturer and the physician today in the area of improper instruction to the physician as to how to dispense the drug which may give a bad result to a patient rather than the question of quality control?

MR. BATE: You kind of beg the question because if a drug didn't act properly in this particular instance, then you make an investigation why it didn't act properly. It might be that this particular drug had certain ingredients that did not have the therapeutic result that was sought by the physician.

ASSEMBLYMAN HERMAN: I think perhaps we are talking about the same thing, but around a different point.

One or two last comments in the form of a question: You talk about this pride in product, this American way. I assume you would give those same standards of pride in the American way and their products to companies such as General Motors, Ford, Chrysler?

MR. BATE: Certainly.

ASSEMBLYMAN HERMAN: Yet the American government has seen fit to enact legislation which enforces recall of automobiles and produces all sorts of enforced safety requirements and other standards that had not previously existed

in the trade.

MR. BATE: Many of which I disagree with totally. For instance, I get real up tight when I can't start the car without the seat belt on. It annoys me. I think I have a right to start my car without the seat belt.

ASSEMBLYMAN HERMAN: A lot of consumers got up tight too when their tires blew and when the steering columns didn't work and when they went into walls and some killed themselves because of no notices.

MR. BATE: I think it is an amazing thing the way our government seems rather than to emphasize some of the positive things that industry has done has continually emphasized some of the mistakes. We all make mistakes. Government makes mistakes. Governmental committees make mistakes. Pharmaceutical as well as automobile manufacturers make some mistakes. Nobody is perfect. But it is an individual's right to determine which of those manufacturers he wants to go to, despite all the mistakes that some of them may have made.

ASSEMBLYMAN HERMAN: Well, we may have a difference of philosophy. I think some of our consumers would rather stay alive and have a little more government regulation rather than having their cars wrecked.

MR. BATE: Who is to decide that, they or you?

ASSEMBLYMAN HERMAN: That's what they sent us here for. Thank you very much. It was very kind of you to appear.

Dr. Frank Malta, please.

D R. I R A N K J. M A L T A: Mr. Vice Chairman, my name is Dr. Frank J. Malta, 541 Lakehurst Road, Toms River, New Jersey. I was graduated from the Tulane School of Medicine in 1955 and I have practiced medicine at the above location for the past 13 years. I am a member of the Medical Staff at Point Pleasant Hospital, Paul Kimball

Hospital, Deborah Hospital, and I am primarily active at Community Memorial Hospital, Toms River, New Jersey, in the capacity of Attending in the Department of Medicine. I am Board Certified in the field of Internal Medicine. I am a member of the Medical Society of New Jersey and also the immediate past-president of the Ocean County Medical Society. I am also a Council member of the New Jersey Society of Internal Medicine. As a member of the Medical Society of New Jersey, I am aware of their testimony presented at a previous public hearing and I wholly support and endorse their stand against Assembly Bill 1257.

As immediate past president of the Ocean County Medical Society, please allow me to read a resolution that has been adopted by our Medical Society on April 24, 1974.

(Reading)

"Whereas, the Ocean County Medical Society is interested in the care and well-being of patients;

"Whereas, there has been a growing concern for rising cost for medications as a result of inflation, whatever the causes therein;

"Whereas, there is a growing trend on the part of those who deal in health care and its delivery to consider generic prescriptions to be equivalent to brand names of its counterpart;

"Whereas, there appears a trend on the part of states in edging towards the concept that they have the right to dictate what physicians shall prescribe for their private patients;

"Whereas, the generic versus brand therapeutic has not been resolved;

"Whereas, Assembly Bill #1257 may increase liability for pharmacists, doctors, and dentists; and

"Whereas, it has not been proven that generic

savings on prescriptions are being passed on to patients;

"Therefore, be it resolved that the New Jersey Medical Society oppose Assembly Bill #1257 until such time as it is established that generic versus brand prescriptions are equivalent in all respects;

"And furthermore, be it resolved that the physician continue to have control and responsibility in writing prescriptions that are his eminent domain and his alone, in the ultimate care and responsibility towards his patients."

Credence is supplied to these positions demanding proven bioequivalence by the World Health Organization in their Technical Report Series #536, and I quote, "Priority should be given to studies of products containing drugs used for treatment or prevention of serious illness, particularly those drugs that have steep dose-response curves, an unfavorable therapeutic index and relatively poor solubility in water. Steroids, antiepileptics, cardiac glycosides, hypoglycemic agents, coumadin, anticoagulants and certain anti-inflammatory drugs and anti-infectives are among the products that require early consideration."

In studying Assembly Bill 1257, our Society feels that the Drug Utilization Review Council falls short in the credentials required for its members. When one begins to think about bioequivalence of such complex drugs as the steroids, anti-coagulants and antibiotics, to mention just a few categories, it is hard to visualize how these eight members could perform the required testing or even evaluate the results of such testing provided by an outside source.

Dr. Schmidt of the Food and Drug Administration in a recent speech states that the FDA would set standards for appropriate conduct of bioavailability studies. It would appear to me that the Council that would be created by this bill is charting a parallel course to the FDA and

their action in establishing a list of bioequivalent drugs, if they could accomplish this task, would certainly be duplicative.

As is stated in our County's resolution, "The physician must continue to have control and the responsibility in writing prescriptions that are his domain and his alone." Any attempt to alter this situation can only impede health care delivery to the residents of New Jersey. There is no substitute for experience and only the physician possesses the experience of treating certain ailments in his patients with certain drugs. The pharmacist, trained as he may be in the areas of pharmacology, does not have this clinical experience. It is respectfully requested that the Committee now considering this bill oppose its passage.

This is the gist of the formal presentation that I have. All I am interested in as a private practicing physician is the best care for my patients. And how does a physician arrive at this position? He certainly cannot just get it out of textbooks. He has to continue with post-graduate education. He has to develop experience. Call it trial and error. Call it mistakes. But it is experience. I think this is a problem we are faced with today.

When I went to medical school in 1951 to '55, Dr. George Birch, Professor of Medicine there, a prominent cardiologist, used to emphasize over and over again to us as students that the most important thing is diagnosis. Once you make the diagnosis, you can call your wife up and she can look up in the book and read off how to treat the patient.

Twenty years have gone by since I graduated from medical school and for many years I have said, "You know, he's right. It is important to make the right diagnosis because everything is predicated on the right diagnosis."

But in the last ten years I think we have gained a lot of knowledge about generics. Before, perhaps nobody gave a second thought as to what generics were. Who cares? But now we are learning a lot. It is an educational process.

Also too, I find there is an education process that only comes with experience and time. But now we also have a situation called interaction drugs. We never heard about this in medical school. At least, if it was presented that way, it was not emphasized to the point it is today.

So I think there are a lot of questions that have to be resolved from a clinical standpoint and I don't think it can be legislated and put into practice. There may come a day when we can prescribe a product generically and have the same confidence in the generic product as in a brand-named. But I am sorry to say, as of today, I very rarely write generically, mainly because I cannot be sure where the drug product is coming from. We have heard testimony this morning about the different problems that do arise. I can cite an example I had three months ago. A patient came to me and said, "Doctor, please write me," - I'll take the brand name of meprobamate - "-- write me the generic because I hear I can get it more cheaply." I guess it must have been one of my weaker days because usually I am quite firm about not writing generic prescriptions because of these problems. I said, "Well, let me write generically." The next week the patient came in and said, "Doctor, I took one pill and it is not the same thing as that brand-name tranquilizer I was taking. I threw all the pills down into the drain."

Call it what you may, psychological, or whether there was a falsification of the generic drug, maybe it wasn't bioavailable, maybe it didn't break down, I don't know. You hear time and time again the story about aspirin. Sure, we could write acetylsalicylic acid, and give any

generic equivalent. But there are people who come in and say, "Doctor, I can't take aspirin, but I can take Anacin or I can take Bufferin." They have aspirin in them. So what is it makes it so different in a different product? It is the formulation.

I can prescribe a penicillin tablet, coated a certain way by a certain company, and I know I will get minimal side effects. On the other hand, I could prescribe a generic and my patients may have all sorts of side effects - diarrhea, vomiting, etc.

There are certain generics that I do not hesitate to prescribe if I can pinpoint the source. For instance, if I write for Parkinson treatment L'dopa, that's generic, but I know there are only two reputable companies that are making it and I know there is good quality control in these reputable firms.

Many times the point is made about the identification of pills. This is very important, important from the psychotherapeutic standpoint. The patient conditions himself to take a certain blue pill or round capsule. They get a psychotherapeutic effect from taking that pill. If you go into a generic prescription, every time they get a different tablet, they lose the psychotherapeutic effect. You can minimize it and say it is neurosis, forget about it, but this is very important in practicing medicine, the psychotherapeutic effect of drugs and the psychtherapeutic effect of a physician. This only comes with a good doctor-patient relationship.

There are many, many problems that I can think of when it comes to free substitution of generics at this time. I think our State Society has made its position, that certainly if the day comes when we can be guaranteed and assured that there will be generic equivalence, etc., certainly we would not object to a patient saving on the

cost of medication. But from my experience, it would seem no matter how you try to implement this law, it is going to be very difficult. In our area we have a certain number of chain drug stores. Many patients come in and say they want to try the chain drug stores because they hear they are a little less expensive, whether it be because more generics are prescribed or not, I don't know, but they are less expensive. But we get the least cooperation from those druggists. They are the least apt to call the doctor up and say, "Doctor, can I renew your medication," and, according to law, we are allowed to renew certain medications over the phone. So you are talking about a law that would allow the pharmacist to even take more time to call a doctor to O.K. substitution. I say it is not going to work. It means more paper work for them, more headaches for them, and it is not going to be done.

If the patient on the one hand is going to get a lower-cost generic prescription, then somewhere else the cost is going to be inflated. In other words, there is going to be another area where costs are going to be added and which the consumer is not going to benefit from. I think again in all fairness we are not ready for generic substitution as this bill proposes.

I am in favor of the doctor being responsible for the care of his patients. If he feels that a generic equivalent in his experience in dealing with certain sources, is satisfactory and he specifies the generic from Schering or generic from SKF or whatever it is, fine - this is his prerogative because he has prescribed this drug a number of times and he knows what to expect in the way of reaction from that medication. So this is his judgment as a result of his experience. You can't take that away from him. Tetracycline and all these different antibiotics have not been proven bioequivalent. In fact, the other day I got a notice

from Eaton Laboratories saying that their Furadantin was found by the FDA to have the most consistent bioavailability. So what is the physician supposed to do, write generic Nitrofurantoin? The problem was mentioned this morning about Digoxin. Are we supposed to write drugs where we can expect by their use certain biological effects and take chances with our patients and one time have a patient get an overdose and another time an underdose. Take Coumadin, an anticoagulant. I would hate to prescribe a generic anticoagulant because this drug is so critical in its effect on the blood as far as the prothrombin time, which is a particular test that we use to regulate the anti-coagulation of blood, that if each time the patient took a different brand-named generic of which we have no way of standardizing the potency, the patient is going to be in danger. One time he might hemorrhage to death and another time he may form clots from being undercoagulated.

So I think this is a difficult thing for a physician in practice in contradistinction to a hospital environment where hospital physicians and pharmacists are there that can help screen out generics and allow the physician to select generics from their formulary, and also allow the physician to select certain proprietary brand names because they have been proven from their experience to be the most reputable and reliable for patient usage. But when you get out into private practice, it is a completely different situation. You are putting the burden of substitution on the shoulders of the pharmacist who does not have the clinical experience in dealing with patients. He can read up on the pharmacology action of the drug, but its consistency in the patient, the uniformity of the medication, the reliability, are what counts.

I think again when we get away from the area of medicine, we all run to the named brands; and, better yet, if you can get a generic appliance and know that it came from

GE or some other brand name, that is tremendous because you have a big saving. This is what is in the back of the minds of most people. You want reliability when you buy a product. You don't want to buy a cheap brand and find after you use it once you have to throw it down the drain. Then you have lost money; you haven't saved anything. You lost money. I think this happens time and time again. When you go out and buy a suit of clothes, it is wonderful to get a suit that was made by some name brand and have some generic label put in it and get it for half price.

Somewhere along the line there is going to be an equalization point. If you suddenly start putting controls on the generic companies to get the guarantees and controls that are on the other drug companies, then the generics are going to have to raise their costs. They can't do it if they are putting drugs out so cheaply. These are the questions I keep asking myself. Thank you very much.

ASSEMBLYMAN HERMAN: You're welcome.

Just a couple of questions: You mentioned tetracycline and your concern about prescribing it. I assume that that concern can't be shared by too many other doctors. I understand from the information I have that out of the first 50 drugs prescribed in the United States, that ranks fourth.

DR. MALTA: I don't know how other doctors conduct their practices. All I can tell you is that I do my best to stay up in my field. I am certified. I subscribe to Clinic Alert, to Drug Letters, and all these things help to point out certain problems with drugs. My experience with the physicians that I deal with in my small locality is that they do not as a rule prescribe generic antibiotics because of the problems that have occurred in the past.

ASSEMBLYMAN HERMAN: Somebody has to prescribe these drugs. And if my information is correct that tetracycline

ranks number four and ampicillin ranks number seven, somebody is prescribing them.

DR. MALTA: Is this in hospital practice or in general practice?

ASSEMBLYMAN HERMAN: Prescriptions.

DR. MALTA: I think that is important to know that because ---

ASSEMBLYMAN HERMAN: New and refilled prescriptions.

DR. MALTA: As I pointed out earlier, if a hospital formulary committee of doctors and pharmacists agree that a certain brand tetracycline, whether it be from Smith, Kline and French or whatever source it is coming from, is going to be filled generically, if that is the big statistics you are getting there, that is not a reflection of what is actually going on in private practice.

ASSEMBLYMAN HERMAN: Let's stop right there, Doctor. As a member of the medical profession, you would be reasonably assured if such a group as you have just described in preparing such a hospital formulary would make such a list, to use it.

DR. MALTA: No, I wouldn't. I would only be responsible to me, to my immediate peers, to the people with which I have contact; I will not be responsible or respond to this Council that is proposed. I certainly would go along with the FDA and what they are trying to do. They have broken the ice on this.

ASSEMBLYMAN HERMAN: If the FDA were to publish a bioequivalent list --

DR. MALTA: Yes, if the FDA approved a bioequivalent, just like I quoted to you the Furadantin, I would accept it. I accepted their work on Furadantin.

ASSEMBLYMAN HERMAN: Then if New Jersey would use such a list, you would have no objection?

DR. MALTA: If they would, but I want guarantee and assurance that there would be adequate controls because we

know there are many laws on the books that are not enforceable. You can say this is the law of the land and everybody is supposed to comply. That may or may not be the case. It is the enforcement that counts. If you can't enforce it, don't put it on the books.

ASSEMBLYMAN HERMAN: Do you have a Physician's Desk Reference?

DR. MALTA: The PDR? Yes.

ASSEMBLYMAN HERMAN: What is the purpose of the PDR?

DR. MALTA: For me, it is just a quick reference for a particular drug product that I perhaps may not be exactly familiar with. For instance, if a patient comes in and shows me some pills he is taking, I might reach for the PDR and quickly identify them.

ASSEMBLYMAN HERMAN: Is it issued yearly?

DR. MALTA: Yes.

ASSEMBLYMAN HERMAN: It is used by doctors as a desk reference for drugs?

DR. MALTA: Yes.

ASSEMBLYMAN HERMAN: And it contains approximately how many drugs?

DR. MALTA: I have no idea.

ASSEMBLYMAN HERMAN: But thousands I would think, and the purpose is to give the doctor an ability to find out in a paragraph or two just exactly what a drug is all about and what it does.

DR. MALTA: In sketch form, yes. It doesn't tell everything about the drug, but has, at least, some of the package insert information that according to law has to be provided with the samples.

ASSEMBLYMAN HERMAN: The reason for the use of a type of - I guess we would call it an encyclical document - is because it is impossible for any profession to keep up

on every drug that is put out.

DR. MALTA: That may be true, but that would not be the Bible as far as I am concerned. It is a desk reference - that's all it is. It is not a text book on pharmacology; it is not a clinical reporting. It is a quick reference for the spelling of a name or quick information on a product, and that's all it is.

ASSEMBLYMAN HERMAN: Can I ask you, Doctor, just as a matter of your practice - and then we will get on to our next witness - how many pharmaceutical representatives do you deal with? Do you limit it to two, three or four?

DR. MALTA: I try to give the courtesy to every pharmaceutical man that arrives at the office.

ASSEMBLYMAN HERMAN: Approximately?

DR. MALTA: I see on the average maybe one or two a week - maybe three or four a week.

ASSEMBLYMAN HERMAN: Do you deal primarily with the same companies?

DR. MALTA: By and large, yes.

ASSEMBLYMAN HERMAN: On an average, if we can break that down - not to pin you to a definitive number - would it be fair to say you primarily deal with maybe three or four companies, reputable drug houses?

DR. MALTA: For prescription purposes?

ASSEMBLYMAN HERMAN: For prescription or educational purposes.

DR. MALTA: No, I don't.

ASSEMBLYMAN HERMAN: What would that number be?

DR. MALTA: I have no idea if you want me to pinpoint it down.

ASSEMBLYMAN HERMAN: As far as the every-day working relationship, I think you have testified to a limited number of companies that you deal with. I assume time is a problem too.

DR. MALTA: That's right.

ASSEMBLYMAN HERMAN: What is that number?

DR. MALTA: Let me put it this way and explain to you - I do not use the pharmaceutical representatives to educate me in pharmacology or what is good for my patients. As I explained to you, I do my best to keep up post graduate training, to be aware of adverse effects, etc. And I feel most of the physicians in our area are doing exactly that. Maybe in remote areas, the pharmaceutical or detail man may perhaps pass on information to the physician in the form of an educational process about the actions of drugs, etc. But I, myself, look at the sales representatives of companies as representatives. I treat them as gentlemen as I do anyone else who comes to my office. I give them a minimal amount of my time because I feel that they want to introduce products to me. I may be familiar with them - I may not - all well and good. Whatever they say to me about products, I do not take as gospel truth. If a representative says this product will result in less diarrhea, I take it with a grain of salt. I wait for my own clinical experience to prove this out.

ASSEMBLYMAN HERMAN: Could we get to the number?

DR. MALTA: I have no way of telling you the number. I would say on the average I spend two to three ---

ASSEMBLYMAN HERMAN: I think your earlier testimony was ---

DR. MALTA: I give them maybe one minute of my time or two minutes, just enough to come in and show me the product and let me worry about the pharmacology and the use, etc.

ASSEMBLYMAN HERMAN: I think you also testified that you deal primarily with a relatively small number of companies.

DR. MALTA: I would say about seven or eight or under a dozen, if you want a specific number. Under a

dozen detail me regularly. This is not to mention the mail that comes in from many, many sources.

ASSEMBLYMAN HERMAN: By the way, as far as sample products that are sent to your office - and I assume that we could use you as an average practicing physician from the standpoint of patient hours and time in the office, etc. - how many pills or sample medicines would you say come to your office per week?

DR. MALTA: I can't give you an estimate. Many of these things I actively solicit for various reasons. One, they are a source of savings to the patient. If a patient comes in who I feel is having a difficult time getting prescription drugs, I may pass on the samples to that individual. The purpose of using these drugs many times is to start them out as samples; that is, a patient taking a drug today is inexperienced. There are problems with allergies and so forth. Many times I would rather not write a prescription for 30, 40 or 50 pills, have the patient go home and take one and find he is allergic to it, that it disagrees with him, that he vomits. I use the samples as starting doses. That is what I believe they are designed for, starter doses. In some instances, I go beyond that.

ASSEMBLYMAN HERMAN: I am interested in unsolicited, coming-through-the-mail, here-it-is sort of pills and medicine. How much of that do you get?

DR. MALTA: Very minimal. Most of the companies now have embarked on a program to do minimal soliciting through the mail and do it only upon specific signature request. So what I get now through the mail is specific because I requested it because I want it for my office.

ASSEMBLYMAN HERMAN: Thank you very much. I appreciate your taking your time to come down.

DR. MALTA: Thank you.

ASSEMBLYMAN HERMAN: Is Sandy Helton present?

(Member of the audience advised she had to leave, but indicated she would submit a statement for the record.)

William R. Jones, McNeil Laboratories.

W I L L I A M R. J O N E S: Assemblyman Herman, I am William R. Jones, Executive Director, Control Division of McNeil Laboratories, located at Fort. Washington, Pennsylvania, a subsidiary of Johnson and Johnson, New Brunswick, New Jersey. I appreciate the opportunity to appear before you today to comment on Assembly Bill 1257.

It is our opinion that AB1257 should not be reported out favorably by this committee. When a physician prescribes a specific drug for a patient, that specific medication should be given to the patient and no other. The judgment of the therapeutic results of a medicine can only be made by the physician in cooperation with his patient, and the quality of the medicine dispensed affects those results. Thus it must be in the best interests of the patient to care for him under a system which continues to permit his physician to select those pharmaceutical products which he knows are of the highest quality and which his experience tells him will deliver the best results.

We are particularly concerned about the provision which

permits dosage form exchange whereby a Council may determine that no substantial therapeutic difference will result when one product is substituted for another. It is our feeling to permit such a provision exposes the residents of this state to a risk that should not be taken. Over my years of experience, which now exceed 25 with the industry plus association in earlier years with the family retail pharmacy, I have seen quite a disparity between so-called product chemical equivalents - that is, chemical equivalents as defined by this proposed bill. This difference relates amongst other things to the quality of the product. The unfortunate part about this is that in many instances the difference cannot be detected by a simple analysis of the product or by a protocol of analysis furnished by the manufacturer.

If I might take a few minutes and relate the basis of a sound quality program as exercised by responsible manufacturers in the business, you may be able to pick out areas which would leave questions in your minds if you were to entrust to a Council (and I in no way want to reflect on

the ability of such a Council) the assignment of assuring that in a dosage form exchange no substantial therapeutic difference would result.

Quality in our operation is based upon the premise that each product, prior to introduction to the market, moves through the clinic in order to establish safety and effectiveness. Once the safety and effectiveness has been established in the clinic for a given product made under standard manufacturing and control procedures, specifications for both the active component(s) and the excipient materials are established as well as chemical and physical parameters for the finished dosage form. Each batch of the product made from that point on must conform to the standards established in order to assure uniform response from the dosage unit over the period of time the patient is exposed to it. In addition a stability profile for the product is developed which enables us to assure the consumer that upon taking the product within its stated shelf life, he may expect the same safety and efficacy results as the day the product is made. Keep in mind the council must

attest to this program in absentia from the plant where the product is made.

Coupled with this, and in my opinion the most important unmeasurable facet of this entire subject, is the philosophy and procedures under which responsible manufacturers operate. It might be simply summarized by stating that we start with the compendial requirements and Current Good Manufacturing Practices regulations as a baseline and build from that point a total quality program to assure a product of highest quality, thus minimizing any consumer risk. If good programs do not exist, if adequate training of personnel does not take place, if top management is indifferent, then there is no telling what can go wrong in a pharmaceutical plant resulting in a defective product even though the product may meet the definition of "chemically equivalent." Ladies and gentlemen, I assure you if something can go wrong it will go wrong and only a concerted quality effort on the part of all personnel will avoid a sub-standard product from reaching the marketplace. Can any person or any group removed from day to day operations pass judgment

on each and every batch and each and every product produced and come up with a list of substitutable products that would be equivalent in all respects? This, I think you will agree, is quite an assignment.

Let me take you on a short trip through a plant and cite a few hypothetical but quite possible examples of how product deficiencies occur, deficiencies not detected by ordinary analytical means. Picture, if you will, a mixture of material passing through a metal screen. The screen breaks and metal enters the product. What are the choices now open to the management of this firm? There is no hesitation in my mind stating the first thought coming to responsible managements mind is the destruction of the entire batch or destruction of the identifiable portion if it can be isolated. Less than responsible management, I suspect, might attempt to cull the material and move on, knowing there will be little chance of having any of the metal present detected. A hazard? Possibly. A risk? No question. A second element also arises in this same situation. The screen must be replaced. If the same

mesh size is available, fine, and a responsible firm's program would require it. Others less diligent might feel if the same size screen is not available, then one close to it will fill the bill. But will it? We have seen differences in our plant on availability of the active component due to minor differences in screen size. Chemically equivalent? Yes. Equivalent availability? Questionable.

Let me close off our plant tour by citing just one more example. Picture, if you will, how misleading an analysis on a final product might be if one checks only for the labeled claim and a gross adulteration has taken place in the manufacturing cycle because of less than diligent quality production. How can one determine, for example, if a lethal dose of atropine sulfate is inadvertently added to an otherwise safe dosage form? No routine analysis will pick this up and only a cataclysmic event will bring it to light. This is where management attitude, sound procedures, and dedicated, competent employees come into play. This is what total control of quality is all about and no "list" will automatically bring it into being.

I hope I have depicted the risk that one assumes in granting automatic substitution powers matching an unknown against a known. We in the business of quality like to feel we are the consumers' representative at the plant, especially since we and our families are also consumers.

And if I might close with a quote taken from a recent talk by Mr. F. B. Whitlock, Chairman of the Board of Directors of PMA and Vice Chairman of the Board of Directors of Johnson & Johnson, speaking on the occasion of the Fiftieth Anniversary of the PMA Quality Control Section, he stated:

"You, ladies and gentlemen, spend your lives enhancing drug quality, raising drug standards, and thereby protecting ill consumers from inferior pharmaceuticals, however unintentionally produced. In a literal sense, you are what this industry is about."

We trust our efforts will not be negated by a blanket authority to use any product in lieu of the one prescribed. Thank you for this opportunity to present these comments.

ASSEMBLYMAN HERMAN: Just one or two questions.

MR. JONES: Yes, sir.

ASSEMBLYMAN HERMAN: Does your company produce generics?

MR. JONES: We have generic products, yes.

ASSEMBLYMAN HERMAN: Perhaps for the record you could give us a generic product which is also produced by other reliable companies.

MR. JONES: I can't think of one in the prescription drug field, Mr. Herman.

ASSEMBLYMAN HERMAN: Now we are talking about over-the-counter drugs?

MR. JONES: Over-the-counter drugs.

ASSEMBLYMAN HERMAN: Would you perhaps enlighten us in that area?

MR. JONES: Acetaminophen tablets.

ASSEMBLYMAN HERMAN: What would be your competitors?

MR. JONES: There are probably 50 or 60 in the market place today.

ASSEMBLYMAN HERMAN: Good ones? Acceptable ones?

MR. JONES: I have no way of judging that.

ASSEMBLYMAN HERMAN: You know that some of them are decent - are acceptable. Are you trying to say that yours is the only acceptable product?

MR. JONES: I think it is the best.

ASSEMBLYMAN HERMAN: Is it the only acceptable product?

MR. JONES: I have no way of telling unless I test the other ones to find out totally.

ASSEMBLYMAN HERMAN: By the way, in your pharmaceutical manufacturing process, do you license any of the patents you hold to others to use?

MR. JONES: Not to my knowledge.

ASSEMBLYMAN HERMAN: Are you a licensee of any particular drug products? I see your counsel or somebody nodding his head in the back of the room.

MR. JONES: In which direction?

ASSEMBLYMAN HERMAN: The gentleman who was seated next to you.

MR. JONES: I know of none.

ASSEMBLYMAN HERMAN: All right. Thank you very much. I appreciate your coming down to spend some time with us.

We will stand adjourned for lunch and start promptly at two o'clock.

(Recess for Lunch)

AFTERNOON SESSION

ASSEMBLYMAN HERMAN: I'd like to call the hearing back to order.

Our first witness will be Mr. Foley from the Department of Health. Mr. Foley.

D O N A L D J. F O L E Y: Mr. Chairman, I am Donald J. Foley, Chief of Drug Control, Division of Narcotic and Drug Abuse Control, New Jersey Department of Health.

I am appearing here on behalf of Commissioner Joanne E. Finley, M.D., Commissioner of Health. Dr. Finley wishes to thank the Chairman and the Committee for the opportunity to comment on the proposed amended version of Assembly 1257.

Commissioner Finley has had an opportunity to review the Department's comments and testimony given before this Committee on June 3, 1974. The Commissioner feels that the testimony is still pertinent. The Commissioner wishes to thank the Committee for the opportunity to prepare a fiscal note regarding the operation of the Drug Utilization Review Council.

If the Chairman or members of the Committee have questions pertaining to the Council operations, the Commissioner would be most happy to reply.

Thank you.

ASSEMBLYMAN HERMAN: Mr. Foley, on behalf of the members of our Committee, I wish to thank you and the Commissioner for taking the time to appear at the last hearing and this hearing, and for the detailed preparation of this memorandum.

I would instruct the stenographer to attach this memorandum, in regard to a proposed cost for a Drug Utilization Review Council, to the transcript of this hearing.

Again, Mr. Foley, thank you very much

MR. FOLEY: Thank you, sir. (see page 40A)

ASSEMBLYMAN HERMAN: Dr. G. Graham will be our next witness.

D R. G A R T H K. G R A H A M: I am Dr. Garth K. Graham. I am a physician. I am a graduate of Harvard Medical School. I am a Fellow of the American College of Physicians and, until about four weeks ago, in the private solo practice of internal medicine. I am now a Manager of Medical Affairs for Smith, Kline & French Laboratories in Philadelphia.

Accompanying me today is Donald K. Fletcher, Manager of Legislative, Pharmacy and Health Programs for Smith, Kline & French.

With the Chairman's permission, I should like to make a short summary statement and, in the interest of time, file for your consideration a longer, written statement of position on Assembly Bill 1257.

ASSEMBLYMAN HERMAN: That will be satisfactory.

DR. GRAHAM: Thank you.

My personal feeling of urgency in being here is born, really, of over 20 years of private practice in medicine, far more than my very brief tenure in the pharmaceutical industry. I would beg you to consider my remarks in the light of the professional relationships between your own physicians and yourself and your family and, indeed, your constituents.

With the vast armamentarium of drugs now at his disposal, the careful practicing physician bears an awesome responsibility both morally and legally in prescribing the safest and most effective medication, or combination of medications, that are possible in the treatment of his patient in a given illness.

The pharmacist bears an equal responsibility

in his area in implementing this treatment program as carefully and as accurately as possible.

The patient also, having been told in many cases - certainly it was my practice frequently to describe, specifically, the medication - what he is to receive and the importance to him of its proper use, should rightfully expect to receive the exact preparation offered by his physician.

The Assembly Bill 1257, as I have read and interpreted it, would certainly dilute these responsibilities and abridge these rights.

On the other hand, in many communities the degree of interprofessional respect and cooperation between physicians and pharmacists is such that by prior consultation and agreement, either case by case or on a continuing basis, substitution of appropriate products known to the physician to be equivalent in efficacy and safety and whose source is generally known to the physician, can be made within the framework of present laws.

However, this prerogative should be the exception, based on such mutual trust and respect and not a legislative rule.

More formal and continuing agreements have, in some communities, been used by physicians and pharmacists toward this agreed degree of substitution. These agreements completely fill the need of both professionals and certainly minimize the risk to the ultimate goal, which is the care of the patient.

I think it was obvious in previous testimony - and it is my feeling - that, certainly, a real core issue of this legislation is the matter of the totality of bioequivalence - one drug equaling another in all areas of effectiveness and safety. The careful and scientific resolution of this issue is, as we

have heard, at this very moment the subject of a major effort at the Federal level.

The Congressional office of Technology Assessment, chaired by Senator Kennedy, is conducting at this time a full-scale investigation and study of this issue. Certainly any decision by this Committee on this legislation could be embarrassingly premature, unless it awaits the final results of the O.T.A. probe.

Mr. Chairman, I appreciate this opportunity to present this summary statement and hope that my written statement herewith submitted will be of further assistance in your deliberations.

I would also like to add, parenthetically, two or three other thoughts that have come to my mind as I have thought about this particular type of legislation.

It has been said in other testimony, and I have heard elsewhere, that comments are made that if a physician in one breath states that he feels strongly about his prerogatives to indicate on his prescription the brand name and the source of a given medication, and then in another breath admits to the occasional use of generic prescribing, that he is contradicting himself. On the other hand, too, I think, really, this is the exercise - if it is done conscientiously - of his prerogative. The use of a generic prescription from time to time is a perfectly reasonable thing to do when there are a number of good products on the market and, most especially, when he knows his pharmacist and when he knows the particular group of products which might be used to fill a generic prescription. So, this is not an inconsistency when we use both.

Also, as I read the law and thought about it in relation to the practice of medicine, it would

seem to me that the communications between the physician and the pharmacist are actually well covered, merely by the fact that it is legal to give telephone prescriptions in most instances.

At this particular time, the only need for the legislation in question would seem to me to be that related to the economics of the costs of prescription drugs. Yet, at this particular stage in the evaluation of bioequivalency - of the evaluation by the physician of various drug preparations, etc. - there certainly would appear to be a very reasonable doubt that equivalency is the same regardless of cost and there would certainly seem to be quite a reasonable question as to whether there may be, to some degree, really a direct lineal relationship between the quality of the product and the price. This takes into consideration matters of the development of the product, quality control, etc.

I thank you for listening to our views.

ASSEMBLYMAN HERMAN: Thank you. Mr. Fletcher, do you wish to say something?

MR. FLETCHER: I am here to help with any questions you may have. We would be happy to entertain them.

ASSEMBLYMAN HERMAN: I have a copy of your very nice booklet - your annual statement. It is a nice deep blue. It does raise a couple of questions which I will get to.

I believe you stated earlier, Dr. Graham, that you believe that the relationship and the ability to substitute - the working relationship - between the doctor and the pharmacist is one that should be left untampered with and unencumbered by legislation, is that correct?

DR. GRAHAM: I don't think I used those words

but I think that is the gist of my comments.

ASSEMBLYMAN HERMAN: Yet, isn't it the New Jersey law, as it now exists, which enables that relationship to exist? Doesn't the doctor prescribe by generic drug if he sees fit? Isn't that a matter of law or legislative permission?

DR. GRAHAM: Legislative permission in this case is fine, yes.

ASSEMBLYMAN HERMAN: But it is a matter of legislation which has created the situation which you say should exist.

DR. GRAHAM: I think, however, one would find that as long, again, as there is a telephone communication and as long as there is a law allowing the legality of telephone communication in a prescription, that this covers all of the eventualities of communication - what should be prescribed and what the physician requires and what the pharmacist, in his good practice, will dispense.

ASSEMBLYMAN HERMAN: And you are not worried about the possible fraud or misuse of the doctor telephoning the pharmacist, or the pharmacist telephoning the doctor?

DR. GRAHAM: I am always worried about this fraud, or misuse, and have been throughout practice. There are good safeguards that he and I have commonly used.

ASSEMBLYMAN HERMAN: But, by and large, throughout the medical profession as well as the pharmacy profession it is not a real concern when the doctor picks up the telephone as long as he knows the pharmacist?

DR. GRAHAM: Day-by-day, I don't think there is a concern.

ASSEMBLYMAN HERMAN: All right. Because there was, earlier, a concern raised by a witness and I just

wanted to get your views on that.

In reference to Smith, Kline and French, I note from this brochure that on page 2 - and I quote from the middle of the fifth paragraph - "Smith, Kline and French continued their strong financial support of research and development programs and established ourselves in developing branded generic market with our 'S-K' line, a line of high quality, low cost, widely used ethical drug products."

Could you tell us, sir, how this line of products differs from your other products? Either gentleman can answer that question.

MR. FLETCHER: Assemblyman Herman, I think our 'S-K' line and the desire for an 'S-K' line was motivated, a great deal, in the same way that, perhaps, your legislation is motivated - to save people money. However, we believe--

ASSEMBLYMAN HERMAN: Excuse me, before you continue -- Do some of the products in this line have branded equivalents manufactured by your company?

MR. FLETCHER: By our company?

ASSEMBLYMAN HERMAN: Yes.

MR. FLETCHER: No, they do not.

ASSEMBLYMAN HERMAN: How about branded equivalents by other companies?

MR. FLETCHER: Yes, they certainly do.

ASSEMBLYMAN HERMAN: And you consider your products equal to or superior to those products?

MR. FLETCHER: We certainly consider them equal, yes.

ASSEMBLYMAN HERMAN: Could you give us a couple of examples, just for the purpose of record, where, your 'S-K' line - your branded generic - would be equivalent to other branded names?

MR. FLETCHER: Well, one such as S-K 65 would be equivalent to Lilly's Darvon.

ASSEMBLYMAN HERMAN: What is the price differential between those two products?

MR. FLETCHER: The price differential on the one example I gave is something like 50%.

ASSEMBLYMAN HERMAN: Could you give us, basically, retail dollars and cents - as best you can?

MR. FLETCHER: Really, I can't.

ASSEMBLYMAN HERMAN: Your product is 50% less?

MR. FLETCHER: It is about 50% less.

ASSEMBLYMAN HERMAN: And, in your opinion, based on your professional expertise, it is as good?

MR. FLETCHER: Yes. It has the assurance and the quality control guarantee and company liability trust of Smith, Kline & French.

ASSEMBLYMAN HERMAN: I am interested. Could you give us a couple of examples?

MR. FLETCHER: Well, it would be a great deal easier if I had some of my literature on the S-K line with me. I think it is sufficient to say that--

ASSEMBLYMAN HERMAN: Excuse me, I don't mean to interrupt you but could you, perhaps, send us some of that literature on the S-K line and, perhaps-- I am sure some of the other members of the Committee would be interested in knowing just exactly what the price differentials are.

Would you do that for us?

MR. FLETCHER: I certainly can, and I will.

ASSEMBLYMAN HERMAN: We would appreciate it.

MR. FLETCHER: The point I would like to make about price differentials is that all you can ever give in the area of pharmaceutical pricing are approximations, because they don't exactly coincide. But as a general rule, this is a fair statement. The price is

approximately 50%, on that particular example that I gave you.

ASSEMBLYMAN HERMAN: Let me ask you this. I am very intrigued by your comment. In this area-- What is your brand again? I am sorry. S-K 65?

MR. FLETCHER: Yes, we are calling it S-K 65. It is a propoxyphene.

ASSEMBLYMAN HERMAN: How much of this would you say is used on a national basis? How much would you say in gross dollars - not just of your product but of that entire product?

MR. FLETCHER: I don't-- Do you mean of the whole area?

ASSEMBLYMAN HERMAN: No, just one particular --

MR. FLETCHER: I can't answer that question, Assemblyman.

ASSEMBLYMAN HERMAN: Well, I would assume that if Darvon sells in the millions of dollars in retail sales, that if everyone used your brand they would save half of that; which means that the many millions, just in that one item alone - without giving you an undue plug here - would produce almost a 50% saving.

MR. FLETCHER: It doesn't exactly work that way though because you have to realize that this is a voluntary situation in which the doctor has accepted the reputation and trust of the manufacturer. He knows what it is and has written for it. He writes for it.

ASSEMBLYMAN HERMAN: The branded generic product?

MR. FLETCHER: Right.

ASSEMBLYMAN HERMAN: Yes. I think we agree there. It is based on his familiarity with the company and the drug representative and all those other things which

would increase his familiarity with a given product over the years, right?

MR. FLETCHER: Well, I would like the examples of what I was speaking of - trust in the company and the guarantee that it gives the product.

ASSEMBLYMAN HERMAN: Yet, with a little more trust and a little more public information, just in that one product alone - using your company's example - the public could be saving millions of dollars a year.

MR. FLETCHER: The idea, of course, of the increase in generic prescriptions - which you, yourself have mentioned on a number of occasions - I think, is an example of the fact that physicians are prescribing them more and are finding occasions where they can trust them.

There are examples, which have been mentioned before, of course, of antibiotics - where there is government testing batch-for-batch and they have some assurance.

I think that some of this is coming and it is coming, perhaps, in a more rational, proven fashion, rather than us being dropped into the pot before we are quite ready to swim.

ASSEMBLYMAN HERMAN: Okay. If public hearings were held by an administrative agency, such as a Drug Utilization Council - assuming that one were created by law - and they were to say, well, these are the drugs that we want to put on this particular list and if they were made available for public inspection and evaluation by the various drug companies, there would be a way that the drug companies would have to come back and say, yes, you can do that, or no, you can't do that - just like you have come in to appear before me today.

MR. FLETCHER: Well, there is a hearing

mechanism established with your law.

ASSEMBLYMAN HERMAN: Yes.

MR. FLETCHER: I think that there is a mechanism, though, that presumes this also can assure equivalence. I think that is a question that you virtually decided on in your legislation. The Federal Government is still asking itself that question.

ASSEMBLYMAN HERMAN: Let's get to the one question that I asked. If I were to say, as part of a Drug Utilization Council, that we intend to consider this particular generic drug - let's take tetracycline as an example - and we are going to consider the following brands as generically equivalent, your company, as well as the other drug companies, would be in a position to say, yes, you can do that; no, you can't do that. You can then appear at a public hearing to give your opinion on that particular drug product, isn't that correct?

MR. FLETCHER: We would show up and demonstrate the evidence of equivalence that each of us has. I think the point has been made that this is difficult and there may not even be technology as yet to assess that.

That, again, is what the O.T.A. study is all about, to determine all of this. A great deal of what we are doing today is on the matter of trust and reputation.

ASSEMBLYMAN HERMAN: But there are some things that can be established and some items that can't be established, correct?

DR. GRAHAM: This we don't know yet.

ASSEMBLYMAN HERMAN: I beg your pardon? I don't think that was your answer.

MR. FLETCHER: Whether or not we know if all of this technology exists or not? We know some of it does not exist.

ASSEMBLYMAN HERMAN: On the other hand, some of it does exist.

MR. FLETCHER: Yes, sir.

ASSEMBLYMAN HERMAN: And for those products for which it does exist, I would assume you don't have any objection to the public getting the best possible product at the lowest price.

MR. FLETCHER: Well, the technology is not always product exclusive. In other words, you often times need several technologies in one product line.

ASSEMBLYMAN HERMAN: But as a general principle I assume you are not against the public getting the best possible product at the lowest price?

MR. FLETCHER: I don't believe anyone here has been.

ASSEMBLYMAN HERMAN: In fact, that is one of the reasons for your S-K line, it is a competitive line, isn't it?

MR. FLETCHER: It certainly is.

ASSEMBLYMAN HERMAN: I'd like to make reference to another paragraph in your report. I quote, starting at the bottom of page 5 - "During 1973, we continued to experience competition to our tranquilizer, Thorazine - our brand of Chlorpromazine - for which the patent expired in 1970. Despite the competition, we were pleased with the performance of this product. We are confident that the continued acceptance of Thorazine by physicians and our wide range of dosage forms will enable us to maintain a strong position in the Chlorpromazine market."

Now, in reference to this particular patented Thorazine, the patent ran out, right?

MR. FLETCHER: Yes.

ASSEMBLYMAN HERMAN: Is the price of Thorazine the same as it was in 1970, today?

MR. FLETCHER: It is lower. We have lowered our price.

ASSEMBLYMAN HERMAN: Why?

MR. FLETCHER: Competition.

ASSEMBLYMAN HERMAN: What do you mean by the wide range of dosage forms in that report?

MR. FLETCHER: There are a number of strengths. There are different dosage forms. There are time release dosage forms; suppositories; liquids, injectables, etc.

ASSEMBLYMAN HERMAN: Just a few more questions, if I may.

You make the print big. You should read it.

MR. FLETCHER: We should have brought our copy.

ASSEMBLYMAN HERMAN: I would be happy to let you look.

On page 26, it says that your sales in 1972 were - I am rounding these off for the record - \$402 million and in 1793 they were \$744 million. They have royalties and other income - 6½ million in 1973. Does your company license other firms to produce any patented product?

MR. FLETCHER: I would say that must be referring to something like that. Our line is so extensive, involving animal health products and electronics, that I can't really give you any details on that.

ASSEMBLYMAN HERMAN: Do you have any idea, without pinning you down here because I assume it is all lumped into one -- It says that your marketing, administrative and general expenses were almost \$171 million in 1973 and over \$152 million in 1972. Research and development was \$40,234,000 in 1973 compared to \$38,400,000 in 1972. Do you know how much of that marketing, administrative and general budget is for

pharmaceutical advertising of product lines or is that all of it, or most of it, or a part of it?

MR. FLETCHER: It is obviously a part of it, Assemblyman Herman. I have no idea how much of it is though.

ASSEMBLYMAN HERMAN: I was just wondering, with all of this talk about research and development as the reasons for stabilizing prices and keeping them up, just why there appears - and it is not just your firm - to be such a substantial increase of marketing costs over research costs. Is there a reason for that in the trade?

MR. FLETCHER: I think you are making assumptions there that I would like to speak to.

I don't know that I can answer the question, but the assumption is that the \$40 million, which is not at all large in the brand name company industry, is part of a product price - any product price - and it is part of the way the pharmaceutical industry carries a very unique research program on. It is not government supported.

ASSEMBLYMAN HERMAN: That is not the point I am raising.

MR. FLETCHER: I don't really know how much we spend on promotion versus research.

ASSEMBLYMAN HERMAN: It just appears that from all these records that I have seen, all these statements - I am not going to burden the record by going through every company - you talk about two and three and four times the amount of promotional costs versus the amount of research and development costs and I just thought there might be a particular reason for the difference.

MR. FLETCHER: You have a lump figure of

one hundred and something million dollars for administration and a number of other items. You are comparing that \$40 million for pharmaceutical research where the heavy burden is. Now, we can't really compare these things. Even if I had the figures, I probably couldn't do a very effective job; I'd want a different setting to compare them in.

ASSEMBLYMAN HERMAN: It appears to be general. I just made the observation.

I want to thank you both for taking the time to appear here today. Your more formal written statement will be spread upon the record. (see page 44A)

If you would be so kind as to, perhaps, supplement the record by way of a letter with regard to your other line, I'd certainly appreciate it.

Marvin R. Friedman, please?

M A R V I N R. F R I E D M A N: My name is Marvin Friedman. I am a pharmacist engaged in community practice. I am a partner in the Frederick Pharmacy, located in New Milford, New Jersey - Bergen County.

I'd like to first quote from "A Talk with Bob Johnson", as reported in American Druggist Magazine, June 15, 1974. I quote - "There is absolutely no sound reason, medically or economically, for the anti-substitution laws to remain in effect today. If a pharmacist is not capable of judging the quality and efficacy of the drug product to be dispensed to a patient, then who is? If we have spent 4, 5, or 6 years of our life obtaining a highly specialized education in pharmaceuticals and then lack the capability of simply selecting the manufacturer of the drug product to be dispensed, we have wasted a hell of a lot of our time and the educational institutions in which we spent these 4, 5 or 6 years have shortchanged us like nothing

in the history of this country".

I responded, in a letter to the editor, as follows: "I agree with Mr. Johnson that there is absolutely no sound economic reason for the anti-substitution laws to remain in effect. There is every sound reason medically for them to remain in force. I submit that a pharmacist is not in any position, nor capable of judging, the quality and efficacy of a drug product to be dispensed.

"Mr. Johnson asks, 'Who is?'. My reply is, the only person who is qualified to so judge is the prescriber thereof. How the hell am I, as a pharmacist, to judge and determine the therapeutic effect of any medication on any patient? I may not even see the patient, if the prescription is picked up by a member of the family, or if I deliver it. How the hell am I to judge effect when I don't know exactly the condition, or extent thereof, for which it was prescribed?

"I don't consider my education wasted as a pharmacist. For a physician, it would be. I am not a physician, nor am I attempting to usurp a physician's prerogatives or obligations. Am I supposed to take the time to travel to each manufacturing plant and inspect its facilities to insure that they conform to certain minimum standards? What are those minimum standards? Am I supposed to check the chemical, biological, and bioavailability assays on each batch of each drug to insure that they meet with accepted standards of purity and therapeutic equivalency? I can't even find the time to go fishing, let alone do all this.

"I am willing to accept the products of major pharmaceutical firms as being of excellent quality and not misrepresented in any manner. Other than the reputation of the manufacturer, what am I supposed to use as a guide to quality? Am I supposed to accept

the legal liability involved in substituting on a physician's prescription? What if the drug I substitute doesn't perform up to the doctor's expectations, and he alleges that, had I dispensed exactly what he ordered, the patient would have responded? I am then legally liable. This I refuse to accept.

"My education enables me to recommend medication, or alternate medication, to the prescriber. The ultimate decision, and responsibility therefore, resides with him. This is what my education has fitted me for; to check on the physician, insure that he is aware of potential drug interactions, overdosages, etc. - in other words, to act as the final safety factor between physician and patient. That is my function. I utterly deny myself the right to do any more."

Mr. Johnson has further stated, "I am not going to suggest that there is necessarily therapeutic equivalence among multi-source drug products. The question I raise is, is potential inequivalence any indication of therapeutic ineffectiveness? To suggest that drug products are of poor quality because there may be inequivalence is an unfortunate delusion that has been perpetrated upon the profession and the public. Our scientists should forthrightly address this question rather than contribute to the prolongation of the 'equivalency smoke screen' fostered by some elements within the drug industry."

My response - "To suggest that drug products are of poor quality because there may be inequivalence, is certainly a delusion. However, to expect the physician to accept any inequivalence in medication for his patient is patently absurd. The physician, who is accustomed to using a particular drug, is familiar with its effects, should continue to be assured that when

he orders that drug, his patient will receive no other. His expectation of results should be founded in fact.

"To dispense any other drug, which may or may not exert the exact therapeutic result, would be an act of criminal negligence, and any pharmacist who would do so, should have his license revoked, as a danger to the community. No pharmacist, scientist, or other, can determine the effect of any medication in any physician's patient. Only the physician, who sees the patient before and after medication, can possibly be the judge of therapeutic effectiveness."

I might add to the foregoing, that there frequently are individual reactions to almost any medication, which, again, only a physician can recognize and allow for in his treatment of a patient.

Recognition of individual idiosyncracies, or untoward individual reactions, decision as to whether to alter dosage and continue or discontinue the specific medication, all lie within the judgment and prerogative of the physician.

As a practicing community pharmacist, it is immaterial to me what brand of drug I dispense. My charge to the patient is based on a fee system, whereby I profit the same, irrespective of the cost of the medication to me. Those proponents of substitution can only argue that substitution, or generic prescribing, would result in substantial economic advantages to the patient. I disagree. As one example of varying prices on the same drug, I submit the following information:

100 Achromycin V capsules 250mg strength, purchased from my wholesaler would cost me \$4.68. The same drug, the same quantity, purchased by me directly from the manufacturer - from Lederle - would cost me \$3.90.

The purchase of a bottle of 1,000 capsules from

Lederle - my cost, \$37.95

Lederle's price, per 1,000 on 3,000 capsules -
\$27.00.

Lederle has available a larger quantity deal, which
I split with another pharmacy - cost per thousand,
\$19.35.

I might point out, that breaks down to a cost
of \$1.93 per hundred, as opposed to a high cost of
\$4.68 per hundred.

The major source of price differential is really
not between brand name and generic drugs, but between
the varying prices charged by the manufacturer himself.
The quantity which any pharmacy purchases, and the price
therefor, is dictated by purely economic and business
factors - how fast will that quantity of drug turn over
in his pharmacy? This situation is typical of the
majority of pharmaceutical manufacturers. Another sore
point regarding price is the wide disparity between
prices, charged by the same manufacturer for the same
drug, to a community pharmacy and to a federal or state
institution. The difference can be more than tenfold.

One specific study of drug prices which came
to my attention, through the courtesy of Assemblyman
Ed Hines, is the Ontario study. This study which
compared prices of tetracycline and stated that there
was a difference between a high of \$50.60 per 100
capsules, and a low of \$4.70 per 100 capsules, was in
gross error. The comparison made used Vibramycin as
the source of the high price. Vibramycin is DOXYCYCLINE,
not tetracycline, and could never be substituted for
tetracycline. The highest price I pay for any brand
of tetracycline is \$16.37 per 100 capsules from my
wholesaler, and is for Tetrex, manufactured by Bristol
Laboratories.

I might add here, that I have seen and read
a copy of the testimony of Joseph D'Amico, President of

the New Jersey Pharmaceutical Association, in which he stated facts on an in-depth analysis of the New Jersey prescription market. The best information that I have been able to obtain regarding the facts and figures which he quoted is that this was not from an in-depth analysis of the New Jersey market, but were figures taken from a national analysis and were extrapolated on the basis of population density to conform and be applicable to New Jersey.

I question, seriously, the accuracy and voracity of the figures he stated.

Certainly, a pharmacist cognizant of the costs of medication and faced with competition from other pharmacies, is going to try to keep costs of medication down as much as possible through good business practices and management.

In line with this, I might add that, according to statistics published by the U. S. Department of Labor, medication and prescription drug costs have increased less than most other phases of the economy. Further, I quote from a letter to me, dated June 5, 1974, from Dr. William R. Barclay, Assistant Executive Vice President of the American Medical Association:

"Insofar as drug price is concerned, the AMA has long supported the position that physicians should be conscious of the prices of drugs and, whenever consistent with good therapy, to order drugs that will cost the patient less. We do not accept the premise, however, that generic prescribing is automatically synonymous with lowest price. Neither are we persuaded that there is enough evidence at hand to automatically assume equivalence by all parameters of measurement of so-called identical drugs. As is well known, the question of bioavailability and therapeutic

equivalence of drugs is far from resolved; many instances come to mind where a lack of equivalence has been demonstrated in the clinical setting."

Certainly, there are times when a physician, for purely psychological reasons, will order a particular brand of a drug. Color, shape, size, taste, etc., may, and often will, affect whether or not the patient will take the medication.

The best medication in the world is useless until it enters the patient's bloodstream. I refer to a situation which took place in my pharmacy last Wednesday, when a physician ordered three prescriptions for three members of the same family - two prescriptions for Sumycin and one for Achromycin-V. Generically the drugs are identical - yet, they are different in appearance. Why the physician chose to do this is his business, not mine.

In the area of generic prescribing, we have learned in recent years that we have to consider not only the active ingredient of a tablet or capsule, but also excipients, fillers, stabilizing agents, disintegrating agents, etc., which are used in combination with the active ingredient, and which may, and often do, affect absorption of the medicinal ingredient and therefore affect therapeutic effectiveness.

Witness the recent change in assay requirements on chloramphenicol and digoxin. What I am afraid of is, how much else do we still have to learn? While it is true that a generic house will purchase quantities of drugs from major ethical manufacturers, they will be the ones, not their supplier, who will formulate that medical ingredient into tablet or capsule or liquid form. As I have stated, the other ingredients used in conjunction with the therapeutic ingredient can have a definite effect on bioavailability

of the drug. If it is not up to accepted standards of the physician, the patient will be the person to suffer.

I do not believe that there would be substantial economic savings to the public involved in a right-to-substitute law. Necessary safeguards incorporated in such a law, costs of testing and assaying, would very possibly exceed any savings to the public. Since these administrative and laboratory costs would be paid for out of tax dollars, it is conceivable that the public might wind up paying more for drugs than it now costs under our present system.

I feel very strongly that physician and pharmacist are a necessary team, dedicated to the health and welfare of the patient. Legal permissiveness to the contrary notwithstanding, I will not substitute on a physician's prescription without his specific consent.

This particular bill is onerous and unworkable, in that it requires a pharmacist to compromise his ethics and places an onus upon him to contact a physician and advise him either of his intent to substitute or of the fact that he has done so after the fact. The amount of paperwork would become not merely unwieldy, but impossible. It would drastically slow down a pharmacist, enable him to fill fewer prescriptions in the same amount of time, thereby reducing his productiveness and, as a consequence, force the price of prescriptions to go up to compensate therefor.

I am sure that you have been amply warned of the possible consequences of permitting open substitution without adequate safeguards. However, I would like to suggest to you a possible solution to the question of substitution which would satisfy all parties concerned, including physicians, and which would not compromise the

ethics of either the medical or pharmaceutical professions. All you would have to do would be to place into law a bill requiring one of the following statements to be printed on each prescription blank:

1. Do not substitute.
2. Generic or equivalent drug substitute may be dispensed.
3. Unless checked here, generic or equivalent drug substitute may be dispensed.

The utilization of either of these statements, would permit the decision of whether or not to permit a pharmacist to substitute to remain wholly within the province of the physician, where it rightfully belongs. The statement used would either permit or deny a pharmacist the right to engage in drug substitution and, if permitted, would be with the physician's specific consent.

There would be no further paperwork involved, and the pharmacist would not acquire any legal liability since he would always be acting according to the specific instructions of the physician.

Of course, the question of which brand to use would be within the discretion of the pharmacist, just as it is now when the physician prescribes a drug by its generic name. Unless you question the quality of those drugs now being dispensed on generic orders, there would be no need for a state formulary, or a drug review council. There would be no additional expense to the taxpayers. The onus of compliance with such a law would be on the prescriber, where it belongs.

It is easy to criticize anything and somewhat harder to suggest a viable solution to an existing problem. I think that I have done so and respectfully submit the same for your consideration. I thank you for

hearing me. If you have any questions, I will answer them to the best of my ability.

ASSEMBLYMAN HERMAN: Thank you very much. I have just a few questions.

In reference to pricing, in your pharmacy do you -- In reference to Penicillin G, is that called Pentids? Am I pronouncing that correctly? Produced by Squibb--

MR. FRIEDMAN: Yes.

ASSEMBLYMAN HERMAN: What does that sell for?

MR. FRIEDMAN: Truthfully, I don't remember the price. It does come in three strengths.

ASSEMBLYMAN HERMAN: How about 400,000 units?

MR. FRIEDMAN: 400,000 units would probably be about 12 or 13¢ per tablet to the patient.

ASSEMBLYMAN HERMAN: What would it be per hundred - about \$13.00 per hundred?

MR. FRIEDMAN: No, it would be less. It would be substantially less.

ASSEMBLYMAN HERMAN: What would you sell it for, approximately?

MR. FRIEDMAN: Perhaps \$6.00 or \$7.00 per hundred.

ASSEMBLYMAN HERMAN: Do you carry Wyeth's Penicillin?

MR. FRIEDMAN: No, I do not.

ASSEMBLYMAN HERMAN: Do you carry any other brand of Penicillin G?

MR. FRIEDMAN: I carry a generic brand.

ASSEMBLYMAN HERMAN: What is that?

MR. FRIEDMAN: It is made by Shine.

ASSEMBLYMAN HERMAN: And how much does that sell for?

MR. FRIEDMAN: Well, 100 to a patient would be approximately \$4.00.

ASSEMBLYMAN HERMAN: I assume, based on your

very thorough testimony that you certainly wouldn't carry anything in your pharmacy that you didn't feel was a good product.

MR. FRIEDMAN: No, I would not.

ASSEMBLYMAN HERMAN: Tetracycline, 250 - is is milligrams?

MR. FRIEDMAN: Yes.

ASSEMBLYMAN HERMAN: Do you carry Bristol's Tetrex?

MR. FRIEDMAN: Yes, I do.

ASSEMBLYMAN HERMAN: How much does that sell for per 100?

MR. FRIEDMAN: Well, it costs me \$16.37 per hundred. If I were to sell a bottle of 100, it would be approximately \$20.00.

ASSEMBLYMAN HERMAN: How about-- Do you carry any other brands?

MR. FRIEDMAN: Many. Too many.

ASSEMBLYMAN HERMAN: How about some that you consider decent and acceptable?

MR. FRIEDMAN: Lederle's Achromycin V. I mention that in my testimony.

ASSEMBLYMAN HERMAN: How much is that?

MR. FRIEDMAN: It costs me \$1.93 per 100. My price for 100 to the patient would be about \$6.00

ASSEMBLYMAN HERMAN: About \$6.00 per 100?

MR. FRIEDMAN: That is correct.

May I point out to you, again, though, the difference is based on my cost. If I were buying 100 Achromycin V, then it would cost me \$4.80.

ASSEMBLYMAN HERMAN: How about Reserpine, 25 milligrams?

MR. FRIEDMAN: That's very inexpensive. Even Serpasil, which is Ciba's brand name of that drug is relatively inexpensive.

ASSEMBLYMAN HERMAN: About \$4.50 per 100?

MR. FRIEDMAN: I don't know the price off hand.

ASSEMBLYMAN HERMAN: How about Lilly's brand?

MR. FRIEDMAN: I don't carry it.

ASSEMBLYMAN HERMAN: How about any other generic?

MR. FRIEDMAN: I carry none other.

May I submit one other thing to you?

ASSEMBLYMAN HERMAN: Sure.

MR. FRIEDMAN: You questioned the price of penicillin. It is a rare situation where any person gets a prescription for 100 tablets. Usually this is limited to a --

ASSEMBLYMAN HERMAN: Well, the price comparatives are relative aren't they?

MR. FRIEDMAN: Not really. It depends on usage. The only person who would be taking 100 tablets of penicillin at a time would be a rheumatic fever victim where they take it for a long period of time. The usual course of therapy comprises maybe 12, 16 or 20 tablets.

ASSEMBLYMAN HERMAN: Let's take that same example. I do not want to belabor this. Tell me what the difference in price would be between the generic brand that you mentioned for Penicillin G and the Squibb brand for the same amount of tablets.

MR. FRIEDMAN: The average quantity on a prescription - let's say it is 20 tablets; that would be five days of therapy for an infection, so it would be about \$3.50 or \$3.75 for 20 tablets of Pentids.

ASSEMBLYMAN HERMAN: That's the Squibb product?

MR. FRIEDMAN: That's the Squibb product. It might be, perhaps, 50¢ less - if that - for a comparable generic brand.

ASSEMBLYMAN HERMAN: And there is that wide divergence when you get to the price of 100?

MR. FRIEDMAN: Simply because there is not that much difference in the cost between 20 tablets of one and 20 tablets of the other.

I take the cost and add a professional fee.

ASSEMBLYMAN HERMAN: But there is a difference between 100 of one and 100 of another - a substantial difference?

MR. FRIEDMAN: Sure.

ASSEMBLYMAN HERMAN: That is a degree of economics that is, perhaps, just beyond me.

I want to thank you very much for appearing and taking your time to come down from Bergen County.

MR. FRIEDMAN: Thank you for hearing me.

ASSEMBLYMAN HERMAN: You are quite welcome.

Dr. Mary Hall.

D R. M A R Y H A L L: My full name is Mary Benson Hall. I am a graduate of the School of Medicine of the University of Pennsylvania. I have been in private practice here in Trenton since 1957 and my practice is devoted 100% to allergic diseases.

I am past chairman of the Pharmacy Committee at Helene Fuld Hospital and since May, I am President of the New Jersey Allergy Society.

I have to say that I am not officially representing the Allergy Society today. We haven't had a chance to convene our Executive Committee, so I am really speaking here today as a practicing physician.

For an allergic patient it is possible that there is absolutely no therapeutic equivalency between generic brands. Medicines, as they are compounded today - tablets, capsules, liquids - contain numerous ingredients in addition to the active principal which gives it its name.

These would be coloring agents, flavorings, fillers, excipients which are added for stability, etc.

Dr. Steven Locke of Lancaster, Pennsylvania, who has a well established reputation in the field of allergy, has devoted a lifetime of work in tracking down the causes of allergic reactions to medicines. He has demonstrated to us, over and over again, that a patient's reaction may not be caused by the active ingredient but, rather, by coloring agents or by some of the other numerous additives, or flavoring agents.

A simple clinical example I could give you, for instance, would be an allowable food coloring - F D & C #5, tartrazine - which imparts a yellow color to food or drug, but if you recall your elementary art, yellow and red make orange and yellow and blue make green. So, this tartrazine may be other than just yellow colored medication. This is capable of causing an allergic reaction, such as hives, angioedema, asthma, rashes, etc. in a patient who is sensitized to tartrazine.

Now, I have to grant you that this sensitivity is not rampant in the general public and it isn't really rampant in the allergic community but for that poor patient who is so sensitized, it is a very important factor. It produces a second illness in addition to the one for which the medicine was originally prescribed in the first place.

To elaborate on this a little bit further - we were talking about antibiotics - tetracycline, for instance - and Mr. Friedman mentioned Achromycin; that is a blue and yellow colored capsule. Some of the other popular colors -- Sumycin is pink; Pfizer's Tetracycline is brown and white. Now, if this patient goes to the drug store with a prescription for tetracycline written generically, or goes with his prescription written for Tetracyn and the pharmacist

is allowed to give this and I'm sure you're likely to have an allergic reaction.

So, there has to be an additional control in here. I don't think the pharmacist should have blanket permission to substitute from their stock because of some of these situations.

Now, this is just a single example. I brought with me some of Doctor Locke's information. I copied it. I am not supposed to copy it without his permission, so I don't think I ought to leave it with the Committee.

ASSEMBLYMAN HERMAN: You are more than welcome, if you do get his permission, to give it to us. We will append it as part of the record.

DR. HALL: All right. I will write for his permission. I could read some of it here.

For instance, the therapeutic Unicaps contain four different potential sensitizers in addition to tartrazine, so if you have a substitution for a therapeutic vitamin this could be a possibility. Premarin, which is an estrogen, contains 7 potential sensitizers. Pyribenzamine, an antihistamine used for allergic conditions, contains two potential sensitizers. Polaramine REPETABS, also an antihistamine, contains about 11 potential sensitizers.

The point I want to make is that there are other ingredients in the medications than just the active ingredient.

This is also very important with pediatric practice where you are giving a patient a liquid preparation. The pharmacist today is very good in the way he compounds liquid preparations for children. Their flavoring agents are terrific. But if you have a child that just isn't going to take licorice flavor but he will take cherry flavored preparations -- I

find in my practice as an allergist, one of the broncho-dilator preparations - one of the very popular ones - is licorice flavored. I find very few children will take this. The competing brand has lemon flavoring. Another one has a cherry flavor. If the pharmacist is allowed to substitute there, I may find that the mother can't get the medicine into the child.

This is also true in antibiotics, with the difference in flavor in antibiotic preparations. I think this is a very important factor. I have had this happen. I have, on occasion, written for a generic prescription for some of the antibiotics and then it has turned out that the pharmacist has dispensed a flavor which was unsuitable for that child and the mother couldn't get the medicine into the child. So, that is a consideration.

Now, to go back to the allergic possibilities - the pharmacist in favor of the bill counters, as on page 5, paragraph 5, that they keep an individual record on the patient, listing their sensitivities, etc. That's great; they do. However, unfortunately, patients today are mobile and not all patients keep all of their prescriptions at one drug store. This is their right in a free society, to go where they want to go. Sometimes it is because they are really shopping around for price; sometimes it is because their established drug store is closed at a time when they become sick; perhaps they are out of town; perhaps they are in a different area of the community. They are at work and the drug store is around the corner. Their regular drug store is way back a couple of miles away, so they go around the corner. That drug store doesn't have the patient's profile on hand. So, this profile is good but it really doesn't cover all the possibilities.

Of course, the ultimate check on this is the patient himself. He should see that this medicine - for instance, if it is a question of the yellow coloring and he shouldn't have it - is a yellow color and he knows that he shouldn't have it.

However, when he picks up his medicine at the drug store it is usually disguised in store wrappings and he can't see what it is. He has to pay for it and he goes home and then he takes it out and then discovers that it is yellow and he knows that he is going to have hives if he takes that medicine. Now, he can't go back to the drug store; maybe the drug store is closed. Furthermore, the drug store won't take returns and he has already paid for the medicine. That means he has to try and reach his doctor and find out whether he should take it, whether this is a medicine that has tartrazine in it, to which he is sensitive, or, perhaps, just a medicine which is colored by one of the other coloring agents.

So, the poor patient here is in a dilemma: should he have faith and go ahead and take the medicine and run the risk of his allergic reaction, or should he just skip it and wait until he reaches his doctor and let his infection get worse over the weekend?

Now, in the hospital situation, where generics as substitutions are allowable, you have open lines of communication for immediate resolution of the problem. The patient notices when the medication nurse brings the medication to him that it is not what he should have. He reports it to the nurse. The nurse can either call the pharmacy or the nurse can check with the physician or, if she can't reach the physician, she can check with the intern or the house officer and this problem can be resolved immediately in the hospital situation.

But in the out-patient situation, it is much harder to carry on those lines of communication.

The second point I wanted to make here is, a great deal of doctor-patient confusion can result from free substitutions. Patients and doctors often exchange their information about the patient's condition and the medicines they are taking when the doctor asks, how many green capsules are you taking? The patient says, what green capsules? I got red tablets. Well, that creates difficulty. That doctor wonders if the patient got the proper medicine. The patient wonders if the doctor is prescribing the wrong thing. It may take time to track that down and find out exactly what was dispensed.

Now, it does say here in your bill - you do have the provision on page 4, paragraph 4 - that the pharmacist, if he makes a substitution, is to notify the physician, either orally - and the problem I anticipate with that is when he is not able to immediately get in touch with the doctor - or by written notice, to be mailed no later than the end of the business day. Well, feature the business day as Friday. He sends it in writing to the doctor. Maybe with the mails the way they are, it may not be on the doctor's desk Monday morning when he comes in. It may be Tuesday or Wednesday. In the meantime several days have elapsed if the patient has been taking his medication - taking it or not taking it, depending upon what the patient decided to do when he discovered the medicine looked different.

The problem isn't solved by requiring the generic name to be put on every medicine bottle. Some pharmacists have a way of neglecting to do this, especially on refills. More often the patient neglects to read this label, perhaps because of an emotional block, perhaps because of a limited intellectual

capacity. But time and again I have had patients -- I have asked them for the name on the label and they say, I don't know; what's the name on the label; oh, yes, here it is; this is what it says. They haven't read it. They haven't paid attention to it. So, it doesn't solve the problem.

Another example I can give you - perhaps it has been given in previous testimony - is not specifically related to the field of allergic disease. It is the patient who is required to take five or six different medicines. The patient may be living alone, slightly senile, have poor eyesight, be debilitated from his illness, but he is trying to live alone and be independent. To help him keep his medicine straight a skillful doctor will arrange that each of these has a different shape and/or color, if this is possible. If the pharmacist has authority to make free substitutions, this very well designed plan can go awry, causing the patient to overdose or underdose himself, or get the medicines mixed up and then take it at the wrong time.

Then, to make it worse, if, on a refill, the pharmacist substitutes from his current supply of the generic brand - which now has a different shape, or color and thus might resemble one of the other patient's medicines - I can see where continuing medical care would be difficult for such a patient.

Another comment, under general medical practice - not specifically allergic practice but which has been brought out to me in my practice of allergy - I frequently use Prednisone. Generic brands, in spite of the U.S.P. standardization requirements, are not always standardized. The patient does not always react in the standardized fashion. One brand may give a patient a proper response, another may be

worthless or cause side effects. I have seen this in Prednisone. It is supposed to be standardized. Generic Prednisone is supposed to be standardized to U.S.P. standards and, yet, I know when I see the patient that this patient must be getting a low quality brand which is probably contaminated with Cortisone.

Maybe there are differences in the patient's ability to absorb the medication from his particular gastrointestinal tract; maybe there are gross contaminants present - low grade contaminants, rather - which are not detected or ignored in the standardization requirements. One tablet may have more insoluble factors. It may fragment. It may disintegrate. It may not hold up well. The basic standardization is there by the U.S.P. standards but it is really minimal. It does not really give the best in high quality control. High quality control doesn't come cheap. You have to pay if you want the best.

Other medicines which have been shown to vary brand-for-brand have been digitalis and thyroid preparations.

My final comment here would concern the cost of medications. The bill specifies that the pharmacist will substitute the brand - the least expensive brand. Well, in my experience this hasn't happened. I have had the exact reverse situation happen. I have written generically for a preparation and the patient comes back to me and complains because that medicine was so expensive. So, I checked back and I found out what was given and sure enough, that pharmacist, instead of dispensing his least expensive quality brand, he dispensed the most expensive brand that he had on his shelf. He said to me, well, you want your patients to have the best, don't you? Well, I do want my patients to have the best but if there are other good brands

which are less expensive and work just as well, I am willing to substitute.

I think that is probably all that I have to say.

ASSEMBLYMAN HERMAN: Thank you very much, Doctor. I do have two or three questions for you.

It appears that one of your primary concerns, that I can understand from your testimony, is the question of the doctor being able, in the end result, if he or she did not want a generic drug, to be able to so specify, notwithstanding the lowest possible price, is that correct?

I will repeat that. You raised the concern with reference to your many examples as to allergic reaction--

DR. HALL: Right.

ASSEMBLYMAN HERMAN: --that there is a specified drug for a specified purpose that, although it may be on a limited basis, would give an individual uncomfortable and bad results.

DR. HALL: Yes. If you had a medication that contained an additive that he was allergic to.

ASSEMBLYMAN HERMAN: So, your concern, as a physician, would be that notwithstanding generic substitute in those given situations, the doctor should retain control to say, with specificity, this and only this?

DR. HALL: That's right.

ASSEMBLYMAN HERMAN: I would assume that if the legislation spoke to that particular issue, that objection which you raised would be overcome?

DR. HALL: Yes, I guess if it really works out that way in practicality. Sometimes it doesn't always work the way you want it to.

ASSEMBLYMAN HERMAN: Perhaps there may be a need for a better uniform prescription blank, which I

understand is a problem in the trade.

DR. HALL: I am not aware of that.

ASSEMBLYMAN HERMAN: There is not one standard prescription blank, is there?

DR. HALL: No.

ASSEMBLYMAN HERMAN: I assume that can be overcome with specificity in a properly prepared uniform prescription blank.

DR. HALL: I would guess you could get around that, yes.

ASSEMBLYMAN HERMAN: Now, you mentioned the fact that patients or consumers float from pharmacy to pharmacy. It is also true that patients float from doctor to doctor.

DR. HALL: Oh, yes.

ASSEMBLYMAN HERMAN: He may be treating with two or more doctors at the same time, sometimes unknown to the doctor because they are embarrassed to say I am being treated by Dr. Jones.

DR. HALL: Oh, yes. That's true.

ASSEMBLYMAN HERMAN: In those situations they may be going to the same pharmacist. You certainly would want to know, as a doctor, from that pharmacist if he is getting prescriptions in from two or three doctors, including yourself, which were not compatible; you would want to know that fact because of the patient's welfare.

DR. HALL: Yes. I think--

ASSEMBLYMAN HERMAN: So, that is a problem too, as well as the ability of the patient to float from pharmacist to pharmacist, that the patient also floats from doctor to doctor.

DR. HALL: Right. That situation exists, yes. That is why these patient profiles are good and it is another check on it.

As an allergist I - because drug sensitivities are a very important part of my problems - always question the patient specifically about what medicines they are taking. I ask, are you taking any medications from any other doctor?

You know, it is true, maybe they are not going to tell me but if the patient has come to me with a condition which I suspect is basically caused by a drug reaction, I will tell them, you bring in to me all the contents of your medicine cabinet and then I can read the name of the drugs.

ASSEMBLYMAN HERMAN: Because of your specialty, your practice - or your situation - as far as the patient communication to the doctor, may not be exactly the same as that of the G.P.

DR. HALL: It may not be , that is correct.

ASSEMBLYMAN HERMAN: It is really a different situation altogether. I assume that they are coming to you for allergies or allergic reactions.

DR. HALL: That's right. But they also are seeing a general practitioner who may also be prescribing for them. But then I always ask them when they come to me -- if they say I have had a cold or I have bronchitis and I went to Dr. X, my family doctor, I always say to them, what did he do for you? Did he give you an antibiotic? Which one did he give you? I will even tell them, bring it in so that I can see it.

ASSEMBLYMAN HERMAN: You, as a doctor in your field, would be more inclined to ask, are you treating with another physician?

DR. HALL: Yes.

ASSEMBLYMAN HERMAN: Because of your specialty, maybe more than a G. P. would.

DR. HALL: That's right.

ASSEMBLYMAN HERMAN: I just want to ask one last question. You commented that high quality control doesn't come cheap - if I remember your statement.

DR. HALL: Well, there is a euphemism that says you get what you pay for.

ASSEMBLYMAN HERMAN: Well, that's the point I want to reach because during testimony that we have had here - even today - Smith, Kline & French, in reference to Thorazine, when I asked them the question, when the patent ran out, was the price cheaper today than it was in 1970, they said yes. When I asked, why, they said, competition.

DR. HALL: Well, you have to use a little common sense. When you apply that euphemism it is obviously not 100% applicable to all situations. There are situations in which -- What can I think of? You go to Abercrombie & Fitch and you buy their tennis racquet and you pay for top quality and theoretically you can get the same one in your local sporting goods store, who doesn't have as big an overhead or as big a mark-up that has to be absorbed into that cost he puts on that particular racquet. It applies in all businesses.

ASSEMBLYMAN HERMAN: I assume Abercrombie & Fitch doesn't have to worry about patents expiring.

DR. HALL: Well, no. That is just a generalized example.

ASSEMBLYMAN HERMAN: I want to thank you for taking the time from what I am sure is a busy schedule to come before us. We certainly appreciate it.

DR. HALL: I hope I have been helpful.

ASSEMBLYMAN HERMAN: Thank you again.

I have before me, directed to the Honorable Byron M. Baer, dated June 25, 1974, a statement of Albert

J. Salzman, M.D., Member, Council of Medical Staffs for Southern New Jersey, which I authorize to be spread upon the record as well as the statement of Sandra Helton, which, likewise, I request be put into the record.

It would appear that there are no more witnesses to be heard. As sponsor of A-1257, rather than making an extensive comment for the record at this time, I am reserving the right to add, as a appendix, to the official public hearings - both public hearing #1 and #2 - an official sponsor's report, which will be included as part of these public hearings.

I want to thank everyone for attending and for the input that they have given. Hopefully, the legislation which I, as sponsor, hope will eventually come to fruition, will reflect the end product of concern and input of all the witness who have testified before this committee. The hearing stands adjourned.

(hearing concluded)

Printing and Office

Stationery & office supplies		\$ 250.00
*Research & reference books		100.00
Printing, office forms	\$ 100.	
**Outside printing	1520.	
	<u>1620.</u>	
		<u>1620.00</u>
		\$ 1970.00

* PDR	\$35.00	** 19000 Items
Red Book	20.00	X8
Blue Book	20.00	<u>152000</u>
Federal Drug Directory	4.50	\$10. per thousand
U.S.P.	15.00	<u>\$1520.00</u>
N.F.	15.00	
	<u>\$109.50</u>	

Travel

Council meetings - 2 a month - each month	
Maximum mileage round trip 150 miles	
150 miles X \$.14/mi. X 24 meetings X 8 members =	\$ 4032.00
Parking, tolls, meals \$8.50	
\$8.50 X 24 meetings X 8 members =	<u>1632.00</u>
	5664.00

Travel of Executive Secretary

Out of State trips	days	per diem	trans.	local trans.	
Baltimore (1)	2	\$ 70.	\$ 20.	\$ 15.	
Washington D.C. (2)	4	140.	40.	30.	
Chicago (1)	3	105.	128.	15.	
		<u>\$315.</u>	<u>\$188.</u>	<u>\$ 60.</u>	563.00

In State travel

4500 miles @ .14 (30 days approx. 150 miles per day)	630.00
Parking and tolls \$4.00/day X 30	120.00
Total travel	<u>\$1313.00</u>

Telephone

Per instrument	\$525.00	
Estimated other charges	500.00	
	<u>1025.00</u>	\$1025.00

Subscriptions

Federal Register	\$ 48.	
Others	102.	
	<u>\$150.</u>	\$ 150.00

Legal and Investigative

Court Reporter \$40. X 8 hearings	\$ 320.	
\$1.50 per page - 150 pages X 8 hearings	1800.	
Hearing office		
\$150. X 8 hearings	\$1200.00	
\$30/hr X 2 hr. preparation X 8 hearings	240.00	
	<u>\$3560.00</u>	\$ 3560.00

Postage

Mailings - 8 the first year
18,000 physicians, osteopaths, dentists, podiatrists,
veterinarians, hospitals, pharmacies, manufacturers
and distributors

18,000 X 8 X \$.061 bulk rate	\$8784.	
Other mailings 1000 pieces X \$.10	100.	
	<u>\$8884.</u>	\$ 8884.00

Rent

700 sq. feet at \$6.00	\$4200.	\$ 4200.00
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Other Professional

48 days @ \$100/day	\$4800.	\$ 4800.00
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Office Equipment:

3 desks - 1 executive	\$ 140.	
2 secretarial @ \$101.	202.	
3 chairs - 1 executive	46.50	
2 secretarial @ \$39.	78.00	
2 typewriters @ \$550.	1100.00	
1 table	76.75	
1 tape recorder	302.00	
1 5-drawer file	75.00	
	<u>\$ 2020.25</u>	\$ 2020.00

Salaries

Executive Secretary	\$16,324.	
\$16,324 - \$22,036 (\$816)		
Principal Clerk steno	7,478.	
\$7478 - 10,096 (\$374)		
Clerk Steno	5,314.	
\$5314 - \$7176		
Total salaries	<u>\$29,116.</u>	\$ 29,116.00

TESTIMONY OF

**GARTH GRAHAM, M.D.
MANAGER OF MEDICAL SERVICES
SMITH KLINE & FRENCH LABORATORIES**

**BEFORE THE N.J. ASSEMBLY COMMITTEE ON COMMERCE,
INDUSTRY & PROFESSIONS**

FRIDAY, JUNE 28, 1974

The controversy over so-called "generic equivalence" and the repeal or amendment of the state antisubstitution laws has been vigorously debated within professional and academic circles for a decade. Professional ethics and the laws of fifty states have allocated the choice of medication to the physician. This choice of medication includes the source of drug product, as well as the type of drug.

This controversy is presently being considered in New Jersey A#1257. The purpose and design of this legislation deprive the physician of one of his most important medical prerogatives--choosing the source of medication for his patient. This prerogative would be assumed by an agency of the state known as The Drug Utilization Review Council and the pharmacist.

The source of the drug product is of critical importance to the physician and his patient. The physician, in the course of his professional practice, learns to depend upon the specific response to a given drug from a known source. He depends upon the pharmacist to dispense the exact medication he prescribes for the patient. If the patient fails to respond to the medication in the manner expected, the physician has every reason to believe that his choice of medication or dosage schedule should be changed. However, if the pharmacist has actually dispensed a different drug, or a drug product from a different source, without the doctor's knowledge, the physician's decision for an alternate therapy may be improper.

At the heart of the generic advocates' argument is the myth of "generic equivalency". They assure that all drugs on the market of a specific type are equal. This assurance is given in the face of official statements from the government and mountains of scientific research to the contrary. A detailed description of the generic equivalency argument is attached to this statement.

The issue at stake for the citizens of N.J. is not economic. It is clearly a decision regarding the caliber of medical care that will be available to present and future generations. This decision is of the utmost importance because the price of an error is not in money but in the health and lives of the citizens of N.J.

The vocal minority that is advocating repeal of the state antisubstitution laws, or generic drug laws, would without just cause "blindfold" the physician in the exercise of his professional skills. This vocal minority contends the pharmacist or the state should decide the source or brand of medication to dispense on a prescription. They assert that the pharmacist or the state is in a better position to select the source of a drug. The pharmacist's knowledge of pharmacology is important and well recognized; however, the pharmacist's access to information related to the patient's individual response to a given medication is seriously handicapped even in N.J. where patient profile records are required in pharmacies. The physician and the physician only can monitor the patient's response to medication.

The advocates of generic drugs, having failed to convince the scientific world of their arguments, are now taking their position to the public and to the legislator. What they fail to acknowledge in their presentations is that the present N.J. law does in no way prevent the doctor from prescribing generic drugs. In fact, physicians commonly prescribe certain medication by generic name. In these cases, the physician has decided this was safe and proper and he knows the source of drug may vary. His professional experience with drugs and patient responses, however, usually leads the physician to prescribe a specific brand or source in the majority of his prescriptions.

The generic advocates frequently describe in great detail the burden placed on the pharmacists who must stock a variety of brands of the same chemical. What the generic advocates do not tell is that the pharmacist needs only to obtain the permission of the physician to substitute, if he is out of stock or wishes to dispense a brand of drug other than the one on the prescription. In this case, the physician may or may not allow his prescription to be so altered. However, in any such case, the physician now knows that such a change has been made. Such mutual agreements between the pharmacist and the physician are entirely proper by law and professional ethics at this time and answer all needs of the physician, the pharmacist, and most important, the patients health. The use of professional agreements between the physician and the pharmacist offers the parties involved the best long term solution. In this manner, only those physicians and pharmacists who wish to be involved need participate. Specific agreement on acceptable product alternatives can be reached by the physician and pharmacist.

The vast majority of professionals in this state involved in the delivery of health care support the present relationship of the physician and pharmacist. They see no reason to alter the critical relationship of the doctor and his patient. The following national associations have taken a position in support of the present state laws prohibiting substitution by the pharmacist:

American Academy of Dermatology
Board of Directors of the American Academy of Family Physicians
Executive Board of the American Academy of Neurology
Committee on Drugs of the American Academy of Pediatrics
American College of Allergists
Executive Committee of the American College of Obstetricians and
Gynecologists
Board of Regents of the American College of Physicians
Board of Trustees of the American Dental Association
Board of Trustees of the American Medical Association
American Psychiatric Association
Executive Committee of the National Association of Retail Druggists
Board of Directors of the Pharmaceutical Manufacturers Association

In many states, the generic advocates already have their "foot in the door" in the area of welfare recipients. State legislatures in their desire to cut costs have decided that generic drugs are good enough for the poor and elderly. We are now being told that prescriptions should be written for generic drugs or at least filled with them even when the patient is paying his own bills. Before this decision is made on the current legislation we encourage the utmost consideration of the issues presented in this position statement.

THE MYTH OF GENERIC EQUIVALENCY

A recent situation in one of the Nation's largest hospitals illustrates once again, the argument of "generic equivalency" is not only specious but dangerous.

Physicians at New York's Harlem Hospital were puzzled by the abnormally high doses of digoxin needed for desired response by some of their heart patients. They asked Columbia University scientists to study the four digoxin preparations being used. One compound was a brand-name product from a prominent manufacturer, three were generic products. Taking the digoxin themselves, the Columbia investigators found striking differences in the serum concentrations produced by these compounds. The brand-name drug gave 4-7 times the peak serum levels of two of the generic products, and, though all met Federal standards, some generic tablets had little effect. Furthermore, there were significant variations between two lots from one generic manufacturer.

Dr. John Lindenbaum and his associates at Columbia University and Harlem Hospital concluded that biologic non-equivalency may exist among all marketed digoxin products. These investigators are urging the FDA to screen all digoxin preparations for biological availability, and they urge physicians to keep a patient on a preparation if he is doing well. Incidentally, of the four products studied, only the brand-name preparation is still dispensed at Harlem Hospital.

So digoxin joins the growing list of compounds for which it is shown that chemical equivalency does not signify biologic equivalency -- diphenylhydantoin, phenylbutazone, bishydroxycoumarin, prednisone, thyroid, tolbutamide, chloramphenicol and oxytetracycline. Only time, research, and sad experience will tell how many other drugs will be added to this list.

The concept of "generic equivalency" has been discredited by many prominent members of the scientific community. Here are just a few:

Academy of Pharmaceutical Sciences, reported that, "Drug products from different sources may differ in quality in several respects. These differences, individually or collectively, may lead to substantial differences in therapeutic effect and/or safety...it cannot be assumed that the product will exhibit clinical acceptability simply because an apparently identical product is already marketed". (The Academy of Pharmaceutical Sciences, American Pharmaceutical Association, May 19, 1969.)

Charles C. Edwards, M.D., Commissioner, FDA, stated that, "It has become increasingly apparent that drug products which purport to be equivalent and which satisfy chemical and other analytical tests of equivalence, may not be therapeutically equivalent. We believe the key to the problem lies in what we refer to as bioavailability." (Meeting of the American Pharmaceutical Association, Washington, D.C., April 15, 1970.)

James L. Goddard, M.D., former Commissioner, FDA, stated that, "There are others who maintain that you can buy any drug in the marketplace and expect it to be therapeutically equivalent to others sold on the same name. I must say that we do not have controlled clinical studies to decide the issue in all cases". (U.S. Senate, Statement to Committee on Finance, September 12, 1967.)

W. B. Castle, M.D., speaking for the AMA's Policy Advisory Committee Drug Efficacy Study, stated that the data reviewed indicates that, "therapeutic equivalence, or biological activity, cannot necessarily be inferred from equivalence in the chemical constitution of different formulations of the same drug". (J.A.M.A. 208 (7), May 19, 1969.)

Alfred Gilman, Ph.D., Professor and Chairman, Department of Pharmacology, Albert Einstein College of Medicine, Yeshiva University, stated that he is "convinced that there is no such thing as a generic equivalent unless proven by adequate experimental data". (Letter to Senator Gaylord Nelson, published in the Congressional Record, September 12, 1967.)

Louis Lasagna, M.D., Chairman, Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, stated that, "The motives behind these generic bills are perfectly respectable. Unfortunately, the science underlying them, and the realistic appraisals of their economic impact, are deficient". (Letter to the Editor, The Baltimore Sun, May 29, 1968.)

In spite of all the evidence against "generic equivalency", N.J. is, unfortunately seeking to deal with the cost of medical care A#1257 which encourage generic prescribing and dispensing -- a case of the cure being worse than the disease. Doesn't the patient in our state, for instance, deserve more than just the cheapest product on the market? Doesn't he deserve to have his physician choose the drug that the physician believes can do the best job?

Unless you, as a legislator, can be positive of the bio-equivalence and other issues involved, you are risking the future excellence of medical care for N.J. citizens if you support A#1257. I urge you to seriously consider all the potential problems before you make your decision.

EXHIBITS PRESENTED BY

DR. MURRAY WEINSTOCK

(pages 50A through 63A)

W. W. W. W. W.

DIGOXIN TABLETS

Many physicians may not be aware that digoxin tablets can be altered by the manufacturer without notice and without changing the appearance or the labeling. Because of increasing concern about poor absorption, some manufacturers of digoxin tablets have reformulated the tablets or changed the manufacturing process. Since all digitalis preparations have a narrow gap between therapeutic and toxic effects, increasing the absorption of digoxin tablets can be dangerous.

BIOAVAILABILITY - Digoxin is more widely used than any other cardiac glycoside because it has a shorter half-life and therefore more rapid dissipation of toxic effects than digitoxin, other oral glycosides, or digitalis leaf. Some digoxin tablets are poorly absorbed, however, and vary considerably in bioavailability, even among different lots of digoxin produced by the same manufacturer. Poor dissolution of tablets appears to be a major cause of this variation in absorption (J. Lindenbaum, Pharmacol. Rev., 25:229, June 1973).

GOVERNMENT REGULATIONS - Because digoxin tablets were introduced before passage of the 1938 Food, Drug and Cosmetic Act, they can be reformulated without a New Drug Application and without notifying physicians or any regulatory agency. New standards of the U.S. Pharmacopeia effective November 15, however, require testing the dissolution time of digoxin tablets. The U.S. Food and Drug Administration can be expected to seek recall of tablets that do not meet the standards and to issue a regulation controlling reformulation.

CURRENT RECOMMENDATIONS - The practicing physician should be aware that either underdigitalization or toxicity may result from changes in the source or even the lot of digoxin tablets. If a patient is responding well to the digoxin preparation he is using, it should be continued. If the physician suspects a change in digitalis effect, serum digoxin concentrations should be measured in blood taken eight hours or more after the last oral maintenance dose (patients receiving 0.25 to 0.5 mg daily of a preparation of good bioavailability usually have serum concentrations between 0.5 and 2.0 nanograms/ml). Serum analyses are available from some large commercial laboratories.

Many cardiologists now recommend Burroughs Wellcome's Lanoxin brand of digoxin, especially for patients taking digitalis for the first time. Different lots of Lanoxin have shown fairly consistent bioavailability.

CONCLUSION - Marked variation exists in the bioavailability of digoxin tablets. Official USP standards have just been revised to include in vitro testing of dissolution rates; the FDA can be expected to seek recall of all digoxin tablets that do not meet this standard. Physicians should be alert to possible digitalis overdosage resulting from changes in the manufacturing process. Lanoxin (Burroughs Wellcome) is fairly consistent from batch to batch and is preferred by many cardiologists, but switching a well-compensated patient from one digoxin product to another is inadvisable.

Dr. Weinstein

FDA drug recalls

(Only products reaching retailers or hospitals appear in this list, excerpted from the FDA listing. Recalls at branch, warehouse or distributor level are not included.)

Name, Form, and Label	Product Type	Lot Number	Manufacturer, Pack-er or Distributor	Reason
Nysta-Cort 1/2% lotion in 1 fl oz & 5 cc sizes, for external use, acid ph, nystatin 100,000 units. (Dome Labs., Div. Miles Labs.)	Rx	1 oz: 017129, 051129, 100090. 5 cc samples: 016129, 017129, 053059.	(Mfr.) Miles Labs West Haven, Conn.	Subpotent (1)
Athea Hospital Lotion in 8 oz btls. (Athea Labs.)	OTC	All lots	(Mfr.) Athea Labs., Inc. Milwaukee, Wisc.	Bacterial contamination (2)
Medisage Hospital Lotion in 4 & 8 oz btls.	OTC	All lots	(Mfr.) Athea Labs., Inc. Milwaukee, Wisc.	Bacterial contamination (2)
Galesburg cottage hosp. lotion in 8 oz sizes.	OTC	All lots	(Mfr.) Athea Labs., Inc. Milwaukee, Wisc.	Bacterial contamination (2)
Three Rivers Hospital Lotion in 8 oz sizes.	OTC	All lots	(Mfr.) Athea Labs., Inc. Milwaukee, Wisc.	Bacterial contamination (2)
Time-Tabs anti-bese, each tab cont. amobarbital 60 mgm; thyroid 150 mgm; methamphetamine HCl 10 mgm. (Dist. Heyl Physicians Supply Co., Erie, Pa.)	Rx	All lots	(Mfr.) Anti-Bese T American Tab and Cap, Brooklyn, N.Y. (now called Ketchum Labs., Brooklyn, N.Y.)	FR Pub 12/3/68 (3)
Anti-Bese T-15 timed disinteg. tabs, each T.D. cont. amobarbital 60 mg; thyroid 150 mg; methamphetamine HCl 15 mg. (Dist. Heyl Physicians Supply Co., Erie, Pa.)	Rx	All lots	(Mfr.) American Tab and Cap Co., Brooklyn, N.Y. and Zenith Labs., Inc. Englewood, N.J.	FR Pub 12/3/68 (3)
Digoxin 0.25 mg in 1000's, 5000's, and bulk. (Zenith Labs)	Rx	2058-02 ✓	(Mfr.) Zenith Labs Inc., Northvale, N.J.	Content uniformity (4)
Same as above in 1000's. (Dist. Aberdeen Pharmaceuticals, Inc., Northvale, N.J.)	Rx	2058-02 ✓	(Mfr.) Zenith Labs Inc., Northvale, N.J.	Content uniformity (4)
Same as above in 5000's. (Dist. Paramount Surgical Supply Corp., Northvale, N.J.)	Rx	2058-02 ✓	(Mfr.) Zenith Labs Inc., Northvale, N.J.	Content uniformity (4)

Same as above in 1000's and 5000's. (Bioline, Inc., Brooklyn, N.Y.)	Rx	2058-02	(Mfr.) Zenith Labs Inc., Northvale, N.J.	Content uniformity (4)
Digoxin 0.25 mg tabs in 100, 1000, and 5000 tab btls. (Richlyn Labs.)	Rx	18448 ✓	(Mfr. and responsible firm) Richlyn Labs., Philadelphia	Content uniformity (5)
Same as above in 1000 tab btls. (United Research Labs., Philadelphia)	Rx	18448	(Mfr. and responsible firm) Richlyn Labs., Philadelphia	Content uniformity (5)
Same as above in 1000 tab btls. (Fremont Labs., Los Angeles)	Rx	18448	(Mfr. and responsible firm) Richlyn Labs., Philadelphia	Content uniformity (5)
Digoxin (Daylin Medical & Surgical Supply Inc., Los Angeles)	Rx	18448 ✓	(Mfr. and responsible firm) Richlyn Labs., Philadelphia	Content uniformity (5)
Metalex Elixir, each 5 cc cont. pentylenetetrazole 100 mg; niacin 50 mg in 1 pint and 1 gal sizes. (Arnar Stone)	Rx	All	(Mfr.) Arnar-Stone Labs, Mt. Prospect, Ill.	FR Pub 9/12/70
H-R Sterile lubricating jelly in 2.8 gm, 4 oz and 5 oz sizes. (Holland-Rantos)	OTC	All lots	(Mfr.) Holland-Rantos Co., Inc., Piscataway, N.J.	Bacterial contamination (6)
Potassium Iodide solution N.F. in 1 pint glass btls. under brand labels of "Stanlabs" and "Stanley". (Mfr. Stanley Drug Products)	Rx	180003; 099002; 257006.	(Mfr.) Stanley Drug Products Inc., Portland, Ore.	Particulate matter (7)
(1) FDA analysis found samples to have average potency of 84.6% of declared and pH below the 5.0 to 7.0 permitted (average 4.9). Problem linked to stability. (2) FDA analysis revealed pseudomonas aeruginosa contamination of product samples. (3) 33 FR 17927. (4) Samples of product indicated potency ranges of from 21.2-242.2% of declared. (5) Product failed content uniformity tests. Range not reported. (6) FDA analysis of samples revealed gram positive aerobic spore bacillus. (7) Particulate matter found by FDA sampling tentatively identified as sulphur.				
Digoxin in 1000s, 0.25 mg. (Dist. Wolins Pharmacal Co., Melville, N.Y.)	Rx	070005 or BS 070005	(Mfr.) Heather Drug Co., Cherry Hill, N.J.	Content uniformity (1)
'Estra-Testrin' estradiol valerate 4 mg./cc, testosterone enanthate 90 mg./cc, inject. (Pasadena Research Labs)	Rx	016, 017	(Mfr.) Pasadena Research Labs., Inc., Pasadena, Calif.	Misbranded/subpotent (2)
'Estra-L' estradiol valerate inject. 20 mg./cc in 10 cc vials. (Pasadena Research Labs.)	Rx	327/331	(Mfr.) Pasadena Research Labs., Inc., Pasadena, Calif.	Misbranded/subpotent (4)
(1) Potency ranges of 10.1 - 127.6 of declared. (2) Analysis revealed no estradiol valerate in the product. The product sample was found to contain however, estradiol isovalerate 3.58 mg./cc and 0.38 mg./cc. (4) Analysis revealed product to contain no estradiol valerate but to contain instead 16.9 mg./cc estradiol isovalerate.				



PHONE

PHARMACY

FOR.....

ADDRESS..... DATE.....

Rx

Dear Murray,

You were right. I would say these

labs supply 50 % of Digoxin in

the area under the names of

many other Co. who rebottle

MAY BE REFILLED

0-1-2-3-4 PRN M. D.



January 1974

DRUG BULLETIN

FDA TO CORRECT DIGOXIN PROBLEMS

FDA APPROVES CEA ASSAY KIT
FOR CANCER MANAGEMENT, DIAGNOSIS

FDA APPROVES PROPRANOLOL
IN ANGINA PECTORIS

WARNING RENEWED ON
ERYTHROMYCIN ESTOLATE

a significant difference between a group (ng. per ml.) and a group (ng. per ml.). An overlap in practice there is no difference in therapeutic activity of the drug. My own experience that patients on one occasion and not on another of the drug. Moreover, the fibrillation to sinus rhythm was revealed latent toxicities, we find the measure of great value in helping patients can safely be increased, and decreased in individuals being misled by our estimation.

Advantages listed by Dr. Fogelin: 1. Diagnostic of digitalis toxicity can ever make a "definitive" diagnosis only if a change in serum-digoxin concentration when the drug is withdrawn. 2. In a recent study. If the diagnosis is reasonable doubt, we must be suspicious between the results of the published series. In the new assay procedures, and their place as an aid

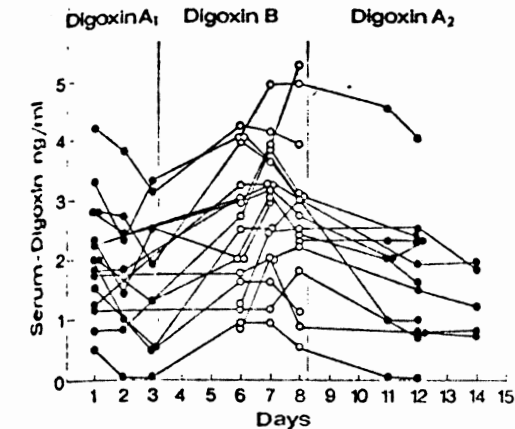
- D. CHAMBERLAIN
- A. REDFORS.
- A. BERTLER.
- J. COLTART.
- R. WHITE.

CONCENTRATIONS IN PATIENTS WITH DIFFERENT PREPARATIONS

It is encountered in up to 10% of patients with digitalis toxicity. As you have emphasized (Lancet, 1971, p. 362), the margin between a toxic dose is very small. It is not possible to evaluate differences between commercial preparations of digoxin—both in tablets of 0.25 mg and in ampoules of 0.25 mg/ml—both in appearance and in effect.

In elderly women in a long-term study because of social problems after cerebrovascular attack, digoxin A for weeks or months. Serum-digoxin concentrations over 3 successive days, denoted hereafter digoxin A was changed to digoxin B.

Then the patients were now denoted digoxin A. The concentration was not changed during the only minor changes in blood-samples were taken at the same time. Serum-digoxin concentrations were not affected by lidium-86 inhibition.³ In



Serum-digoxin concentrations in 19 patients during treatment with two different digoxin preparations.

The results were checked by radioimmunoassay.⁴ The figure summarises the results. There was a definite increase in serum-digoxin concentration in 15 of the 19 patients during treatment with digoxin B, while in the remaining 4 patients no change in concentration occurred. When the serum-digoxin concentrations during the different stages in each individual patient were paired, the mean difference \pm S.E. in ng. per ml. between digoxin A₁ and digoxin B was 0.89 ± 0.19 ($n=19$), and between digoxin B and digoxin A₂, 0.78 ± 0.16 ($n=19$). The respective mean serum-digoxin concentrations were 1.85, 2.74, and 2.5 ng. per ml. During digoxin B treatment, 3 patients showed clinical signs of digitalis intoxication which were reversed by discontinuation of the drug. In one the mean serum-digoxin concentration rose from 2.6 to 3.7 ng. per ml., in the second from 1.0 to 4.0 ng. per ml., and in the third from 2.8 to 3.0 ng. per ml.

This investigation shows that the absorption of digoxin from apparently equivalent preparations may be different. If the patient is well established on a given preparation, unnecessary changes may increase the hazards of digoxin therapy and should be avoided. The costs of digoxin therapy are low for an individual patient, but for large-scale therapy the best absorbed preparations may be economically worth considering.

Tuburi Research Institute, Helsinki 14, and First Department of Medicine, University of Helsinki, Helsinki 29, Finland.

VESA MANNINEN
JOHN MELIN
GOTTFRIED HÄRTEL.

NEW SIGN OF IRON DEFICIENCY ?

SIR,—Over the past year or two I have noticed that blue whites are a useful guide to iron deficiency. My attention was first drawn to this relationship in a woman with severe rheumatoid arthritis and malabsorption who had a vivid blue tinge to the whites of her eyes. The colour was so striking that I even wondered if she had osteogenesis imperfecta. Since then I have confirmed the relationship between "blue whites" and sideropenia on many occasions, and have found the sign valuable in diagnosis and treatment. I expect the sign has been described previously, but I can find no reference to it in the standard works, and it deserves to be better known. The blue tinge disappears on iron replacement: but don't shoot it in until you've seen the whites of their eyes.

The Quadrant, 100, London Road, Exeter EX2 4LE.

G. H. HALL.

Smith, T. W., Butler, V. P., Haber, E. *New Engl. J. Med.* 1969, 281, 1212.

RADIO-ONE THERAPY

SIR,—The thought of being restored to consciousness by continuous administration of Radio One is indeed an appalling one. Should people be advised to add to the cards which indicate their blood-group, that they are taking M.A.O.-inhibitors, &c., the statement: "Please revive with Radio Three (or Four)?"

27 Willoughby Road, London N.W.3.

J. McFIE.

ASSESSMENT OF EQUIPMENT

Mr. PHILIP KITTREDGE, editor, *Respiratory Care* (Box 125, Mendocino, California), writes: "Mr. Thorne (Sept. 11, p. 605) and Dr. Gilston (Sept. 25, p. 713) and others concerned with performance of medical equipment might be interested in a publication called *Health Devices*. Issued monthly by the non-profit Emergency Care Research Institute of Philadelphia, this publication provides a test, evaluation, and advisory service to its subscribers. The service is supported by the health community. It does not accept funds from the medical devices industry and its employees may not act as private consultants or own stock in medical device firms. The publication carries no advertising. This independence of advertising revenue or other support by vested interests puts the subscription price at \$250, but a subscribing institution gets not only the publication but also consultation services and such tools as a pro forma clinical equipment control programme for hospitals. Investigations have been carried out on external cardiac compressors, single-channel versus three-channel cardiographs, hypothermia machines, portable oxygen analysers, operating-room conductivity testers, oxygen-powered resuscitators, portable battery-powered defibrillators, ventilators, resuscitators, operating-tables, blood-gas analysers, and other items. For those interested, the address is The Emergency Care Research Institute, 913 Walnut Street, Philadelphia, Pa. 19107, U.S.A."

Obituaries

HUGH STANFORD BRYAN M.R.C.S.

Dr. Hugh Bryan, first psychiatrist and director of the department of psychiatry at Alder Hey Children's Hospital, Liverpool, died on Sept. 27 at the age of 79.

Dr. Bryan took the Conjoint diploma in 1918 from the London Hospital Medical College. His interest in behaviour disorders in children began when he was a school medical officer in Derbyshire, and when the first county child guidance clinic in Britain was established there he became the first doctor to hold the official title of county child psychiatrist. He was a member of the Child Guidance Council, which later merged into the National Association for Mental Health; Dr. Bryan was a founder member of the Association and was elected to its inter-clinic committee, which dealt mainly with child guidance. In 1948 he became the first medical director of the newly established regional psychiatric clinic at Alder Hey Children's Hospital, which was one of the first of such clinics, and he was also appointed adviser in child psychiatry to the Liverpool Regional Hospital Board. He retired in 1958.

A. E. McC. writes:

"At the inception of the National Health Service there was a difference of opinion as to whether child guidance should be run from mental hospitals, or should come under the authority of the director of education. Dr. Bryan firmly believed that child psychiatry was a branch of children's medicine, and that it should be run by the school

VARIATION IN BIOLOGIC AVAILABILITY OF DIGOXIN FROM FOUR PREPARATIONS

JOHN LINDENBAUM, M.D., MARK H. MELLOW, M.D., MICHAEL O. BLACKSTONE, M.D., AND VINCENT P. BUTLER, JR., M.D.

Abstract The unexplained association of unusually large maintenance doses of digoxin and low serum digoxin concentrations in several patients prompted a study of the biologic availability of various digoxin products recently available for use on the wards of a New York City municipal hospital. In crossover studies in which 0.5 mg of digoxin was administered orally to normal volunteers, marked differences in

serum digoxin levels achieved over a five-hour period were demonstrated. With one product peak serum levels were seven times those obtained with another. Significant variation between different lots prepared by a single manufacturer was also observed. Evidence of biologic as well as chemical equivalence of digoxin products for use in man should be required.

AMONG the conditions reported to be associated with increased dosage requirements for cardiac glycosides are hyperthyroidism,¹ impaired intestinal absorption,^{2,3} supraventricular arrhythmias,⁴ infancy,⁵ altered digoxin metabolism^{6*} and the presence of circulating antidigitoxin antibodies.⁹ We recently observed several patients at Harlem Hospital Center who required large oral maintenance doses of digoxin (as much as 1.0 mg daily) despite the absence of any of the conditions known to increase digitalis tolerance. Low serum digoxin concentrations¹⁰ were found in these patients. Digoxin tablets produced by a variety of manufacturers were available for use in patients at our hospital and other New York City municipal hospitals during the past year. In view of increasing reports in recent years of marked variation in the biologic availability of a number of other therapeutic agents,^{11,20} we decided to study the intestinal absorption of digoxin from several of these preparations. The results of our crossover studies in normal subjects indicated striking differences in the serum digoxin levels achieved after oral administration of various digoxin products.

SUBJECTS

Our healthy male members of the Harlem Hospital Center Medical Service house staff, 26 to 32 years of age, with no history of gastrointestinal or other disease, volunteered as subjects. Fully informed consent was obtained after discussion of the studies in detail with each subject.

METHODS

Absorption Studies

After an overnight fast 0.5 mg of digoxin as two 0.25-mg tablets was given with 100 ml of water to each subject. Blood for serum digoxin concentration

was obtained at zero, 1/2, one, 1 1/2, two, three and five hours. Subjects were allowed to eat breakfast at four hours. Serum digoxin levels were measured by the radioimmunoassay method of Smith, Butler and Haber.¹⁰

In each volunteer the digoxin absorption test was performed in an identical manner on four occasions, the only difference being the digoxin preparation given. The tablets used, all of which were from supplies available on the wards of Harlem Hospital Center for administration to patients during the period June, 1970, to February, 1971, included Burroughs Wellcome digoxin, lot No. Z180 (A), American Pharmaceutical Company digoxin lot No. B15703 and OA12933 (B₁ and B₂) and Davis-Edward digoxin, lot No. 24928 (C). The order of administration of the various preparations was randomized (Table 1). Repeat absorption studies were performed at intervals of eight days or more; in no subject were detectable digoxin levels present in zero-hour serum. No subject complained of ill-effects during or after the test.

Mean serum digoxin concentrations at various times after the oral administration of each preparation and the standard error of the differences between mean levels were calculated, and the Student "t"-test applied to determine significance. In addition, the area under each absorption curve was measured by polar planimetry, and the areas under the curves for the different products evaluated by multiple comparison technics with the use of Bonferroni "t"-tests.²¹

In Vitro Studies

The concentration of immunoreactive digoxin in

Table 1. Order of Administration of Digoxin Products

SUBJECT	ORDER OF ADMINISTRATION			
	1	2	3	4
M.B.	A	B ₁	B ₂ *	C
H.R.	B ₁	A	C	B ₁
C.H.	C	A	B ₁	B ₂ *
S.S.	A	C*	B ₁	B

* Administered 8 days after preceding study; on all other occasions interval between tests was 3-4 wk.

From the Medical Service, Harlem Hospital Center, and the Department of Medicine, Columbia University College of Physicians and Surgeons (address reprint requests to Dr. Lindenbaum, at the Medical Service, Harlem Hospital Center, Lenox Ave. and 135th St., New York, N.Y., 10037).

Supported by grants-in-aid from the New York Heart Association, the American Heart Association (69-824) and research grants (HE-10608, HE-05741 and MH-17957) from the United States Public Health Service (Dr. Butler is the recipient of a research career-development award [HE-11315]).

lets from each of was determined h preparation had e digoxin was ext added to digoxin. nunoassay. In adde an ratio was dete C. A 1:1 mixture n was added to fi for two hours at re allowed to se ter and chloroform concentration by rad idies, crystalline nner to the grou a reference point.

Absorption Studies

The peak serum c er oral administra rkedly with the p ak concentration 0.52 ng per millili ven times that ac 0 ng per millilita er). The difference re highly signific each case). The oxin product B₁ er) were lower th 5), and signific up less than 0.0

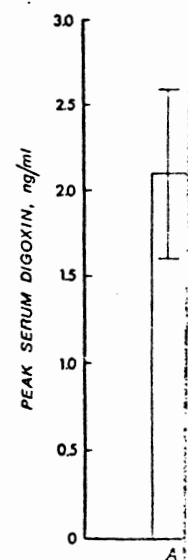


Figure 1. Mean Peak Serum Digoxin Concentration after Oral Administration of Digoxin Product A. Vertical crossbars represent standard error of the mean.

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Tablets from each of the four lots given to the subjects was determined after 10 0.25-mg tablets of each preparation had been ground to a fine powder. The digoxin was extracted in alcohol or chloroform and added to digoxin-free pooled human plasma for immunoassay. In addition the chloroform water partition ratio was determined for preparations A, B₁ and C. A 1:1 mixture of distilled water and chloroform was added to finely ground tablets. After agitation for two hours at room temperature the mixtures were allowed to separate after standing, and the water and chloroform phases measured for digoxin concentration by radiimmunoassay. In all in vitro studies, crystalline digoxin, handled in identical manner to the ground digoxin tablets, was included as a reference point.

RESULTS

Absorption Studies

The peak serum digoxin concentrations achieved after oral administration in the four subjects varied markedly with the product used (Fig. 1). The mean peak concentration attained with product A — 2.1 ± 0.52 ng per milliliter (mean ± 1 S.D.) — was four to seven times that achieved with products B₂ (0.30 ± 0.10 ng per milliliter) and C (0.50 ± 0.42 ng per milliliter). The differences between A and either B₂ or C were highly significant statistically (p less than 0.005 in each case). The peak serum levels reached with digoxin product B₁ (mean 1.4 ± 0.14 ng per milliliter) were lower than with product A (p less than 0.05), and significantly higher than with either B₂ or C (p less than 0.01 in each case). There were no

significant differences in peak levels achieved between products B₂ and C.

The mean serum levels attained with each of the four preparations during the five hours after drug administration are shown in Figure 2. Serum levels after product A differed significantly (p less than 0.05 or less) from those after products B₂ and C at every point on the curve after the zero-hour determination except at three hours. Although the mean serum levels for product B₁ were lower at each point than those for product A, none of the differences were significant. The mean levels attained for product B₁ significantly exceeded those for product B₂ at every point except at three hours, and significantly exceeded product C at 1/2, one and five hours. B₂ did not differ significantly from C at any point.

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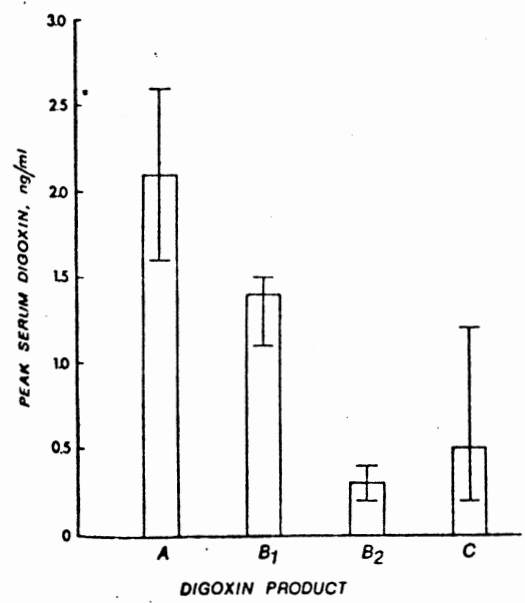


Figure 1. Mean Peak Serum Digoxin Concentrations Attained after Oral Administration of 0.5 Mg of Each of Four Digoxin Products to Four Subjects. Crossbars represent the range of observations in the four volunteers.

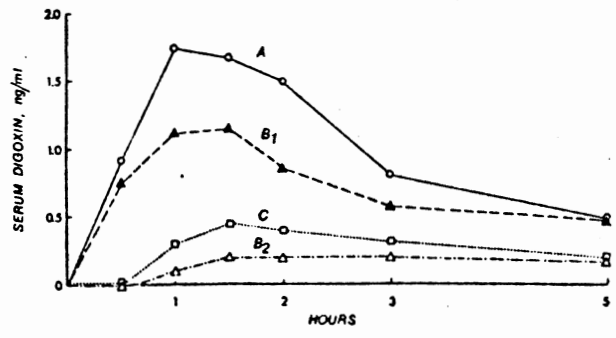


Figure 2. Mean Serum Digoxin Levels over a Five-Hour Period after Oral Administration of Four Digoxin Products to Four Volunteers. Each line represents the mean of four curves.

The absorption curves for the four preparations in each of the four subjects are shown in Figure 3. With products A and B₁ substantial radioimmunoassayable digoxin concentrations were attained at 1/2 hour, and peak levels reached at one to two hours, with subsequent levels falling off sharply. With products B₂ and C serum digoxin was usually absent or barely detectable at 1/2 and one hours, and the absorption curves had a "flat" appearance at subsequent points—with the exception of the curve obtained in one subject (H.R.) with product C. When the areas under the curves were compared, significant differences (overall error level, 5 per cent) were noted between A and B₂, A and C and B₁ and B₂.

In Vitro Studies

The digoxin concentration of the tablets, expressed as proportion recovered with crystalline digoxin as 100 per cent, was 91.9, 91.9, 82.7, and 96.5 per cent for products A, B₁, B₂ and C, respectively. The differences between the four products were within the range of error of the method. The chloroform-water partition coefficients for crystalline digoxin were 57a

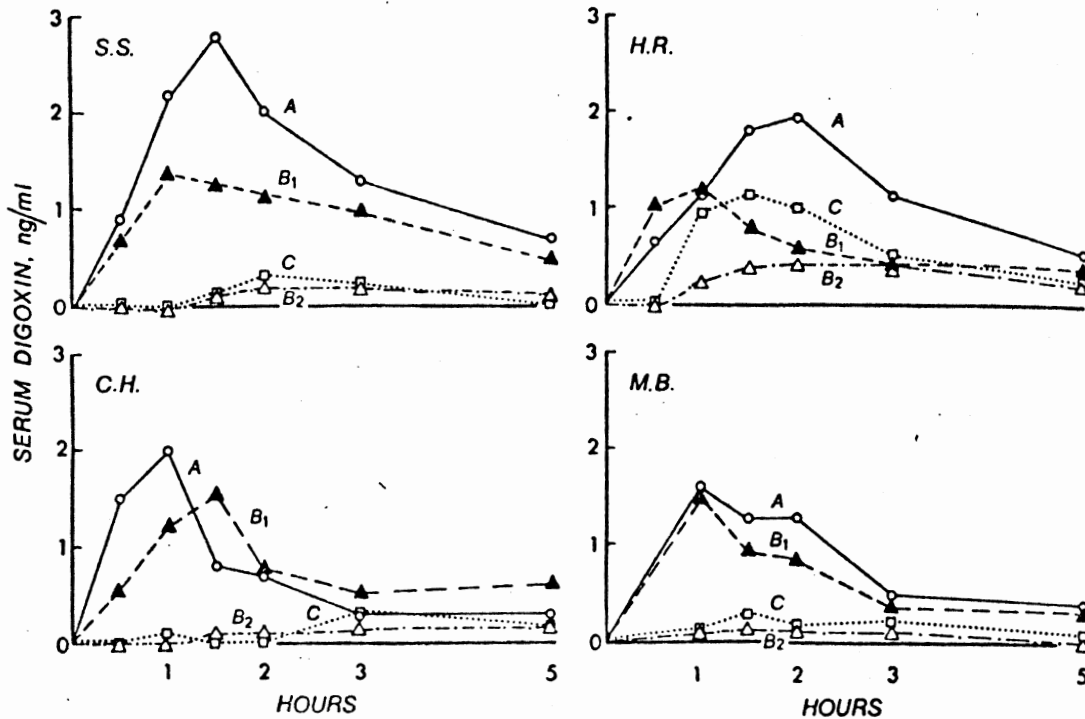


Figure 3. Individual Absorption Curves after Each of the Four Products in the Four Volunteers Studied. Serum digoxin levels at ½ hour were not obtained in M.B.

digoxin and products A, B₁ and C were 16.6:1, 15.2:1, 15.2:1 and 16.0:1, respectively.

DISCUSSION

These findings indicate that differences of as much as four to seven times in serum digoxin levels may be achieved in vivo after the oral administration of various preparations despite essentially equal digoxin tablet concentrations as measured in vitro. The variation was noted not only between preparations supplied by different companies but between different lots (B₁ and B₂) obtained from the same manufacturer. Similar discrepancies in the biologic availability of drugs, including diphenylhydantoin,^{11,12} bishydroxycoumarin,¹³ phenylbutazone,¹⁴ prednisone,¹⁵ thyroid,¹⁶ tolbutamide,¹⁷ chloramphenicol^{11,18} and oxytetracycline,^{19,20} have been reported.

The reason for the differences in biologic availability of the digoxin preparations studied has not yet been determined. A number of factors other than chemical potency have been shown to be responsible for variability in the absorption of other drugs, including particle size, disintegration and dissolution rates, and the effects of various "inert" excipients and other additives.^{12-15,17,18}

In our studies a recently developed immunoassay for serum digoxin levels was applied to the investigation of drug absorption. Our results with product A were similar to those recently reported by White and his colleagues²² in normal subjects, who used the same product and assay, indicating that digoxin, administered as well formulated tablets, is rapidly

absorbed in man, with peak levels usually attained within one hour of administration, as was previously found by Doherty and his associates² and Marcus et al.²³ with the use of tritiated digoxin in alcoholic solution.

White and his colleagues observed that when the peak level had been reached after the administration of 0.5 mg of digoxin, plasma glycoside concentrations fell sharply, and began to reach a plateau within four to six hours.²² The blood digoxin levels at these later times appear to reflect a developing equilibrium between blood and tissue concentrations. It is of interest that whereas the five-hour serum levels attained after the ingestion of products A and B₁ were significantly greater than those after C and B₂ (Fig. 2), the values after A and B₁ did not differ from each other at that time. This may indicate that the total digoxin absorbed over the five-hour period was similar for the two products. The apparent differences in blood levels at earlier points in time between A and B₁ (Fig. 2) were also not statistically significant, the number of subjects studied being small.

The observed variability in absorption of digoxin preparations represents a potential hazard to the patient. Changes in the source of manufacturer's digoxin (or even from lot to lot of the same manufacturer, as with product B) may occur without the knowledge of physician or patient and result in toxicity or underdigitalization, depending on the product substituted. The Food and Drug Administration has established a list of drugs²⁴ in which biologic

availability, as demonstrated in the stated conditions, follows: the product for the control is a solid form, soluble; and nonequivalent. We believe that for digoxin, the list of availability is cor

We are indebted to Beth Grimme, Andre Varma, M.D., and to Rabinovich and associates for the st

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availability, as well as chemical potency, should be demonstrated as a requirement for use in patients. The stated criteria for inclusion on this list are as follows: the product is a "critical" drug required for the control of disease; it is generally dispensed in solid form; its active ingredient is relatively inalterable; and there is reason to suspect biologic inequivalency of various available preparations.²⁴ We believe that all these criteria have been fulfilled for digoxin, and recommend that digoxin be added to the list of drugs in which proof of biologic availability is considered crucial.

We are indebted to Miss Francine Perriman and Miss Elizabeth Grimmer for nursing and technical assistance, to Dr. Vire Varma and Mrs. Livia Turgeon for biostatistical advice, and to Drs. Steven Shafer, Coleman Henley, Harris Levinovich and Mack Bonner, who served as volunteer subjects for the study.

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DIETER ENZMANN

We think that the results of our survey and the observations of Hersh et al.⁶ and of Heathcote and Sherlock¹² provide strong circumstantial evidence that hepatitis-B virus may be transmitted sexually. Two questions remain unanswered; the way in which the virus is transmitted and the importance of the sexual route of transmission in the epidemiology of hepatitis B in the U.K. We think that the concept of hepatitis B as primarily a sexually transmitted infection should be carefully considered. Such well-recognised means of transmission as transfusions, the unsterilised syringes of drug addicts, and tattooing could be incidental and may not contribute significantly to the maintenance of virus in the community. These parenteral methods of infection may possibly carry a greater risk of clinical illness.

We thank Dr T. E. Cleghorn for permission to publish results from the North London Blood Transfusion Centre and Miss M. Collings for help in coding the data.

Requests for reprints should be addressed to D. S. D.

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RATE OF DISSOLUTION OF DIGOXIN TABLETS AS A PREDICTOR OF ABSORPTION

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JOHN MCCRERIE

HUGH GREER
CAROLE BYE

ARTHUR FOWLE

Wellcome Research Laboratories, Beckenham, and
Wellcome Development Laboratories, Dartford, Kent

Summary Five experimental batches of 0.25 mg. tablets demonstrated large differences in the rate of dissolution of their digoxin content in a described apparatus. In twenty healthy volunteers, following treatment periods of one tablet every 12 hours for 14 days, plasma-digoxin concentration and urinary excretion were significantly correlated with tablet-dissolution rate. Mean plasma concentration ranged from 1.07 ng. per ml. on tablets of the lowest dissolution-rate to 1.49 ng. per ml. on those of the highest dissolution-rate. Similarly, mean urinary excretion ranged from 86 to 146 μ g. per dosage interval. It is suggested that a minimal acceptable level of dissolution-rate be established for digoxin tablets.

Introduction

LARGE variations in the quantity of digoxin available

for gastrointestinal absorption from tablets of identical nominal digoxin content have been reported in several countries.¹⁻³ Differences have been shown between and within brands, emphasising the unreliability of quality-control standards and leading to suggestions that human bioavailability should be incorporated into the requirements of drug-regulating authorities.^{1,4} Experience in our laboratories with a technique for determining the rate of dissolution of digoxin from tablets suggested a potential in-vitro method of predicting human bioavailability. We have found a strong correlation between tablet-dissolution rate and measures of bioavailability.

Methods

Dissolution-rate

The apparatus used was based upon that specified in the *U.S. Pharmacopeia*.⁵ Six tablets from any batch to be studied were placed in a stainless-steel basket attached to the shaft of a stirring motor. The basket was placed in 600 ml. of distilled water in a 1 litre flat-bottomed straight-sided vessel and rotated at 120 r.p.m. The temperature of the dissolution medium was maintained at 37°C, and 5 ml. samples were withdrawn at selected times. Digoxin was determined by modification of a fluorimetric method.⁶ A coefficient of variation of 3.4% was recorded after repeated examination of tablets from one production batch.

Treatments

Sixteen experimental batches of 0.25 mg. digoxin tablets were made, so that the batches covered a wide range of dissolution-rate. All batches were subjected to full pharmaceutical analysis, and five were selected which covered a suitable span of dissolution-rate and at the same time complied with the *B.P.* monograph for digoxin tablets⁷ in terms of assay, uniformity of weight and digoxin content, and disintegration-time.

Human Studies

Twenty healthy volunteers received one 0.25 mg. digoxin tablet at 9 A.M. and 9 P.M. daily for 14 days. Each volunteer underwent three consecutive treatment periods in randomised sequence, taking three of the five available treatments as determined by a balanced incomplete block design. During each treatment period, plasma was obtained immediately before 9 A.M. on days 13, 14, and 15, and urine was collected during the 12-hour periods

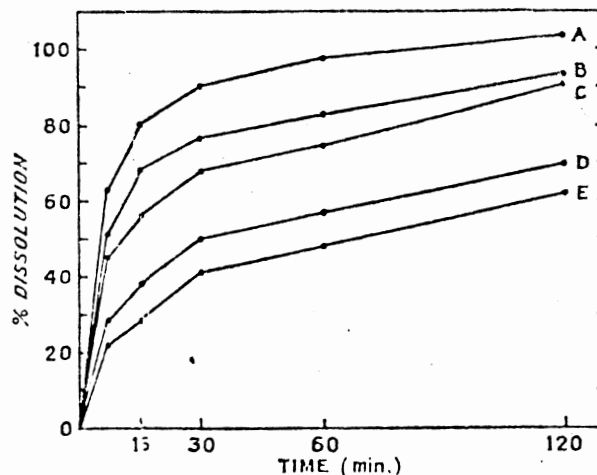


Fig. 1—Percentage of digoxin dissolved at various sampling-times from five experimental batches of tablets.

Each dissolution value is the mean of three determinations.

tolerance is permissible in rate and extent of absorption. Ideally, drug products with identical labeling should have identical rates and extents of availability, just as they should have identical assay potencies. But, differences in the sensitivities of bioavailability tests and differences in the seriousness of disease states make it impossible to establish tolerances that are applicable to all drug products. Each drug must be evaluated as a separate entity, and the practitioner's judgment must be employed to determine what tolerance he is willing to accept in each case.

In 1968, C. M. Martin *et al.*³ reported significant differences in the bioavailability between different brands of sodium diphenylhydantoin, sulfisoxazole and chloramphenicol. Figure 7 (right) shows the results obtained with diphenylhydantoin. In this case, one of the chemically equivalent diphenylhydantoin formulations produced blood levels approximately twice those of the brand (innovator's) product, while the other chemically equivalent product produced approximately 20 percent lower levels.

In 1972, MacLeod *et al.*⁴ reported greater than 20 percent difference in peak concentration and area under the curve for three ampicillin products. These investigators compared two chemically equivalent ampicillin products with a recognized standard. The results are graphically presented in Figure 8 (right).

More recently, Wagner *et al.*⁵ showed that there was a 59 percent difference in peak plasma levels and a 55 percent difference in areas under the curve between two digoxin products (Figure 9, opposite page). These two digoxin products passed all USP specifications and also were assayed in the laboratories of the Food and Drug Administration.

While many of the studies documenting differences in drug product bioavailability have been performed on products made by different manufacturers, problems have been uncovered in different batches of products of the same manufacturer. The now well-known increase in tetracycline bioavailability when dicalcium phosphate was replaced as an excipient is one such example. Other recent examples of differences among batches from the same manufacturer include the increase in bioavailability of diphenylhydantoin when the excipient was changed from calcium sulfate to lactose⁶ and the 100 percent increase bioavailability of digitoxin when a well-known British manufacturer changed his formulation.⁷

Two reports were published nearly simultaneously which commented on the

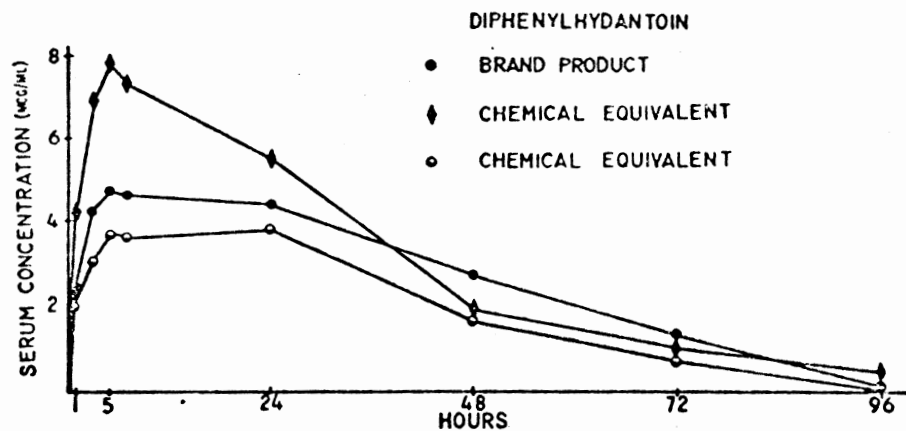


FIGURE 7—Comparative bioavailability of three brands of Sodium Diphenylhydantoin Capsules. Average serum levels were obtained from twelve volunteers following single oral doses of 500 mg. This graph was drawn from values estimated from the curve presented in reference 3.

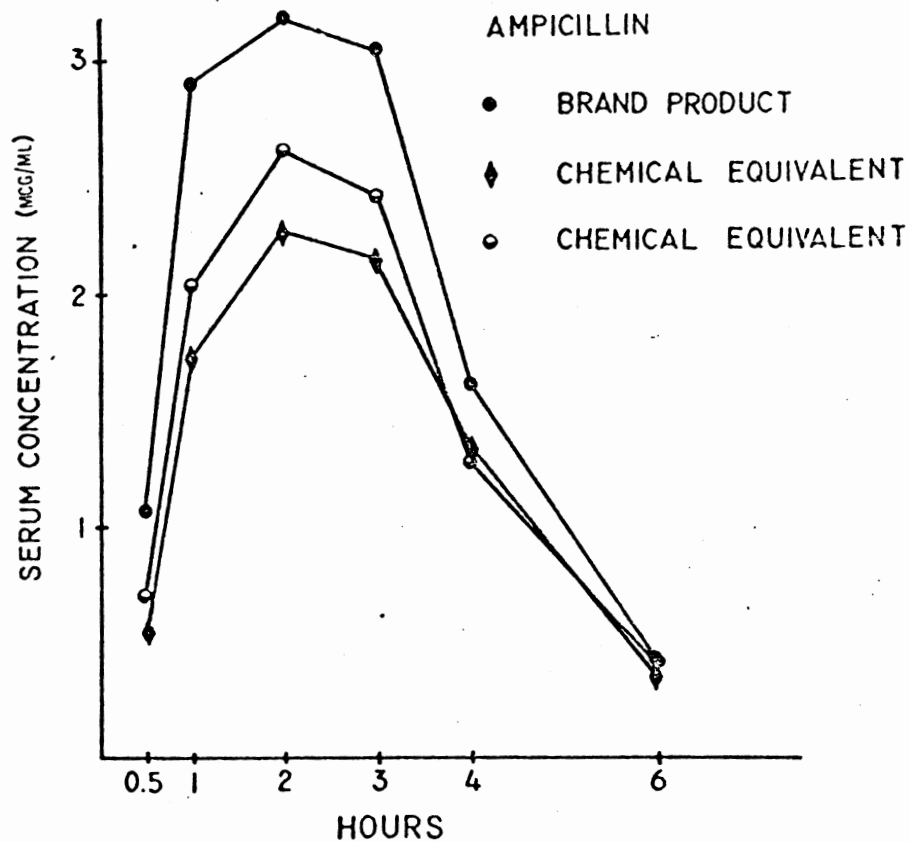
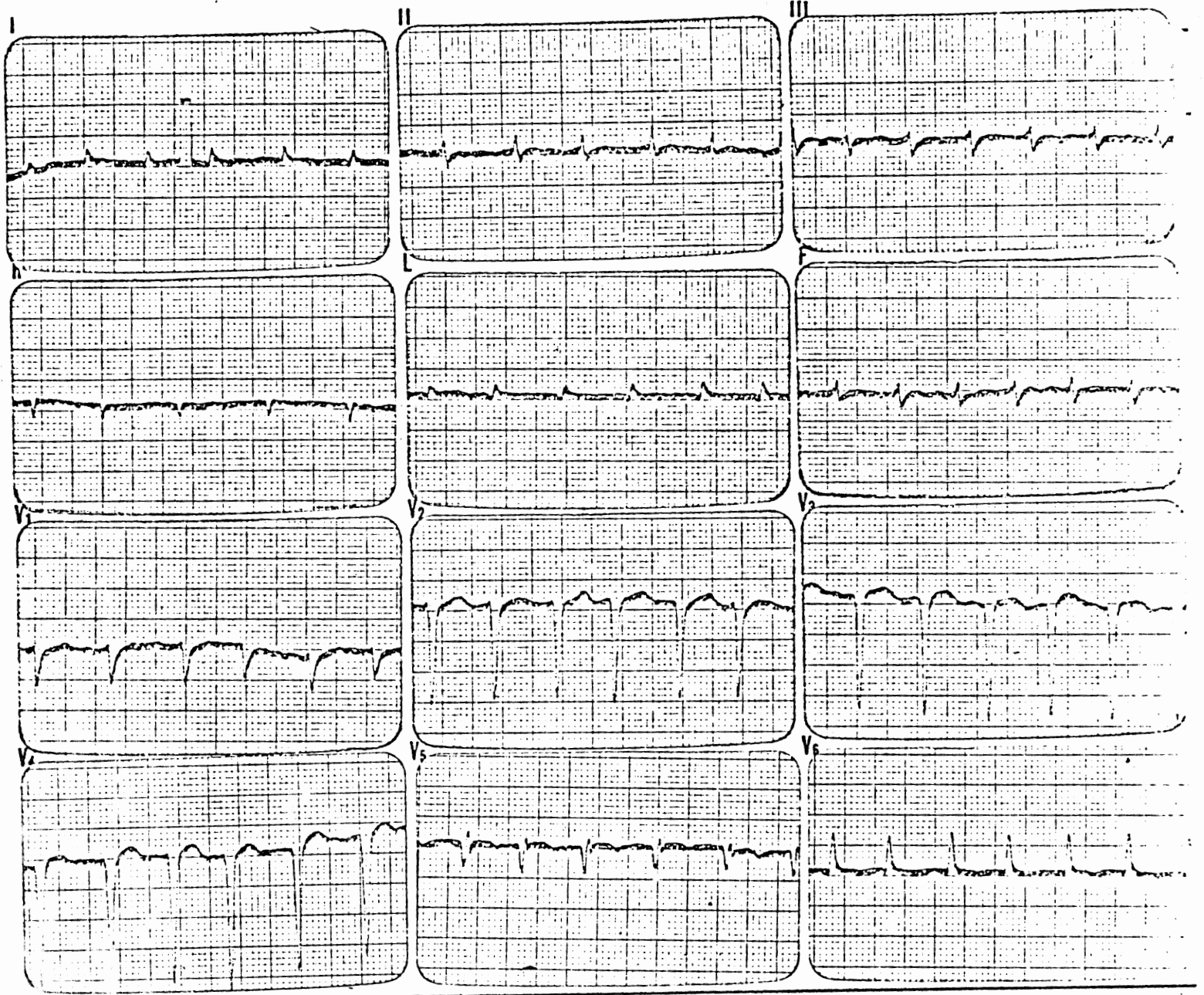


FIGURE 8—Comparative bioavailability of three brands of Ampicillin Capsules. Average serum levels were obtained from eighteen volunteers following single oral doses of 500 mg. Based on data in reference 4.

lack of a full clinical effect for two brands of tolbutamide marketed in Canada^{8,9}. These tablets were shown to have long disintegration times as well as slow dissolution characteristics.¹² An experimental tolbutamide tablet representing only a slight change in formulation was shown¹³ to produce significantly lower blood levels and less hypoglycemic response.

Factors Influencing Drug Product Performance

A drug product such as a tablet or capsule consists not only of the drug itself, but fillers, binding agents, lubricants and other substances which can affect the drug product's performance. For example, lubricants are used to



ELECTROCARDIOGRAPH REQUEST

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 CLIN. DIAG.: _____

SEX _____ B. P. _____
 ORDERED BY _____

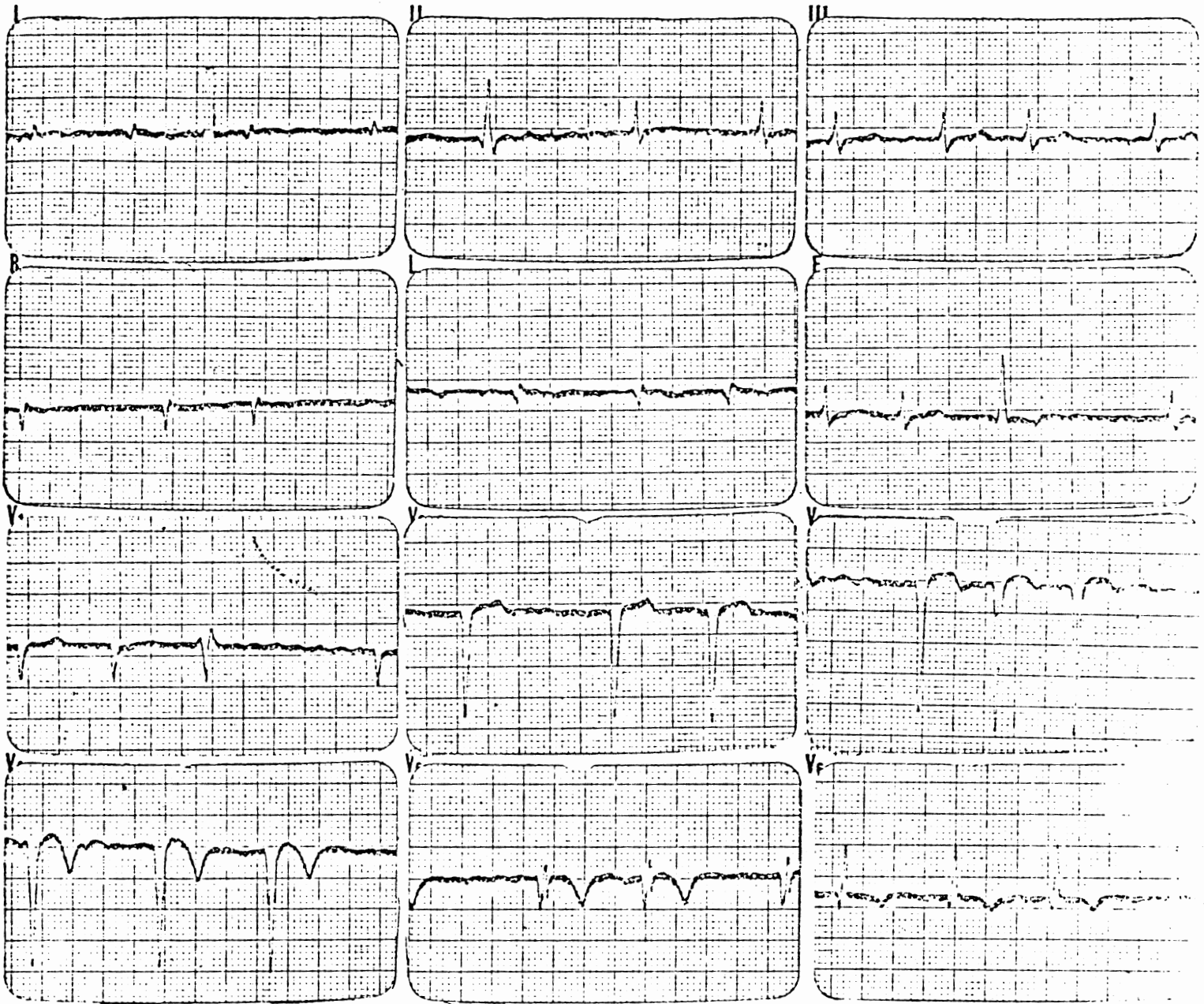
DATE _____

M. D.

ELECTROCARDIOGRAPH REPORT

RHYTHM: SINUS OTHER _____

DATE: _____



ELECTROCARDIOGRAPH REQUEST

PREV. ECG YES NO AMB. BED. EMERG. DIG. QUIN. AGE _____ SEX _____ B. P. _____ DATE _____
 CLIN. DIAG.: _____ ORDERED BY _____

ELECTROCARDIOGRAPH REPORT

DATE: _____ INTERVALS: _____ AXIS: _____

CHART # 1

(Refer to page 2 of Mr. Hunt's Statement)

- 12% Refers to NEW Rx's ONLY
- 10.6% Pharmacy Times Figure
- 9.2% Percentage of NEW and REFILLED Rx's

CHART # 2

(Refer to page 3 of Mr. Hunt's Statement)

67,415,000 New and Refilled Rx's in New Jersey

Average of 9 Per Person

National Average = Approximately 7

CHART # 3

(Refer to page 4 of Mr. Hunt's Statement)

NEW JERSEY DRUG STORE SALES 1973

\$464,954,000

R_x Market \$300,000,000 = 64.5% of Drug Store Sales

National Average 45%

Using National Average

New Jersey R_x Market - \$212,855,000

CHART # 4

(Refer to page 4 of Mr. Hunt's Statement)

New Jersey Per Capita Drug Store Sales

\$63.00

National Average \$70.00

Per Household:

New Jersey \$195.00

National \$217.00

CHART # 5

(Refer to page 4 of Mr. Hunt's Statement)

R_x Sales New Jersey \$300,000,000

Less: Avg. Mark Up \$135,000,000
45%

Less: Whsle. Mark Up 27,000,000
9.2%

Manufacturers Sales \$138,000,000

60% Branded 82,800,000

40% Generic 55,200,000

Savings \$ 15,000,000 = 27%

Generic Market 55,200,000

National Average Return on R_x Products 9.5%

CHART # 6

(Refer to page 6 of Mr. Hunt's Statement)

New Jersey Rx Market		\$212,000,000
Less: Avg. Mark Up 45%	\$95,400,000	
Less: Avg. Whsle. Mark Up of 9.2%	19,504,000	
Manufacturer Sales		97,096,000
Less: non-Generic (60%)		<u>58,257,600</u>
Generic Market		38,838,400

Savings	\$15,000,000	= 38.6%
Generic Market	<u>38,838,400</u>	

↓
4 X National Average of
9.5%

CHART # 7

(Refer to page 6 of Mr. Hunt's Statement)

1973 Generics =

4.3% Drug Store Purchases of Rx Drugs

35% Vitamins and Nutrients

6.5% Antibiotics

6.5% Laxatives

FRANK L. BATE, Attorney-at-Law, State of New Jersey.

Admitted as an attorney in 1950.

Counselor-at-Law, 1953

Partner, Shanley & Fisher, 570 Broad Street,
Newark, New Jersey 07102 since 1954.

Residence: Essex Fells, New Jersey
Marital Status: Married, four children
Age: 53

Member of the Essex County, New Jersey, American Bar Associations
and the Bar Association of the City of New York.

Member of the Supreme Court, Advisory Committee on Profes-
sional Ethics and member of the New Jersey House of Assembly,
1961-1962.

Education: Hamilton College, Clinton, New York, A.B., 1942
Harvard Law School, Cambridge, Massachusetts,
L.L.B., 1949

A major activity since my admission to the Bar has been in the field of combating industrial espionage, counterfeiting and substitution, primarily in respect to the development, manufacture and distribution of pharmaceutical products. I had a major part in drafting two important pieces of legislation in this field. The first was R.S. 2A:119-5.1, et seq. (theft of trade secrets act) which has been a model for legislation in several other states. The second was R.S. 24:6D-1 (New Jersey Drug Counterfeiting Act). I have written and lectured in the field.

My firm does extensive work in the field of product liability.

EDITED AND FINALIZED STATEMENT SUBMITTED BY FRANK L. BATE
OF HIS ORAL STATEMENT.

STATEMENT OF FRANK L. BATE
IN OPPOSITION TO ASSEMBLY BILL 1257

The American system has been built in many respects upon the individual's pride in the product he produces and his willingness to put his name on that product as evidence of that pride. That name is an assurance that the manufacturer stands behind and is responsible for its quality. Pharmaceutical products are not analogous to bacon. Yet housewives or husbands choose between Shop-Rite or Swift or Armour bacon at greatly varying prices depending on their balancing of judgments as to the factors of price and their confidence in the quality of the goods represented by the name. Pharmaceutical products are not as simple as bacon, and it is not the housewife but the physician who makes the judgment. Active ingredients in most capsules and tablets which cause the so-called therapeutic equivalence or bio-availability referred to in the present legislation constitute a minute fraction of the total ingredients of a capsule or tablet most of which are the inert carriers of the active ingredient. How these carriers and the drugs are formulated, mixed together, encapsulated or tableted, packaged and marketed in quantity is a complex operation in which the manufacturer or distributor can demonstrate widely varying meticulousness

or lack thereof and have a widely varying degree of quality control at every step and have widely varying degrees of performance even when not under the close supervision of the various governmental agencies concerned.

A physician may have confidence that a particular brand name, therefore, represents in his mind quality and hence he prescribes a drug by that name. If, however, under the proposed legislation he slips up and fails to put the nonsubstitution legend on the prescription in his own handwriting, the druggist must under Section 4 of the present Bill, substitute another drug and not even on the basis of his professional judgment but on the basis that it is cheaper.

Hence, for example, if the druggist in his judgment were to agree that the initially prescribed drug were of the highest quality, the druggist would have to substitute a cheaper, different drug. And this is not the end. As I read the final paragraph of Paragraph 5 of the Bill, even if the physician were to decide that the next to cheapest drug on the whole list of "therapeutically equivalent drugs" were the appropriate one for the patient and neglected to put the handwritten legend on the prescription the druggist would have to substitute the very cheapest product omitting any option to substitute any of the higher cost items again without regard to his own or the physician's judgment as to quality.

In view of the nature of what we are talking about, i.e. life saving or life destroying agents, it would seem that this should be the last area where the sole criteria that should be applied is that of cost.

Secondly, this Bill would create a council that would make judgments concerning the therapeutic equivalency of various products. I will pass over for the moment the question of how effective \$7,500 which is appropriated for the expenses of this council will go in making the complex, including double-blind, clinical studies on each and every one of thousands of drugs available on the market today.

Let us assume, however, that this council like every other governmental (or non-governmental) agency, being human, might make an error on this subject and that a consumer/patient suffers because of this, possibly even fatally. Who is responsible? Hitherto the physician has been the pivotal point of responsibility or liability under the law. In a supposed case, the physician has attempted to discharge his responsibility by prescribing a drug which he thought was well made, of high quality and of appropriate therapeutic effectiveness and was correct in his judgment. The council, however, has made a judgment that other drugs are of similar effectiveness and hypothetically is wrong. It seems to me probable that the physician (hitherto the pivotal point) has no liability unless it would be negligence for the

physician to omit the nonsubstitution legend. If that were true, however, there would be no reason for this legislation because every physician would then feel he would have to write the legend to protect himself. That would render the present legislation meaningless. No--the more likely result would seem to be a ruling by a court that the physician or druggist is entitled to rely upon the findings of the council and that, hence, to fail to put on the legend is not even evidence of negligence. So the physician escapes liability.

The druggist similarly might well have no liability because he has done only what the statute required him to do, i.e. substitute a cheaper product, possibly even against his personal judgment that the original prescription was more appropriate.

The manufacturer of the product on the other hand simply warranted that the product was what he represented it to be, i.e., for example, that it contained specific ingredients, with certain effectiveness, side effects, dangers, etc. He has presumably given the physician adequate warning about the proper use of the drug, its effectiveness, side effects and the like as required by the FDA. The fact that this drug worked in particular circumstances in a manner other than the one the physician had in mind might

not be relevant to the liability of the manufacturer. Of course, if one could prove that the particular drug was negligently manufactured, this might create liability on the part of the drug manufacturer but it would seem to me to be very difficult to prove such negligence even if it existed. It may well be that the problem is that the drug administered was simply manufactured in a different way, perhaps with different inactive components, than the prescribed drug giving a different overall effect. Therefore, the manufacturer also escapes liability.

This would leave us with the council itself or the individual members of the council as potential defendants. Both of these might well be protected by the provisions of the New Jersey Tort Claims Act, R.S. 59:1-1, et. seq. Thus, for example, public entities as well as public employees are not liable for injury resulting from the exercise of judgment or discretion vested in the body or the individual, for legislative or judicial action or inaction or administrative action or inaction of a legislative or judicial nature. See R.S. 59:2-3a and b, and 59:3-2a and b. Also the limitations of actions sections of the act are most strict. Ordinarily the injured claimant must file a claim with the public entity within 90 days of the accrual of the claim, which may be extended only to one year upon application to the court provided that the public entity has not been substantially prejudiced by the delay, R.S. 59:8-8 and 59:8-9. Great difficulty has been

experienced by the courts in determining the statute of limitations problems even in private medical malpractice cases where the results of the allegedly wrongful medical acts are often difficult to perceive and analyze, sometimes for extended periods of time. See, for example, one of the latest opinions in the Appellate Division, Seaberg v. Baldwin, _____ N.J. Super. _____ (App. Div. 1974). In actions against private defendants, however, equitable principles ameliorate the harsh limitations as to the time within which the action must be brought. The New Jersey Tort Claims Act, on the other hand, is a deviation from the principles of sovereign immunity and the discretion of the court in respect to the limitations of action problems will undoubtedly be governed by the strict provisions of the Act. In actions brought under the Tort Claims Act, also the injured party's right to recover for pain and suffering is severely restricted. R.S. 59:9-2. Of course in the area of medical malpractice, pain and suffering is a normal concomitance of negligence.

In conclusion, not only does this Act by emphasizing cheapness over quality in this delicate field increase the hazards to the patient, but in addition it severely limits the recovery that the patient may have against anyone should a mistake be made. For this reason, I strongly urge

that this committee give much further study to this matter and after such study, I am sure that the committee will realize that the Bill should not be reported out favorably.

Atlantic Radiologists, P.A.

Atlantic City Medical Center — Division of Radiology and Nuclear Medicine

1925 Pacific Avenue — Atlantic City, N. J. 08401 — 609/344-4798

June 25, 1974

Honorable Byron M. Baer
Chairman
Assembly Committee on Commerce,
Industry and Professions
Assembly Chambers State House
Trenton, New Jersey

Dear Sir:

As representative of the Council of Medical Staffs for South Jersey, I am writing you regarding Assembly Bill A-1257 to be considered by your committee on June 28, 1974. I wish this letter to be made part of the Public Record.

I feel there are several sections of the Bill which are impractical and not in the best benefit of the public. It would appear to me that the practicality of establishing a drug utilization review council consisting of the members that you have outlined in Paragraph 2 becomes redundant and unnecessary in view of the fact that there are at present, in every hospital, pharmacy committees which have already prepared lists of approved drug products. It seems to me an incursion on the practice of medicine to have the council in any way specify the number of times a prescription may be refilled by a pharmacist when not specified by the physician. Standardization of dispensing quantities may often be impossible without the knowledge of the physician who, after all, has to make the therapeutic decisions involved as to how often and how long his patient should be treated.

Regarding Paragraph 4, allowing the pharmacist to substitute an equivalent drug product not specified by the prescribing physician strikes me as being again an interference in the practice of medicine by the pharmacist. The only way a prescription should be changed from that given by the physician should be with the express consent of the physician and not by the pharmacist with notification of the physician as a second thought.

Diagnostic Radiology and Nuclear Medicine

Albert J. Salzman, M.D.
Charles S. Walkoff, M.D.
Richard A. Di Meo, M.D.
Marc R. Peck, M.D.
Terry A. Johnston, M.D.

**Radiation Therapy
and Gynecologic Oncology**

Joseph G. Stella, M.D.

Radiation Physics

Jonathan N. Law, B.S.

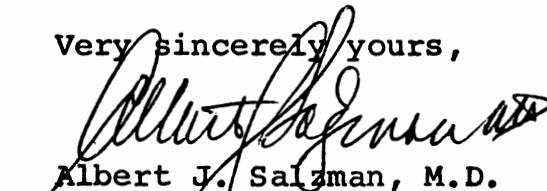
Honorable Byron M. Baer

-2-

June 25, 1974

As an aside, it would appear that the monies to be paid to a drug council and the money established to fund this council are unrealistic. I think that the creation of such a council may grow into an expensive undertaking that is not presently anticipated by the members of your committee.

Very sincerely yours,



Albert J. Salzman, M.D.
Member, Council of Medical Staffs
for Southern New Jersey

AJS:dew

cc: Mr. Martin A. Herman
Mr. C. Guss Rys
Mr. Phillip M. Keeyan
Mr. Robert M. Ruane
Mrs. Barbara A. Curran
Mr. Arnold J. D'Ambrosa
Mr. Morton Salkind
Mrs. Mary Keating Croce

Chairman of the Assembly, Commerce, Industry and Professional Committee

My name is Sandra Helton. I reside in Montville, New Jersey and I appreciate this opportunity to present my opinion on A. B. # 1257 for this issue is of great and grave concern not only to me but to those like myself who must be on drug maintenance programs to combat infections that are detrimental to our health.

Over 30 years ago I was born with the birth defect, Spina Bifida. Spina Bifida is a birth defect leading to multiple disabilities in one in every five hundred newborn for a total of about eleven thousand live births in the United States each year. Spina Bifida has probably existed as long as the history of man and yet only recently has there been any public awareness of its existence much less its consequences. There is a simple explanation. Most spina bifida infants used to die within weeks of birth, far too soon for society to acknowledge their presence. Within the past decade or so, surgical techniques have been perfected which have increased the survival rate of these infants. Each year forward until the cause of spina bifida can be found and eliminated, an estimated 11,000 spina bifida babies will be born, will live, will mature and for better or for worse, will enter the mainstream of American life. They all start out in this world much for the worse.

For the sake of brevity, I would simply state that they are born with a malformation of the vertebrae and spinal cord. Spina Bifida is often euphemistically referred to as "open spine." At best, the spina bifida child will experience reduced sensation and muscle control below the waist. It is more likely that he will be paraplegic. The spina bifida child is incontinent of bowel and bladder. He is the frequent victim of kidney infections which threaten his life.

A child born with spina bifida travels a difficult road. It is also a very expensive road for the cost of treating him . . . of turning him into a productive and useful citizen will reach into the hundred of thousands of dollars during his lifetime. I know for I speak not only for the families of spina bifida children (here in New Jersey there are several hundred) but the voice of experience. I am a spina bifida myelomeningocele

considered the most damaging form of spina bifida. Behind me are some 20 years of medical treatment and some 67 operations. But today I am a tax-payer.....not a tax-burden. I lead a full and productive life. For over 10 years I have worked for a company that has never indicated in any manner that I am " Handicapped." To my company I am an employee fully capable of meeting the requirements of my job and to to it well.

I am active in my church and in my community. I also participate in national organizations whose goals are to help the disabled person lead a more productive life, especially the child with spina bifida. I helped to form the Spina Bifida Association of America, the national organization for spina bifida and am the only one with spina bifida serving as an officer. This organization represents some 100,000 children with spina bifida and their families. Here in New Jersey I am also actively working to help establish a home for disabled adults....the first of its kind in this country.

I know what children born with spina bifida will be up against in life and because I am more fortunate than most of them, I feel it is my responsibility to do what I can....where I can.... when I can. I am greatly concerned about the high cost of drugs and medical care. I remember only too well the years my family was heavily burdened by such bills. But my own life and those ^{of the} 11,000 children born every year with spina bifida depend on the medication we must take every day for the rest of our livesand when it comes to life....which I value most highly....nothing is too costly if it means my health. I don't want any phoney bargains....I want assurances... the assurance that the medication I am taking will do the job for which it is intended...namely keeping me free of urinary infections that are disastrous to my health. I am also concerned about the potential harm that drug substitution can do. I wrote to the U.S. Printing Office to obtain copies of drug recall lists which I am now receiving. These lists inform me which drugs are recalled by the government for some reason. I also found out that most of the cheaper generic drugs have been placed on the market without any clinical trials in man....I just can't afford to take that kind of chance. So I made it my business to know the pros and cons of the drug substitution bill

and I have come to the conclusion that for the little amount of money, if any, one saves by substituting, it was not worth the risk to my health. Besides, what good ^{would} the money saved do me if I am dead? Death for the older person with spina bifida is often due to kidney and renal failure caused by a history of urinary infections. In order to combat these infections... in order that we might live to reach adulthood and become tax-payers, we need the assurances of quality controlled drugs that have been clinically proven to be effective in treating urinary infections.

From my own experience, I can tell you what can happen when a drug substitute is made. For over 20 years I have been on a quality name drug that has kept me free of urinary infections. One time, I was in another city and had to have my prescription refilled. The druggist, knowing nothing of my medical history, advised me he was out of the prescribed drug but was substituting a similar drug that was "just as good" only less expensive. I used this drug for one month and ended up in the hospital for 4 months with a severe urinary infection that almost cost me my life. The doctors thought at first it was caused by a breakdown in the urinary tract.

No one thought to question what medication I had been taking... after all I had used ^{the same} medications for years with no sign of infection. Surgery proved there was no breakdown and a study was done on everything I had done during my trip. Upon learning of the drug substitution, my doctor hit the roof and immediately placed me back on the drug I had used for years. The infection cleared up and because I use only those drugs he prescribed, I have had no further problems with infections. But it taught me a lesson and an expensive one.

That happened some years ago but I can still remember my doctor's words. He taught me the differences between generic drugs and quality drugs. He taught me why I must use drugs and his reasons for wanting me to take certain drugs because as he indicated: "Your life depends on it."

My life depends on the medication I must take. From the moment of birth of a child with spina bifida, the struggle begins to convert a potential welfare dependent and ward of the State into a productive contributing citizen and

*Oil, Chemical and Atomic Workers
International Union AFL-CIO*



RAHWAY LOCAL NO. 8-575

236 W. SCOTT AVENUE
RAHWAY, NEW JERSEY
382-1222

June 25, 1974

The Honorable Byron M. Baer
420 Lantana Avenue
Englewood, New Jersey 07631

Re: A.1257

Dear Assemblyman Baer:

I recently received a letter from Thomas P. Bryan, Committee Aide to the Assembly Commerce, Industry and Professions Committee of which you are Chairman, inviting me to testify at the committee's second public hearing on the proposed amended version of A. 1257 on Friday, June 28, 1974 in Trenton. I very much appreciate the invitation, but unfortunately prior business commitments prevent my attending the Committee hearing personally.

However, I do wish to express my views on this proposed legislation and ask that this letter be made a part of the record of the public hearing on June 28, 1974.

It is my understanding that A. 1257 would establish within the New Jersey State Department of Health a Drug Utilization Review Council which would prepare and distribute a list of generic equivalents of brand named drugs. All pharmacists in the State would then be required to substitute a lower priced drug from such list, notifying the physician orally or by mail only after dispensing the product to the patient.

Such proposed legislation is based solely on the assumption that prescription drugs which are chemically equivalent are also therapeutically equivalent, that is, that they produce the same desired results in the patient. Unfortunately, we believe that this basic assumption has not yet been proven to be true.

As citizens of New Jersey, you and your family would be denied the assurance you now have under present law that the drug product your family doctor prescribes is precisely the product he knows and trusts. This is important. For example, at the June 3 public hearing on A. 1257, testimony was presented showing that differences among various manufacturers' versions of chloramphenicol were so great that at least one of the so-called "generic equivalents" was virtually useless. A child with typhoid fever receiving this "equivalent" drug, instead of the one his doctor thought he was taking, could easily die before the substitution was discovered. Studies showed similar differences in a wide range of products. In fact, studies more often showed differences than equivalence.

As consumers, you know there is hardly a product made that couldn't be cheapened by eliminating some steps in the manufacturing process, or by reducing the number of people involved in quality control and inspection, thus permitting the product to be sold at a lower price. But at Merck and other reputable pharmaceutical houses, quality is the paramount consideration--as the large number of jobs directly related to quality improvement and quality control illustrate. If price were to become the only consideration, less attention would have to be given to quality--to the detriment of employment in the industry and to the detriment of people who rely on the products the industry produces.

For all of these reasons, therefore, it is our considered opinion that adoption of A. 1257 would be a mistake and we would like to register our opposition to passage of this bill.

Very truly yours,

Edward Kross

Edward Kross
President, Rahway Local No. 8-575



WILLIAM M. WEINSTEIN, *Prescriptions*
PHARMACEUTICAL SERVICES, INC.

55 EAST MT. PLEASANT AVENUE
LIVINGSTON, NEW JERSEY 07039

June 21, 1974

The Honorable Byron M. Baer
420 Lantana Avenue
Englewood, New Jersey 07631

Dear Assemblyman Baer:

I am submitting this for public record, because I am concerned about A. 1257, which affects the public and my profession in a profound manner. I do not have any information as to what qualifies an individual to speak on a specific issue other than being an interested citizen. In addition to my citizenship, I offer the following qualifications:

1. A Registered Practicing Pharmacist in New Jersey since 1946.
2. A former member of the faculty of the College of Pharmaceutical Sciences, Columbia University.
3. Presently, a visiting adjunct Professor of Pharmaceutics at Rutgers College of Pharmacy.
4. Practicing pharmacist at the present time, in my Pharmaceutical Center, Livingston, N.J.
5. A member of the Board of Governors of the Essex County Pharmaceutical Society.
6. A member of the APhA, NJPhA, Academy of General Practice, Fellow of the American College of the Apothecaries, and Rho Chi.
7. My civic responsibilities include serving as President of Temple Beth Shalom, Livingston, N.J.

I am cognizant of the time and effort devoted to the rationale that prompted the legislation contained in this proposed law. I am in complete agreement as to the intent, but I question if this can be accomplished in a practical manner as A. 1257 is presently written.

There are a number of areas that I feel require further clarification, possibly a different approach or complete reconsideration. I will just involve this correspondence with certain sections by referring to them by letter or number or both.

Para. 1. c

In the definition of prescriptions, there is no allowance for a designee of the authorized medical practitioner to communicate the order to the pharmacist.

Para. 1. g (1)

"Such standards shall where possible include" leaves the determination of how much criteria is truly required in each case to be interpreted.

Para. 1. g (1) (b)

The fifteen minute interval of clinical testing is in many instances unwarranted and unnecessary. The remaining subtitles present an attempt to direct a research program which I believe is not the intent of the proposed legislation. Competent research is based on accepted methods and procedures long established as necessary.

Para. 2.

The proposed members of the Health and Drug Utilization Review Council certainly give a broad representation to varied opinions, but I find the lack of expertise in pharmacokinetics to be of critical importance. A knowledge of drug availability from dosage forms - not drugs themselves is vital. I sincerely doubt the scientific input of the two practicing physicians, two pharmacists and two public lay persons. Their expertise and comments probably would not be constructive to the scientists involved in the bio-availability comparisons.

Para. 3.

Determination of a list of approved drugs is a monumental task and, unless certain specific ground rules are established, the extent of evaluating medications could possibly be non-ending. How does a council determine refill authorizations and standardize dispensing quantities? These are in the purview of the prescriber. Every situation is an individual one.

Para. 4

I must address myself to this section by asking certain questions:

1. How does the pharmacist base a lower cost - how much lower is low - and lower than what?

June 21, 1974

2. How many choices are available and are they all required to be stocked in the pharmacy?
3. How is the pharmacist compensated for contacting the practitioner for the change of prescribed medication? The time and money may create a problem.

Para. 6.

In attempting to legislate that the full savings in cost be passed on to the consumer, how is that to be determined? Again, I must say that this creates an almost impossible regulatory demand.

I regret that I was not able to be present at the hearing. I do have an appreciation for the problems that the committee is attempting to solve and I am hopeful that you will be able to use my comments and suggestions in creating a workable and equitable set of regulations.

Thank you for whatever consideration you give my correspondence. I am hopeful that the committee will react and enact the most practical legislation that is required to fulfill the intent contained in A. 1257.

Sincerely,



William M. Weinstein

TO: Commerce, Industry and Professions Committee
New Jersey Legislature
State Capitol
Trenton, New Jersey

FROM: Professor Sidney H. Willig, Temple Law School, Philadelphia

In Re A-1257, New Jersey legislative proposal, as per your inquiry by phone, 3 June 1974.

Corrections and Other Suggestions

In definitions section 1.c.

follow "disease" in line 5 with "in accordance with prerogatives noted in the practitioner's governing practice act of the State of New Jersey,"

follow "duly" on line 2 with "New Jersey"

In definition section 1.e.

follow identical with "and whose inactive ingredients, adjuvants, binders, coating shall not in the belief of the council, be substantially different from the reference drug product."

In definition section 1.g.

follow "product" on the 3rd line of (1) with "Such standards shall be established by the Council and/or adopted from those provided by the reference drug product manufacturer, those provided by the Federal Food and Drug Administration; those provided by official compendia."

In section 2. This section betrays some naive. At least 2 members should be pharmaceutical chemists with 5 or more years of experience in pharmaceutical manufacturing and quality control. Physicians, pharmacists and pharmacologists could not contribute any such knowledge as required by the Council inasmuch as their knowledge is limited to the pharmacological significance of a given quantity of an active ingredient. The physician among the three has the additional opportunity for clinical evaluation, but that tends to be post hoc.

Section 3. Following "drug products" in the first sentence, add a new sentence. "The council shall be authorized to use all current scientific means including plant inspection, product sampling, examination of manufacturing and quality controls data, that will serve such determination. It may in its good judgement accept such results as provided by federal or other state agencies." Manufacturer's protocols of assay may be self serving and are usually insufficient. The Council must be prepared to carry out product testing independently.

In the second paragraph, the concept is not fair to consumer interest organizations and residents of the state. The copies of the list should be publicized in the lay press and individual copies should be distributed to everyone who requests same without any charge therefor.

In the fourth paragraph, substantial changes and deletion is required. Since a prescription may not be refilled without a physician's order, the Council would be disregarding a supervening Federal Law, Section 503(b) of the Federal Food Drug and Cosmetic Act and would be aiding and abetting misdemeanor thereunder. However it is reasonable to recommend to physicians that they prescribe quantities which more nearly reflect the patients' exact anticipated needs. This will preclude waste of precious pharmaceuticals and help conserve this resource for the public.

Dosage form exchange is an area that should be treated warily and governed by the same criteria under g.(1) in Section 1. foregoing. That is the only way to assure that no substantial therapeutic difference will result. That is too much additional task for the Council to undertake.

Section 4 starts off with "Notwithstanding any other law" and is a direct challenge as it is written, to the Federal Food Drug and Cosmetic Act, a supervening federal law in this area. By the total effect of section 503(b) of the FFDC Act, 502 and 301 of that law make it a misdemeanor for anyone to provide any dose of a prescription drug to another human being unless:

1. It is by the order of a physician so to do
2. It is the exact drug named by the physician in his order, as to identity, strength, dosage etc.

To accomplish what you wish to in 4. you must require under the language of the New Jersey Medical Practice Act that physicians prescribe by established name only, or that they accept the proviso that in exchange for practicing in New Jersey they must agree to prescribe only in accordance with a New Jersey formulary prepared by the Council. In exchange, the Council for the State of New Jersey should offer each physician a "save harmless" agreement to free him from liability for damages which accrue from products dispensed pursuant to his order.

Likewise in fairness to the New Jersey consumer, pharmacists should be permitted to dispense a different brand name or non brand name drug product of the same established name if it shall reflect a higher quality to the consumer and is contained in the latest list of Council approved drugs. In

respect to this act the pharmacists of the state should be offered encouragement in the form of "save harmless" agreements by which the state of New Jersey would assume liability for product harm allegedly due to the drug product substituted.

Also in Section 4, since physicians notoriously are poor letter readers with respect to notices of the kind mentioned herein, such prescription should not be refillable with the substituted drug until the physician acknowledges with approval the pharmacist's notice of the substitution. This will better assure the consumer of a satisfactory substituted product.

Section 5 is very poor as written. It should be rewritten to encourage pharmacists to contact physicians for a new prescription when the pharmacist believes the prescriber is unaware of the dangers or inefficacy of the prescribed drugs with due concern for the particular patient's record in his possession. Since every pharmacist can already do this in both federal and state law, it ought simply to be deleted.

Section 6 could be taken care of easily also by a regulations in the present N.J. Pharmacy Practice Act since it is in keeping with the anti-misbranding language of that law and the Federal law. However the loose part dealing with passing full savings in cost along to the consumer is too difficult to judge and police since it depends on many variables such as apply to purchase and sale of goods.

Section 7 utterly fails to comprehend the realities of deterency and the needs of the Council. It needs at least two zeros added to every figure cited.

Miscellaneous:

Have your legislative drafting group carefully read 21 USCA 331, 21 USC 352, 353(b). Also suggest they read Willig in Journal of Law Reform published by Michigan University Law School, Page 1, Fall Issue 1972.

Since only those drugs whose patents have expired can be substituted for by drugs the Council finds chemically and therapeutically equivalent, there should be language here assuring that the federal and state trademark acts and patents will be respected.

Further, to protect the individual members of the Council, they should be cloaked with whatever sovereign immunity extends to the Council or any other N.J. agency.

Further, the consumers of drugs for the state of New Jersey should be assured that by adoption of such statute it is not

Commerce, Industry and Professions Committee
New Jersey Legislature
State Capitol
Trenton, New Jersey

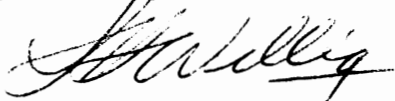
Page 4

the legislative intent, nor will they waive their rights to recovery under all remedies usually permissible in this jurisdiction, against any and all parties engaged in the supply, prescription and dispensing of drugs to the residents of that state.

Bear in mind that in *Mary Griffin v. U.S.*, the federal court granted a 2 million dollar judgement against U.S. because the federal agency had erred by certifying the antibiotic as meeting established standards of safety and efficacy.

Finally, that continuing the constitutional prerogatives of New Jersey residents relating to equal protection under the laws, the proposed law will not contemplate distribution of any misbranded adulterated or unapproved drugs as defined in pertinent state and federal laws.

Respectfully recommended,



Sidney H. Willig, Professor of Law
Director, Food Drug Cosmetic Unit
Temple Law School
Philadelphia, Pennsylvania 19122

SHW:bbe

Christ Hospital

176 PALISADE AVENUE
JERSEY CITY, N.J.

June 26, 1974

Mr. Byron Baer
Chairman of Assembly Committee for Commerce,
Industry and Professions
State Capital
Trenton, New Jersey

Dear Mr. Baer:

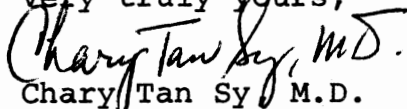
Since I am unable to come to the hearing on Bill AB1257 this Friday, June 28th, I would like to express my feelings in writing. My present position is as the Director of the Internship Training Program at Christ Hospital, Jersey City, New Jersey.

As I understand it, the AB1257 Bill would result in the repeal of the anti-substitution drug law permitting pharmacists the right to select the brand of medication rather than the M.D. In effect, the M.D. is limited to picking the class of medication used by the patient but the pharmacist decides the quality. The practice could be quite dangerous in patients with serious conditions where the quality and bioavailability are extremely important, eg. Digitalis.

Should the Bill be passed, the manufacturers would be forced to compete with the small backyard generic outfits. To cover such a loss of revenue the large companies would have to cut costs, notably in the areas of research. We would be hurt by this.

Thank you for your courtesy.

Very truly yours,



Chary Tan Sy M.D.
Director, Internship Training Program

CTS:lm

