

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

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HEARINGS
BEFORE THE
SUBCOMMITTEE ON MONOPOLY
OF THE
SELECT COMMITTEE ON SMALL BUSINESS
UNITED STATES SENATE
NINETY-SECOND CONGRESS
FIRST SESSION
ON
PRESENT STATUS OF COMPETITION IN THE
PHARMACEUTICAL INDUSTRY

PART 20

JANUARY 18, 19, FEBRUARY 1, 2, AND 3, 1971

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COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

MONDAY, JANUARY 18, 1971

U.S. SENATE,
SUBCOMMITTEE ON MONOPOLY OF THE
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C.

The subcommittee met, pursuant to recess, at 10:10 a.m., in room 1318, New Senate Office Building, Senator Gaylord Nelson (chairman of the subcommittee) presiding.

Present: Senator Nelson.

Also present: Benjamin Gordon, staff economist; and Elaine C. Dye, clerical assistant.

Senator NELSON. The committee will now open its hearings. Our witness today is Dr. Charles Edwards, Commissioner of the Food and Drug Administration.

I apologize, Doctor, for being delayed on the way over here. I appreciate your taking time to come.

The Monopoly Subcommittee of the Senate Small Business Committee is resuming its hearings today on drug usage and purchasing by the Federal Government.

Testimony by the Agency for International Development, the Public Health Service, the Veterans' Administration, the Department of Defense, and the Office of Economic Opportunity indicated that many millions of dollars were being spent on drugs which have been found by panels of specially qualified medical experts to be ineffective, unnecessary, or unacceptable.

For example, the National Academy of Science/National Research Council found that Darvon in its "32 mg. dose has often been found indistinguishable from placebo." Yet, the Defense Department and the Veterans' Administration in 1968 and 1969 paid \$678,000 for this ineffective dosage form.

The NAS-NRC has also found that Darvon "in doses of 65 mg. to 100 mg. has usually, but not always, proved superior to placebo in reasonably sensitive human analgesic assays. * * *" Expert testimony before the subcommittee on November 24th held that there is no "particular reason to use it (Darvon) routinely in preference to aspirin, acetaminophen, or codeine or some combination of codeine with one of the others."

Yet, the Defense Department alone spent \$4.4 million for Darvon in 1968 and 1969.

The Veterans' Administration purchased the tranquilizer meprobamate from Denmark for \$1.55 per 500 tablets. VA, at the same

time was purchasing Meprospan, the sustained release form of meprobamate, from Carter-Wallace for \$34.25 for 500 tablets, or 2,300 percent as much as plain meprobamate. Neither the USP nor the National Formulary recognize the use of long-acting preparations as good medical practice, and the NAS-NRC panel of experts told the subcommittee that "most of these oral preparations of this type are not doing what they purport to do" and that their use can be dangerous.

The Defense Department spent about \$3 million in 1968 and 1969 on demethylchlortetracycline (Declomycin), oxytetracycline (Terramycin), and chlortetracycline (Aureomycin). If the Department heeded the advice of the medical experts and used the drug of choice of this family of antibiotics, that is, plain tetracycline, \$2.3 million would have been saved.

The Department of Defense bought \$133,584 of Equagesic, a combination of aspirin and meprobamate. The NAS-NRC report says that "this combination may be no more effective as an analgesic than the amount of aspirin present." The comparable total for aspirin would have been \$2,721, or a saving of \$130,863.

Both the VA and the DOD spent \$683,632 for Peritrate, a drug used for angina pectoris, which, according to expert testimony, is "not effective compared to a placebo." It may be mentioned also that the American public spent \$22 million in 1968 and \$19.5 million in 1969 for this drug.

These are only a few examples of the large number of ineffective and unnecessary drugs being bought and used by the Federal Government in many of its programs.

Our witness today is the Commissioner of the Food and Drug Administration, who will discuss problems of rationality in drug usage. Our witness tomorrow will be the Comptroller General, who will discuss problems of rationality and competition, and small business in drug procurement.

On February 1, 2, and 3, the Government agencies will be returning to discuss the various changes they have made to bring about more rational and economical drug use and procurement.

Dr. Edwards, your testimony will be printed in full in the record.¹ You may present it however you wish and if at any time you desire to extemporize on it or elaborate on anything you have said, feel free to do so and we will be glad to take time for any comments of your counsel, Mr. Goodrich or Dr. Simmons. Go ahead.

STATEMENT OF DR. CHARLES C. EDWARDS, COMMISSIONER OF FOOD AND DRUGS, PUBLIC HEALTH SERVICE, U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE; ACCOMPANIED BY DR. HENRY SIMMONS, DIRECTOR OF BUREAU OF DRUGS; AND WILLIAM W. GOODRICH, ASSISTANT GENERAL COUNSEL, FDA

Dr. EDWARDS. Thank you, Mr. Chairman. I would like to introduce the gentlemen with me. On my right is Dr. Henry Simmons, Director of our Bureau of Drugs. On my left, Mr. William Goodrich, who is the General Counsel of FDA.

¹ See pp. 8444-8465.

We certainly appreciate this opportunity to discuss with you the important issue of safe and effective drugs. These are certainly issues that touch directly on the lives of all of us.

I think no one would question that the discovery and development of new drugs and new antibiotics over the past three decades have contributed enormously to the eradication and control of disease and to the relief of patient suffering.

However, over this same period of time, drug misuse has become a major national problem. I speak not just of drug abuse in the conventional sense, but rather of the promotion, the prescribing, and the use of drugs of limited or no value, and, of course, equally important, the consumption of too many drugs, often for no purpose or for the wrong purpose. I think few things are more tragic than the prescribing and administration of a drug of no proven effectiveness followed by a serious and even sometimes fatal adverse reaction.

We at FDA are concerned first with drug safety, but we must constantly bear in mind that considerations of drug effectiveness and drug safety cannot be separated.

I would like this morning to briefly discuss where we are today, how we arrived at this point and how we plan to proceed in the days ahead.

Our goal is to achieve the objective of excellence in drug quality, honesty in drug promotion, and rationality in drug use at the earliest possible time. We are striving for a uniform and high standard of safety and reliability of all drugs. Of course, this requires us to be concerned with all phases of the drug scene:

We are concerned with all manufacturers large and small;

With the discovery and investigational use and development of all new drugs;

With the evaluation of safety and efficacy of new products offered to the medical profession;

With the quality controls that assure the identity, the strength, the quality, the purity, and the reliability of the product that comes off the production line and into the hospital, and the community pharmacy;

We are concerned with the labeling and promotion of these products;

With the experience of these drugs in the hands of the practicing physician;

And indirectly, of course, with the costs of these products.

Although we have no specific responsibility relating to drug costs, it is well to recall that Senator Kefauver's investigation a decade ago focused attention on the causes of the high cost of prescription drugs. They were poor quality research, excesses, and exaggeration in promotion and the difficulties encountered by prescribers in obtaining reliable information that would facilitate rational drug therapy. All of these important areas are responsibilities of the Food and Drug Administration.

Senator NELSON. May I interrupt a moment? Isn't an additional problem, which relates to costs, the result of brand name prescribing? That is to say, in 40 or more States—the legislatures have passed anti-substitution laws. So then, if you have a situation in which the

doctor prescribes by the brand name, the pharmacist is required by law to give that brand even though the same compound meeting all appropriate USP or NF standards is being sold at a fraction of the price. Brand name prescribing is an important factor in keeping the price up.

As you know, we heard lengthy testimony on prednisone, which varied in price from 59 cents a hundred to \$17.90 a hundred to the pharmacist; which is a radical price difference. Yet the Medical Letter said they were all equivalent—all met the same standards.

How do you get around that kind of a problem?

Dr. EDWARDS. Well, I think there is probably no simple answer to solving that problem. Certainly, one of the answers is to better communicate to the medical profession the fact that in today's drug scene the brand names and the generic name drugs that are approved by the Food and Drug Administration are for all practical purposes equal drugs in terms of their potency, uniformity, et cetera.

I think frankly, we have not done enough in communicating this kind of information to the practicing medical profession but I think it has to be done and I think until that message is satisfactorily or adequately conveyed to it, we are likely to have this discrepancy in prescribing patterns.

Senator NELSON. You do not have any evidence that indicates, generally speaking, that between brands and generics, one is better than the other?

Dr. EDWARDS. No. I think in today's drugs, certainly in the case of the antibiotics that are certified by the Food and Drug Administration, we can certainly say there that brand and generics are equal. I think that any drug that goes through the New Drug Application process is equal, be it brand or generic.

I think there are some of the "me-too" drugs that we are coming to grips with via the National Academy of Science drug efficacy study that present a little different problem and we cannot make quite that statement in reference to those drugs, but certainly on all drugs that have been approved through regular processes we can make this statement.

Senator NELSON. You may proceed.

Dr. EDWARDS. Moreover, as the investigations of this subcommittee have shown, the Federal Government is a very substantial purchaser of prescription drugs. We at FDA have a responsibility to do what we can to assure that the Federal purchasers are fully informed about the products they buy.

We do have problems in the use of prescription and nonprescription drugs in this country. It is a serious problem and threatens to become more so if vigorous steps are not taken to correct the basic problem.

Mr. GORDON. Dr. Edwards, may I interrupt? What is the evidence of the existence of these problems? How are they manifested?

Dr. EDWARDS. I am about to allude to some of the problems in my statement. They include the fact that the American public is currently receiving approximately 2 billion prescriptions per year and it is estimated that in 5 years this is likely to increase some 50 percent to over 3 billion prescriptions a year, this figure excludes

over-the-counter drugs which are sold in even greater quantities. I think just the volume itself speaks somewhat to the problem.

The subject of adverse reactions to drugs is an important subject. This complication rate has been estimated at some 10 percent, and further that approximately 5 percent of all patients admitted to general hospitals are admitted because of some form of drug reaction.

As I have indicated in my testimony, studies have shown that the average hospital patient receives between eight and 10 drugs per hospital admission and this, of course, may go much higher.

I think all of these indicate, to a degree, the magnitude of the problem we are talking about this morning.

Mr. GORDON. You also state:

We have a responsibility to do what we can to assure that Federal purchasers are fully informed about the products they buy.

What have you done to keep the Government agencies informed about the merits and demerits of drugs on an absolute as well as relative basis?

Dr. EDWARDS. Well, as you know, at least as it relates to the current drug efficacy study, we have sent to each of the purchasing agencies in the Federal Establishment that purchases drugs, our list of drugs classified by NAS-NRC as "ineffective." We intend to keep them up to date on this.

We also intend at the completion of this study to publish a document on the study per se listing all the drugs and their classification by the National Academy of Sciences.

In terms of our day-to-day activities, and Dr. Simmons might want to address himself to this particular question, I do not believe we notify Federal agencies on a day-to-day basis of the new drugs we have approved. Is that correct?

On a periodic basis they are notified but not with each drug as it is approved by the Food and Drug Administration.

Senator NELSON. What kind of a response, if any, have you gotten from any of the professional organizations, the medical profession, or from individual physicians across the country when you have listed a drug that has been widely used and then taken off the market as "ineffective" or "possibly effective?" Those two categories go out of the market forthwith, if they are classified as such; is that right?

Dr. EDWARDS. Possibly. In the case of those drugs classified as "ineffective", the manufacturer has 30 days in which to submit new evidence to us to justify a change in that classification. With "possibly effective" drugs, 6 months are allowed for submission of new evidence; and for the "probably effective" drug 1 year is allowed.

Senator NELSON. Of those that have been removed from the market because they were found to be ineffective or because companies could not come up with evidence to sustain any claim that they were effective, what kind of a response have you heard from the profession?

Dr. EDWARDS. I suspect it is a little early to make any blanket statements. We have certainly heard from the American Medical

Association and Medical News, their weekly publication, they have been very cooperative with us. The response we have gotten from the profession per se has been rather limited but I must be very frank to say that most of the response has not been particularly complimentary to the Food and Drug Administration.

I think there has been an unwillingness, at least by some of the profession, to accept these findings of the National Academy of Sciences and the Food and Drug Administration as being final and as authoritative.

Senator NELSON. I am sure you saw the December 21 article from the New York Times with the heading: "Many Doctors Ignore U.S. List of Hazardous or Useless Drugs".¹ It states:

A list of 369 drug products considered ineffective or hazardous by the FDA apparently is being ignored by a large number of doctors and their patients across the country. Some doctors go so far as to say they consider the Federal agency's action in issuing the list unethical.

Reports from 18 cities one month after the list was issued, also indicate that most people are unaware of the list's existence and are continuing to rely on the advice of private physicians on which drugs to take.

Dr. William Limberger, President of the Pennsylvania Medical Association, commented that:

However, this at times injudicious release by the FDA does not enhance the confidence in the medical profession.

I am curious about this reaction, not being a doctor myself. I wonder whether this is a typical reaction of the medical profession to the judgment of the most distinguished clinicians in the country on the use of drugs. Do you have any comments as to why the profession would not enthusiastically follow the lead of their most distinguished authorities in the field rather than, as apparently many do, take the attitude that there is something wrong with what the FDA is doing?

Dr. EDWARDS. Unfortunately—

Senator NELSON. May I interrupt? There is something wrong either with the communication of the information to the doctors or their understanding of it or the medical profession's effectiveness in telling doctors:

For heaven's sake, follow the advice of the most distinguished scientists on this matter.

What do you think about that, Doctor?

Dr. EDWARDS. I think all the points you just made are very real ones, very legitimate ones. I think in addition to that we have to appreciate or at least hope that the opinion the doctor in Pennsylvania expresses is not necessarily the opinion of the majority of the medical profession. But I certainly would find his statement a very difficult thing to explain and as I say, I just hope that it is not the unanimous opinion of the medical profession.

Senator NELSON. It seems to me, if the President of the Pennsylvania Medical Association is accurately quoted, that it would have an unfortunate effect on the rest of the doctors of the State since he is elected by the profession.

¹ See p. 7993.

Have you gotten this reaction from other State medical societies?

Dr. EDWARDS. As I attempted to indicate a moment ago, the reaction has been mixed. We have had some very nice things said about what we have done. Some other people that have been very critical of what we have done. And I do not know just exactly, as we have not really surveyed the profession in a meaningful sort of way, what the overall reaction is, nor do I think the gentleman who wrote that article really had a sample that was meaningful that would allow him to make a statement quite like he made.

I think we have to communicate the fact to the medical profession that our ultimate aim is to assure the physician that when he prescribes a drug, on which certain claims are made, that he can depend on those claims. I mean, he can depend that these claims will be fulfilled by the drug that he is prescribing. So it really is in the best interests of the profession that they support us and support the National Academy as well.

Senator NELSON. I have not had the opportunity to look at the professional journals. How have they handled the continuing release of the information respecting NAS-NRC studies and the decisions made by the FDA respecting these drugs?

Dr. EDWARDS. I think their handling to date has been pretty much a straightforward reporting job. I do not think there has been a great deal of editorializing.

Do you want to comment on that, Dr. Simmons?

Dr. SIMMONS. Generally, the journals that report this information, specifically the AMA Journal, the Journal of the American Medical Association, and also the Journal of Internal Medicine, merely report what has been said without editorializing. If you ask what kind of support there has been in the medical community generally, I would echo the Commissioner's statement that it varies from faint praise to loud damning.

The New England Journal of Medicine recently ran an editorial stating that with all the difficulties the FDA had in these drug evaluations and other things, the title of the editorial was, "Homage to the FDA," that even with this difficult job the profession did look to it for that kind of guidance. I think generally what it might be reasonable to say is that if anybody thought of going back to the old system before FDA had authority to look to efficacy, almost no one would be willing to go back to that system.

We know that change is difficult to accept.

Senator NELSON. Go ahead, Doctor.

Dr. EDWARDS. I would now like, Mr. Chairman, to speak briefly about the drug efficacy review per se. The Drug Amendments of 1962 required that drugs be proven effective for their intended uses, as well as safe. Thousands of drugs introduced between 1938 and 1962 had been marketed on proof of safety alone with no obligation upon the manufacturer to prove the truth and validity of their promotional claims of effectiveness.

Surely the most important provision of the 1962 Amendment was to define the kind and the quality of medical evidence that is to be required both to justify the introduction of any new product and to sustain the continued marketing of products already on the

market. Congress decreed that claims of drug effectiveness must be supported by "substantial evidence"—meaning evidence derived from adequate and well-controlled clinical investigations on the basis of which it can fairly and responsibly be concluded by experts that the particular drug will have the effectiveness it is represented and purported to possess.

The task set forth before the Food and Drug Administration was a monumental one, to say the least.

In 1966 the Agency turned to the National Academy of Sciences/National Research Council for help. NAS-NRC agreed to undertake the evaluation of the more than 3,000 marketed preparations approved by the Food and Drug Administration between 1938 and 1962, that were still on the market, and to determine whether they were effective for the indications claimed in their labeling. The Drug Efficacy Study was established by NAS-NRC in June 1966 and some 30 panels were set up to evaluate various categories of drugs.

The results are summarized in *Drug Efficacy Study, A Report to the Commissioner of Food and Drugs from the National Academy of Sciences*, which was given to us in 1969. As the report notes, this review made "an audit of the state of the art of drug usage that has been uniquely extensive in scope and uniquely intensive in time" and is applicable to more than 80 percent of the currently marketed drugs.

Senator NELSON. You mean 80 percent of the different compounds? Is that what that means?

Dr. EDWARDS. 80 percent of all dosage forms that are available in the pharmacy.

Senator NELSON. Of all kinds of compounds.

Dr. EDWARDS. Right.

The report noted that the quality of the evidence of efficacy, as well as the quality of the labeling, was poor. Many of the presentations submitted by manufacturers in support of the claims made for the use of their drugs consisted of reports of uncontrolled observations and testimonial-type endorsements. There was a conspicuous lack of substantial evidence based on well-controlled investigations by experienced investigators. The panels specifically criticized the labeling of about two-thirds of the drugs that they evaluated. They have found too many of the package inserts to be poorly organized, repetitive, out-of-date, evasive, and promotionally oriented. The majority of the inserts were found to fail in their primary purpose of providing the physician and the pharmacist with authoritative and objective guides to prescribing or dispensing the drugs in question.

Senator NELSON. May I interrupt again, Doctor? Under the law the Food and Drug Administration has the authority to require that the package insert be accurate and make only justifiable claims and be in sufficient detail. In other words, you have the authority to control what goes into that package insert?

Dr. EDWARDS. That is correct.

Senator NELSON. What is the practice? The company makes up the insert—then when does the FDA get around to looking at it?

Dr. EDWARDS. Prior to approval of any new drug the company, the manufacturer, and the FDA sit down frequently in numerous

conferences to work out the labeling of the particular drug in question. All of the labeling claims on these some 2,000 drugs that are under review in the drug efficacy study, which will remain on the market in one category or another for the time being, will be reviewed and appropriate changes made in the labeling.

Senator NELSON. So, any labeling—

Dr. EDWARDS. I was going to say in addition to that, our current labeling policy on new drugs is a much tougher one than that in previous years in the FDA.

Senator NELSON. So, all labels that have been criticized by the NAS-NRC as being inaccurate for one reason or another will be revised.

Dr. EDWARDS. All of those will be revised and we are moving as I indicate later in my testimony, toward class labeling. In other words, and tetracycline is probably the best example, for a tetracycline drug, be it a brand name or be it generic, the labeling should be the same. I think this will do a great deal to clean up and to make more meaningful the labeling for drugs.

Senator NELSON. I do not know that I follow you on that. You mean that now if there are several brand names of tetracyclines that they may have different labeling?

Dr. EDWARDS. There may be some differences in labeling between various brands of the same drug. We are changing this. We are moving in the direction of class labeling across the board.

Senator NELSON. I do not know what the present practice is. It never occurred to me to look.

Does the labeling require, then, that the generic name of the compound be on the label?

Dr. EDWARDS. Yes. Do you want to add anything to this Dr. Simmons?

Dr. SIMMONS. Yes. Mr. Chairman, on the class labeling specifically, what we are trying to accomplish is this. At the present time—take tetracyclines for example, on which you had a lot of testimony, there are about five different chemical formulations of tetracycline. Now, all of them have minor differences which present and old labeling show, and on which advertising claims have been made.

The important thing, however, is that these minor differences, though there, are clinically insignificant. Therefore, there is no reason why a physician should choose one as opposed to any other.

Now, since there are, I think, over 50 tetracyclines available in these five different chemical classes, what we are trying to do is to simplify the labeling to point out to the doctor, in a simple, concise way, that basically they are all the same. He can expect the same result from any of them and he should base his therapeutic judgments on that statement.

That is what class labeling is and that is what we are trying to accomplish with it.

Senator NELSON. Well, if the distinctions in the formulations are of no clinical significance, are they permitted to make a claim in the labeling that they are?

Dr. SIMMONS. They will no longer be allowed to.

Senator NELSON. They will not be permitted to do that any more.

Mr. GORDON. Is there any evidence that the physician bases his prescribing practices on the contents of the label?

Dr. EDWARDS. I think we have to remember that the Physicians' Desk Reference, which I believe is probably the most commonly used source of drug information by the practicing physician, is made up principally, or composed of, the labeling on various drugs. So, I think looking at it from that standpoint, I suspect that we could say that he does use the labeling.

How frequently the physician uses the package insert per se I do not know. I do not think we have any basis for a statement on that. Dr. Simmons points out, and it is an extremely important point, that the labeling does in fact indicate what may be in the advertising and promotional material for the drug. This is doubly important, not just for the physician per se, but also in terms of all promotional material for a particular drug.

Senator NELSON. I do not follow that. You are saying that they cannot promote the drug—make claims for the drug beyond what are authorized in the label?

Dr. EDWARDS. What is in the label, exactly.

Mr. GOODRICH. And they must make the same warnings and with the same emphasis and the same words in the promotion as in the package insert. So, the package insert sets the stage for all promotions and controls over promotion. That is, the journal advertising, the mail-outs, detailing, and so on.

Senator NELSON. Who uses the insert? The physician usually does not see it, does he?

Dr. EDWARDS. The physician or the pharmacist may or may not see it depending on what his own habits happen to be, but we hope the majority of physicians see it, particularly with more potent drugs.

Senator NELSON. Does the PDR print the whole package insert?

Mr. GOODRICH. In general, yes. They are not required to have some of the things in the insert, like animal studies and things of that kind, but the essential indications, contraindications, warnings, precautions, et cetera, all are required to be in the PDR exactly the same as in the labeling.

Senator NELSON. You say they are required to be in the PDR.

Mr. GOODRICH. If the drug is advertised in the PDR. There is no requirement that anything be put in the PDR but if the company desires to advertise by listing their drug in the PDR they must use the prescribed information.

Senator NELSON. It is required, then, that if a company places an ad in the PDR, that the ad must conform to the labeling FDA has approved for that particular drug. Is that correct?

Mr. GOODRICH. Yes.

Senator NELSON. And, therefore, if they are going to advertise, they have to include certain parts of the package inserts.

Mr. GOODRICH. Our position is that the PDR really serves the purpose of labeling on the physician's desk and, therefore, it must be in conformance with the labeling requirements. We do not allow in the PDR a brief summary that might be permissible in a prescription drug ad, but even in the prescription drug ads you are seeing

the brief summary more and more containing the full story about the warnings and precautions because the regulations do require the same emphasis and the same wording for those essential warnings.

Senator NELSON. Go ahead, Doctor.

Dr. EDWARDS. Continuing on with regard to the drug efficacy study per se, the panel reports evaluated the indications for use as "effective," "probably effective," "possibly effective," "ineffective," "ineffective as a fixed combination" and "effective but." The results of the evaluations are the following. Again, I emphasize, too, here our percentage numbers are based upon the total number of claims on these drugs of which there were some 16,500. Of those 16,500 claims, approximately 14.7 percent were found to be ineffective. Approximately 35 percent were found to be possibly effective. 7.3 percent, probably effective. 19.1 percent, effective, and 24 percent, effective "but."

I might say at this time that we have returned the "effective but" ratings to the National Academy of Sciences for clarification but we did begin to implement the other reports in 1968.

The NAS-NRC reports and our medical reaction to them are not self-executing. They trigger the administrative process of labeling and product reform.

As soon as the first report classifying a drug as "ineffective" was announced, industry resistance appeared. The first line of defense was to throw the issues into hearings, from which protracted delays could be anticipated. There were court suits seeking exemption of a great number of drugs from the efficacy review—on the ground that they were excused by the grandfather clauses.

The real test of the Agency's determination and ability to translate the scientific reviews into patient benefits came in mid-1969 with the now quite famous *Panalba* case. The Agency took two important steps to minimize hearing delays. It defined the scientific content of adequate and well-controlled clinical investigations to provide a regulatory base against which medical documentation would be measured, and it established summary rules to limit its hearing procedures to those cases in which the sponsor of the drug could establish that there was a genuine and substantial issue of fact requiring a hearing.

The *Panalba* case was taken first to the district court and then to the court of appeals. After an expedited appeal, FDA prevailed. The principles on which we would proceed were then firmly established.

There was a temporary setback in the District Court in Wilmington, Del., a short time before the *Panalba* decision came down with the consequence that we had to repromulgate the interpretive and procedural rules. In May 1970, the rules were reissued; a pharmaceutical manufacturers association challenge failed when the district judge sustained the rules in late October. Thus, only 8 months ago the roadblocks were removed and the stage was set to move ahead with the administrative proceedings in an expeditious fashion.

From the drug efficacy study arose two areas of special concern; fixed dose combination drugs and the elimination of unnecessary internal delays in processing cases.

Senator NELSON. May I ask a question, Doctor? The table on page 6, appears to show that almost 60 percent of the claims lack adequate

evidence of efficacy. That is, if you take the categories "probably effective," "possibly effective," "ineffective." Dr. Simmons, in his December 29 speech¹ said:

Of the 16,000 therapeutic claims evaluated by the panels, approximately 11,000, or 70 percent, were found to lack adequate evidence of efficacy.

Do you have a reconciliation of those two figures?

Dr. EDWARDS. I suspect he was including in that category the "effective but" drugs. You see, on some of these drugs that were categorized by the Academy as "effective but," the staff of the FDA made an interpretation of their comments and placed them into the "possibly," "probably," "ineffective" or "effective" categories.

Senator NELSON. I see.

Dr. EDWARDS. So, I think that would account for the discrepancy in numbers.

Senator NELSON. Thank you.

Dr. EDWARDS. Moving on to these two problem areas, combination of drugs account for about 50 percent of the products involved in the National Academy of Sciences reviews. Though the NAS-NRC panels in general ruled against fixed dose combination drugs, 40 percent of America's best selling drugs are fixed dose combinations. It has been estimated that 40 to 50 percent of the prescriptions call for drugs in fixed combination dosage form. The limitations of effectiveness, the limitations of rational use and the built-in hazards that attend the use of some fixed combination dosage forms have long been recognized. They are discussed in the NAS-NRC report, they are discussed in resolutions by the AMA's Council on Drugs, in testimony before this committee, and certainly by many experts in the medical literature.

I would, however, like to make it abundantly clear that FDA is not against all fixed dose combinations. Our problem is to develop and to implement a reasonable policy for dealing with fixed dose combination drugs to make rational prescribing possible.

Senator NELSON. Is it not correct, however, that the NAS-NRC position thus far on fixed combination dosage forms is that the fixed combination that they have endorsed have been an exception to the rule?

Dr. EDWARDS. That is correct.

Essentially, our problem is to allow the marketing of those fixed combination drugs which fill a need among that patient population requiring concomitant therapy with multiple drug ingredients at the particular dosage levels offered. This must be done without permitting the marketing of irrational fixed dose combinations intended for patients who may have a condition amenable to treatment by one or more of the components but who has no need for the others. Certainly, the hazards of unneeded drugs are all too well known to require any extended discussion today.

Mr. GORDON. Dr. Edwards, what is your new policy with respect to combinations and what do you hope to accomplish by it?

Dr. EDWARDS. We are in the process of developing guidelines, if you will, as to what we consider an adequate combination drug. We will probably be publishing these in the Federal Register within the

¹ See pp. 8426-8443.

next 2 weeks. The Pharmaceutical Manufacturers Association has asked that we look at what they suggest, which we will do with them the latter part of this week.

In essence what we are saying is that in any combination drug, the various ingredients of the combination must be shown to exert some effect on the total effect of the drug.

Mr. GORDON. You mean an additive effect or more than an additive effect?

Dr. EDWARDS. Well, that any ingredients of a combination must in fact have some effect on the ultimate or total effect of the drug. Dr. SIMMONS, do you want to add to that?

Dr. SIMMONS. That no drug should be present in a fixed dose combination unless its presence clearly enhances safety or efficacy. And unfortunately, most combination drugs to this point have not developed that type of efficacy.

Mr. GORDON. But convenience is not sufficient.

Dr. EDWARDS. I think convenience is a factor. It certainly has to be considered all else being equal. I think, for instance, in pediatric drug therapy convenience frequently can come into play, but it certainly is not a factor upon which we would base our decision.

Senator NELSON. I am puzzled about that. If it is a fixed dosage form, are you saying that adequately controlled studies would have to be submitted to demonstrate that the combination of these drugs is additive or synergistic?

Dr. SIMMONS. That is right. Mr. Chairman, maybe the simplest way I might be able to explain it would be that if you put two drugs together to treat pain, we would expect you to provide evidence that you get a better result with those two than you would with either of the active ingredients if that particular drug were used in an adequate dose. This is basically what we wish to have provided to us.

Senator NELSON. But here you are reciting the case of an analgesic.

Dr. SIMMONS. Yes.

Senator NELSON. You are not talking, then, about establishing some rules to permit fixed combinations of anti-ineffectives?

Dr. SIMMONS. Yes. That would follow the same rule, that you do not put two antibiotics together unless you can show that those two provide a better result than either one of the ingredients, either a better result in increased safety or increased efficacy.

Senator NELSON. In order to put two antibiotics together in a fixed dosage form, do you mean to say that both of these antibiotics must be effective against the target organism?

Dr. SIMMONS. That is right.

Senator NELSON. So that you would not permit the situation that occurred in the fixed combination of novobiocin and tetracycline which was Panalba.

Dr. SIMMONS. No, we would not. There are two parts to the combination policy, one, that there should be evidence that both contribute to the therapeutic effect, and two, that that specific formulation can be used rationally. In other words, where you must increase the dose of one antibiotic to take care of a certain organism, you do not carry along with it an increase in the dose of the other for which there is no indication to increase the dose. So, there are two requirements in our combination policy.

Senator NELSON. In the studies thus far of the NAS-NRC, apart from topicals, were there any fixed combination drugs that met the standard that you are talking about?

Dr. SIMMONS. Mr. Chairman, out of, I believe, over 1,300 combination drugs reviewed, excluding topicals and parenterals only a handful were rated effective.

Senator NELSON. A handful?

Dr. SIMMONS. Yes.

Senator NELSON. By the standards that you are reciting here.

Dr. SIMMONS. By the NAS-NRC standards themselves. You see, they had a basic standard at the beginning of the study that there should be substantial evidence that each drug contributes to the therapeutic effect claim.

Senator NELSON. And this is the standard that is being adopted or proposed for adoption by the FDA?

Dr. SIMMONS. Yes.

Senator NELSON. Now.

Dr. EDWARDS. Right.

Mr. GOODRICH. With some refinements. We want to improve on that to make sure that the combination itself is rational. For example, the oral contraceptive is a fixed combination product in which both components serve a useful purpose and for which the patient requires concomitant therapy in that combination.

What we are essentially saying is that a fixed combination should not be giving the patient a variety of drugs when he or she needs only one, and if a variety are given, there must be a situation in which the patient requires concomitant therapy with the two drugs in this particular dosage form as Dr. Simmons said, either in terms of increased safety or increased effectiveness.

Senator NELSON. Thank you.

Dr. EDWARDS. We have spoken briefly of the combination problem. The problem of internal delays is frustrating, as you know, to all administrators. We have provided extra resources in the Bureau of Drugs to expedite the handling of these cases. This has and continues to have high priority and these cases are handled as rapidly as possible. We have already published reports on 1,200 drugs and about 700 others are ready for publication. The remainder should be in the public domain by March of this year.

But only last Thursday, the District Court here in Washington heard the American Public Health Association's complaint that we are not moving fast enough. That suit seeks to set aside the internal rules we have developed which allow additional time for the development of appropriate medical evidence to support claims evaluated as "possibly" and "probably" effective.

Senator NELSON. These are the two that are questioned in the suit or are all standards you have set questioned?

Mr. GOODRICH. These are the main ones questioned. Actually, the suit questions the 30 days on the ineffectives and it does not question the rulings of effective. The suit says that once there is a finding by the NAS-NRC of anything other than wholly effective, we should take the product off the market without further delay. Our response was that in those products classified possibly and probably effective

we should exhaust the scientific method to get an answer one way or the other before moving those drugs out of the marketplace, since they do have some real possibilities of proving out effective.

Senator NELSON. Let us see. What is the time schedule now?

Mr. GOODRICH. 6 months on the "possibly effective" and 1 year on the "probably effective," and those times may have to be adjusted at the end of that time frame, depending upon what research has come out during the 6 months or during the 12 months.

For example, if at the end of 6 months there is good research underway giving a reasonable assurance that it will prove out the effectiveness, the Commissioner has said he would extend the time in terms of what would be needed to finish that piece of research.

Dr. EDWARDS. I think this is terribly important. We certainly do not want to take any effective drugs off the market. By the same token, we certainly are not going to procrastinate any longer.

I realize it is very reasonable to say, look, they have had 6, 7, 8 years in which to develop this particular evidence but I think the fact of the matter is that the industry by and large did not take this very seriously until recent months, and I think that we have a responsibility at this point in time to the patient and we certainly do not want to be caught in a position of having taken effective drugs off the market.

Now, granted, how many of these are effective is another question.

Senator NELSON. Go ahead.

Dr. EDWARDS. Moving on to the subject of drug quality, reliability of claims of effectiveness, of course, are of first importance, but we must be equally concerned with product reliability.

We have developed and published improved regulations applicable to good manufacturing practices.

We have several programs to enforce those requirements. The first is the Intensified Drug Inspection program. This is an effort to improve overall industry performance by concentration on specific manufacturers. In this process the FDA learns practical problems of implementing what may be considered theoretical requirements. The industry learns what concerns the FDA in a concrete rather than an abstract fashion. I think object lessons may be applied across the board. Marginal operations can be brought into compliance and hopeless ones identified and eliminated.

Since July of 1968, FDA has initiated intensified inspection of some 287 drug manufacturers and associated commercial testing laboratories. In 147 of the terminated cases, voluntary compliance with the Good Manufacturing Practices regulations was achieved through a dialogue between FDA district personnel and plant management. In some 44 remaining cases are 23 firms which are now the subject of legal action, and 21 firms which are giving up the drug business because of their inability to come into compliance.

Senator NELSON. You refer to an intensified drug inspection program and improved regulations applicable to good manufacturing practice. Can you elaborate on that a bit?

Dr. EDWARDS. Would you like to, Dr. Simmons?

Dr. SIMMONS. Yes. The current Good Manufacturing Practice regulations which we have just repromulgated, Mr. Chairman, are

such that if a firm follows these, it can reasonably be expected that they will produce an up to potency product batch after batch. This is what we aimed to achieve. We try to capture the best available techniques in drug manufacturing into these current good manufacturing practices.

Senator NELSON. I note that a number of producers—21 firms—are giving up the business because they could not comply. Is most of the production for most of the drugs in most of their dosage forms fairly mechanized and automated at this stage?

Dr. SIMMONS. By and large, yes.

Mr. GOODRICH. That is quite variable in terms of different methods. The regulations do permit the use of highly automated equipment, highly automated testing procedures, but they are not designed to require that degree of technology if drugs of adequate quality can be produced through other systems.

The Good Manufacturing Practices regulations deal with the nitty-gritty of good production, that is, a proper building, proper equipment, proper cleaning of the equipment, proper controls of the raw materials going into the mixing batch, proper control over the labeling, regulation of the type of personnel, and so forth. They are designed to be compliable by the small manufacturer as well as the large but there are certain minimum things that must be observed by all manufacturers to assure drug quality.

Now, the 21 firms that have not been able to comply either have not had the willingness or the finances to meet these minimum requirements and the public can accept nothing less.

Senator NELSON. Are there any requirements that must be met by a manufacturer of a drug prior to marketing his drug?

Mr. GOODRICH. Oh, yes.

Senator NELSON. What are they?

Mr. GOODRICH. Of course, if it is a new drug, then he has to make a commitment at the going-in stage of production that he will observe a protocol of manufacturing control that will assure reliability. If it is an antibiotic drug he must submit each batch to us for batch certification. If he is dealing with drugs that are not new drugs, that is, the old products, he must for all drugs meet the conditions of current good manufacturing practice and if he does not, the drug is adulterated and can be taken off the market, he can be enjoined or prosecuted.

So the good manufacturing practices are the basic rules that apply to every drug manufacturer, large or small.

Senator NELSON. But when somebody decides to go into the business of manufacturing drugs, at what stage do you become acquainted with this?

Mr. GOODRICH. He must register with us before he starts. We have to react with an inspection as soon as possible to make sure that he does have the knowledge of what it is all about and he is inspected against the standards of current good manufacturing practices.

The law requires one inspection at least every 2 years, which is far too infrequent, but we are putting the resources into this as we have been to improve on the performance. The Intensified Drug Inspection program is one that concentrates at points where we think the risks of violation are the highest.

Dr. EDWARDS. But the manufacturer does not have to provide us with a list of those products that he is manufacturing.

Senator NELSON. He does not?

Dr. EDWARDS. Does not. That is why, when looking at this from a little longer range, I think that the Food and Drug Administration eventually will have to have at least the opportunity to certify all drugs. That does not mean that we, in fact, would want to certify every drug through a certification program, but rather to selectively certify, and I think that some kind of a registration program is certainly necessary.

Senator NELSON. Well, in effect, you have that authority now, do you not? That is to say, you go into the marketplace or go into the factory and select a sampling of drugs and have them assayed to see whether they meet USP standards. If they do not, you have the authority to say you cannot put them on the market or if they are already there, you must take them off.

Dr. EDWARDS. We certainly do.

Mr. GOODRICH. We have the authority as you say, to go there and obtain samples and analyze the samples. If the product is not under new drug or antibiotic control it can be distributed and if we find it in violation, we have the legal mechanisms to take it off the market. But there is an opportunity, if we had the resources, to expand our inspection authority which would concentrate on these points of drug manufacture where the importance of the performance to the patient is the highest and the likelihood of failure of the drug is the highest, something comparable to the certification, without having that express authority.

Yes, we do have that ability if we had the personnel and the funds to carry it out. We have recently had an episode with digoxin, which Dr. Edwards will discuss, in which we found it necessary to examine the products of all manufacturers to bring them all into compliance.

Senator NELSON. I was just trying to get it clear, Doctor, what you were saying about this.

Dr. EDWARDS. I really was not referring so much to certification per se as the registration process as such. I think that while we have to inspect them once every 2 years, we have very little to say in terms of what they are manufacturing.

Mr. GOODRICH. And the other point he had in mind there was that with certification the burden is on the company itself to make an analysis, submit that analysis plus the sample to us.

Now, with our existing mechanisms we would have to go in and obtain the sample, make our own analysis, and, of course, we could check the analysis that the company made under its Good Manufacturing Practices requirements. But certification has advantages in that the company must submit batch by batch the product to us rather than our sending inspectors out to obtain the sample, and they would be under an embargo from shipping the drug until they got back the results of our certificate.

Those are points of difference.

Senator NELSON. Is it correct that under present law a firm could go into the business of manufacturing drugs, and if they were an old established drug, could put them into the marketplace and the

firm might be in business for two years before it had any contact with the FDA?

Mr. GOODRICH. Possibly. We do have internal instructions on how to deal with a newly registered firm which bring the inspection as soon as the district can handle it, but it does not assure that there will be an inspection before the company makes its first batch of pills or before it makes its first interstate shipment. We certainly should strive to have that carried out as an internal matter.

Senator NELSON. Would it not be sound law to simply require that nobody can put drugs into the marketplace until there has been an inspection?

Mr. GOODRICH. Yes.

Dr. EDWARDS. That is really what I primarily had reference to. We have to have some control over these products before they actually get into the market, more than we have now.

Mr. GORDON. Do you also envisage registration of each drug? In other words, as it is now, you merely register the plant but do you envisage having each drug registered? Is that what you are aiming at?

Dr. EDWARDS. This again, is what I was referring to. In other words, we register the plants.

Mr. GORDON. That is right.

Dr. EDWARDS. We have to have some inventory, if you will, as to what the plant is doing. The only way we can do that is by having some idea of the particular products that are being manufactured by the plant.

Mr. GORDON. As it is now, you do not know who is manufacturing what, is that it?

Dr. EDWARDS. Well, in some cases we do, in some cases we do not actually.

Mr. GOODRICH. Anything that is an antibiotic or new drug, of course, we know. The products that we may not know about are the products for which there is no requirement that they inform us in advance. Those drugs that were under the basic grandfather clause of the 1938 Act, that is, any drug produced prior to that date did not require new drug clearance, and there are some grandfather provisions in the 1962 Kefauver-Harris amendments.

We are litigating in that area to narrow those exemptions as much as we can, but to answer quite specifically, yes, there are some producers of phenobarbital and thyroid and other products that we do not have a full inventory of and we do not have a full inventory of their labeling or of their medical justification for putting the particular labeling into the marketplace.

There was no requirement for that and we have an after-the-fact enforcement responsibility on those drugs.

Dr. SIMMONS. Mr. Chairman, you asked what control does the FDA have on a new drug. On any New Drug Application that comes in, before that drug can be manufactured we do inspect the plant to make sure that they can turn it out as they claim they will in the New Drug Application.

In addition to that, we have a continuing surveillance mechanism whereby we have a regular inspection system nationwide. We will

take a sampling of a class of drugs from the market, analyze it and find problems that way. What we do not have is the mechanism we have in antibiotics where every batch produced must be cleared by us before it is marketed. Other drugs can be marketed and then we have to find the problem after the fact. And this is what we are referring to.

Senator NELSON. What kind of mechanical problem does it present to the FDA to batch-test all anti-infectives?

Dr. SIMMONS. Well, we do 21,000 a year here in Washington and we are able to handle that quite expeditiously. It works quite well.

Senator NELSON. That also applies to all imported anti-infectives, too?

Dr. EDWARDS. Right.

Senator NELSON. Go ahead, Doctor.

Dr. EDWARDS. The Food and Drug Administration's drug sampling and testing programs constitute another effort to find out just how well this system of quality assurance is working. While we appreciate that no monitoring system is without deficiencies, we are seeking the best approach, both medically and statistically, in this important part of the program of quality assurance.

Our National Center for Drug Analysis (NCDA) located at St. Louis, plays an important role in our total effort to assure the quality of drugs. We are very hopeful that this center can be significantly expanded in the months ahead.

At this center we have a modern, sophisticated, facility equipped with automated analytical instrumentation to which we are adding computerization. This will enable us to conduct a large-scale national drug surveillance program.

This program is already underway and we hope to expand it for use in conjunction with our new formulator oriented drug analysis program.

What this is in fact, Mr. Chairman, is that heretofore we in our drug analysis have gone to the retail level to get our drug samples. Under this new program we are going straight to the manufacturer to obtain our sampling materials.

Compliance operations continue to encourage industry cooperation to the maximum extent possible. Voluntary recalls have been the most commonly used method for removing defective or mislabeled drugs from the market and usually the quickest and most effective way to protect the public. There were some 951 recalls during the current fiscal year, some 707 in 1969, and some 711 in 1968. Every recall is reviewed to see how it could have been prevented. When one is found that illustrates an important problem, a recall case is prepared and distributed throughout the country. Drug firms have welcomed such guidance and 40 case studies were available at the end of fiscal 1969, 46 at the end of fiscal 1970. The very important drug, digoxin, has presented an interesting problem that I think gives you some idea how our drug surveillance and National Center operate. Digoxin tablets, an important pharmaceutical drug, are manufactured by some 37 firms. For more than a year content uniformity difficulties resulted in many recalls. Nearly all the manufacturers of this product were having serious difficulty meeting product uniformity specifications.

Our National Center for Drug Analysis, and our Washington laboratories, led the investigation of this problem. It became evident that manufacturing problems resulted from the mixing of the ingredients, which contained only about one active part to 400 inactive parts. All the firms involved cooperated by voluntarily withholding distribution, and discontinuing the manufacture of digoxin tablets, until the problem could be solved.

FDA met with industry representatives to discuss both manufacturing and analytical techniques. Our people recommended a modification of the mixing techniques in the early stages of manufacture which provided the solution. In order to check the process, FDA, with the concurrence of industry, has certified each batch since then before shipment.

Both the U.S. Pharmacopeia and the National Formulary are seeking clinical tests such as excretion and absorption profiles on human beings to evaluate clinical effect. In addition, they are attempting to develop *in vitro* tests which approximate the *in vivo* situation.

Senator NELSON. You mean the USP and NF are seeking these tests on all drugs?

Dr. EDWARDS. I think eventually that would be their ultimate goal. They are doing this by drug categories at this point in time but they are attempting to increase the scope of what are the various factors that go into developing uniformity for these drugs.

Senator NELSON. Well, then, will these become additional factors in meeting USP and NF standards?

Dr. EDWARDS. That is right; yes.

We have made our own efforts to assure that chemical drug equivalents, when administered in the same amounts, will provide essentially the same availability as measured by blood levels, excretion, and absorption profiles, et cetera. We have developed certain in-house biological availability requirements for abbreviated new drug applications but information and techniques thus far in this whole area have been slow in coming and must be considered preliminary. On the basis of currently available evidence, the quality of marketed drugs in regard to their purity and the uniformity of content of active ingredients is not suspect. This includes all marketed drugs, generic as well as brand name. Even though there have been indications that different brands of a few drugs in chemically equivalent formulations have given significantly different biological responses, we have reason to believe this is not a frequent phenomenon.

The next subject I would like to briefly address ourselves to, Mr. Chairman, is this problem of communications with the profession and other Federal purchasers.

All of the Food and Drug Administration's scientific work in new drug approval and surveillance, and all of the NAS-NRC evaluations, are in fact to no avail unless the results are communicated to the prescribing physicians.

Drug information is communicated in a variety of ways—in full disclosure package inserts, in advertising messages, and, of course, by detail men.

The package insert is the key to what can and what must be communicated to assure safe and effective drug therapy. As I indicated,

the NAS-NRC noted that most of the current package inserts require significant revision. As I say, that is being done. Too often they are promotionally slanted. They sometimes are models of clarity when it comes to claims of effectiveness, but models of obscurity in the discussion of limitations, side effects, contraindications, et cetera. In our judgment, our interim labeling regulations will help to correct this problem.

Our first task here is to develop uniform labeling for classes of drugs so that the prescriber will understand that tetracycline, for example, by whatever trade name it is sold has the same indications and the same warnings, et cetera. We are developing such labeling in the course of the NAS-NRC reviews.

We have also increased our advertising surveillance to make sure that the appropriate message, as approved in the package insert, is reflected in the important phases of promotion.

We and the manufacturers involved are studying the problem of detailing, to attempt to assure a balanced oral message to the busy practitioner.

And finally, we have the important problem of adverse reaction reporting from the prescribers themselves and of communicating the experience so reported in a timely fashion to others who use the drug. We can offer no solution to this at the moment, but we are in the process of planning and developing the system necessary to solve this problem.

Communication to other Federal officials involved in drug purchasing, of course, is a simpler problem.

The Federal Register is the official vehicle through which we first publish our position with respect to the safety and efficacy of drugs. We have recently supplemented this in an effort to make sure that affected people are notified with a list representing those drugs which lack substantial evidence of effectiveness, or that an unfavorable benefit-risk ratio exists.

Mr. GORDON. Dr. Edwards, do you tell the press about important actions which you announce in the Federal Register?

Dr. EDWARDS. Practically all of the time a press release is prepared when any important drug or other important announcement is placed in the Federal Register.

Mr. GORDON. I am thinking specifically of the potassium thiazide combination diuretics about which you had some kind of an agreement with the industry recently. You had a notice in the Federal Register but I did not notice anything in the press. I did not even know about it until someone told me about it. And then also the Darvon. I did not even know that there was a statement in the Federal Register about Darvon, which I understand appeared in April 1969, until I got the NAS-NRC report last summer.

Mr. GOODRICH. On the thiazide diuretics, the two leading brands in the market, Esidrex-K, Hydro-diuril-Ka, were removed from the market soon after the *Panalba* case was decided back in the spring of last year. One product still is in controversy with us, a Squibb product under which they have submitted some data.

I do not know what you have in mind in terms of an agreement. The agreement was that they would take the product off the market,

recall it from the marketplace. This was with Esidrex-K, Ciba, and Merck & Co., Inc. did the same with Hydro-diuril-Ka.

In the case of Darvon, that announcement was made, as you indicate in 1969, I believe, and we did not have a press release at that time. We are trying to be more alert to the important drugs as they come out to attempt better communication. But the NAS-NRC evaluations themselves are made available both to the press and to the affected people and anyone else who is interested enough in them at the time they are published in the Federal Register.

Dr. EDWARDS. We have established a working relationship with the AMA Medical News in which weekly or every other week they will publish in that publication a list of products that were found ineffective. In the case of Darvon we are currently again revising the labeling on Darvon, but—

Mr. GORDON. Is this information reaching the hands of every doctor in the country?

Dr. EDWARDS. Probably not. I suspect that we should be using far more than we have the "Dear Dr." letter, and our new "Current Drug Information" letters which as you know, we started in 1970. We are working to publish that more frequently on a number of different subjects. The "Dear Dr." letter is another, of course, mechanism for communicating with the practicing physician. We have not been totally impressed with the value of this as such. It is a very expensive way of doing it.

We are trying to come to grips with what method is the most dollar wise—considering the limited dollars that are available in the Agency, what is the most effective way of communicating with physicians. It is a tough problem to come to grips with.

Mr. GORDON. How about States and municipalities? They have a similarity of interests, do they not?

Dr. EDWARDS. This information was sent to State purchasing officials, Secretary of State Departments of Health, and Secretary of State Boards of Pharmacy.

Mr. GORDON. We are not sure doctors are getting this information, are we?

Dr. EDWARDS. No, we are not, very frankly. It is a weakness and one that I can only say at this time that we are trying to correct. I think over the years the practicing physician has not looked to the FDA enough for reliable drug information and this is one of the areas in which we have got to reestablish our image as being in fact the center for reliable, meaningful drug information. Unfortunately, in the past I think it has tended to be the drug detail man and in our judgment, we have to swing this back.

Senator NELSON. What is the legal status of a dosage form that is no more effective than a placebo? In other words, NAS-NRC says a 32 milligram tablet of propoxyphene hydrochloride, that is Darvon, was shown to be no more effective than a placebo. It is in the marketplace. What is the legal aspect of that?

Mr. GOODRICH. The legal aspects are that any claim of effectiveness for any type of drug must be supported by substantial evidence as we have indicated. As I understand the justification for the 32 milligram, it is to permit some dosage flexibility, but this is a matter that we must look into in terms of going over the claims.

I think there is no question that if Darvon in whatever dosage is claimed to be an effective analgesic, there must be evidence that it performs better than a placebo as an analgesic.

Dr. EDWARDS. As I indicated, Mr. Chairman, we are in the process right now of negotiating with the manufacturer to further revise the labeling on this particular product.

Senator NELSON. I shall put in the appropriate place in the record the news release¹ from the Eli Lilly Co. in response to criticism of that drug. There are a couple of interesting sentences in it. I will not bother to read it all, but it says:

The fact that some investigations fail to show a difference between 32 milligrams of Darvon and a placebo or "sugar pill" is not surprising. All analgesics give similar results at their lower ranges of effectiveness. Thus, a placebo often performs as well as a single aspirin tablet. This does not mean that the aspirin tablet is a placebo. It merely shows that analgesia research, being based on subjective evidence, is not at all that precise at the lower ranges of dosage.

As for the view that Darvon should not be prescribed "routinely" in preference to other analgesics, we agree.

The evidence is that we prescribe Darvon routinely as the analgesic of choice in Veterans hospitals around the country. All you need to do is look at the amount. But it is being studied further, is that what you are saying?

Dr. EDWARDS. Absolutely, and as I said, the labeling on this drug will very shortly be changed again. Dr. Simmons, do you have any other comments in that direction?

Dr. SIMMONS. No.

Mr. GOODRICH. I might make one more point. In our adequate and well-controlled study regulation, there is a requirement for comparing the drug, the claims of effectiveness, either with a placebo or with something else and if it is claimed to be an effective drug, it must be and is compared with a placebo. Of course, it must perform substantially better in order to have any claim supported.

Senator NELSON. Have the physicians been informed that the 32 milligram propoxyphene hydrochloride is not more effective than a placebo?

Dr. SIMMONS. Mr. Chairman, Darvon is a very interesting subject from its inception. If you ask us, has the physician been adequately informed of the late changes in Darvon, I think we would honestly have to say no, and we are taking steps to see that that gets accomplished.

Dr. EDWARDS. I think that Dr. Simmons did not go quite far enough. When Darvon was initially placed on the market and it was promoted as a drug compared to codeine, and as having the potency of codeine, and yet was a non-narcotic drug, I think that this was probably the first error as it relates to the subject of Darvon.

We have come to grips with that particular problem in labeling. We have not as yet come to grips with this problem of its effectiveness relationship to aspirin, and so forth, but I think very shortly we will have that problem corrected, at least as far as the labeling is concerned.

Senator NELSON. Thank you. Go ahead.

¹ See p. 7993.

Dr. EDWARDS. Mr. Chairman, we have gone on in our testimony to indicate what the Department of Health, Education, and Welfare has done as it relates to the list of ineffective drugs which I will not go over at this point in time, but will conclude by answering specifically the questions that you posed in your invitation that we appear here.

Namely, we have learned that constant attention must be given to all forms of drug promotion to keep it current, reliable, and useful. We believe that a future NAS-NRC evaluation can only be avoided by constant surveillance and timely action. Federal policy toward rational prescribing requires attention to drug quality, to sound medical documentation of all allowable promotional claims, and to greatly improved communications with the physicians prescribing these drugs. Government, as a major purchaser of drugs, should and must insist upon the least expensive of equivalent drugs and upon rational choices among different drugs which satisfy the same medical needs. Our role is to assure the reliability of all drugs available in the marketplace and the dissemination of fully informative labeling and promotion to enable the prescribers to make wise choices among the array of products available to them.

Thank you.

Mr. GORDON. What lessons have we learned from the drug efficacy study?

Dr. EDWARDS. Well, I think as I indicated in my concluding remarks, I think that we have learned that, first of all, the two subjects of safety and effectiveness have to be considered together and you cannot consider one without the other, and I think that unfortunately, this was not appreciated prior to 1962 and put us in the position that we are in right now.

I think it also indicates, as indicated to us, that a far better definition has to be had of such subjects as what are adequate and well-controlled studies, and the meaningfulness of monitoring. I think all of these things have been highlighted in this drug efficacy study. Dr. Simmons, do you want to add anything to that?

Dr. SIMMONS. I think in addition to what the Commissioner has already said, basically what we learned was that there are many problems that currently exist in therapeutics that need solutions. I think it taught us that the old system of having authority only to pass on safety was not adequate to the task, that somebody needed the authority to pass on efficacy.

We also learned that the uncontrolled observations and testimonial endorsements are not adequate to the needs of the 20th century, that we do in fact need substantial evidence, well controlled evidence, before we know what we are doing with drugs.

We learned that, as the Commissioner already mentioned, labeling in the past has generally failed in the primary purpose of letting those who have to use the drug know how to use it intelligently. I think it also told us that the combined efforts of the Federal Government and the private sector can help improve this system and in fact, is necessary. I think the most important thing it showed us was that the medical profession needs a better, more balanced and objective source of good drug information.

This is what we hope to be able to provide in the months ahead.

Dr. EDWARDS. I think another thing, Mr. Chairman, that I would have to add is that the Food and Drug Administration is a regulatory agency having the responsibility of monitoring a multibillion dollar industry. In order to do this we have to have adequate resources which I do not think in the past we have necessarily had.

Senator NELSON. For example, the inspectors that inspect the plants are paid for by the Government?

Dr. EDWARDS. Yes.

Senator NELSON. There is no assessment.

Dr. EDWARDS. There is no assessment, although we have been looking into various financing mechanisms that could be utilized by the Food and Drug Administration. It still is not assessable to the manufacturer.

The only part of our operation that is paid for by the manufacturer is our antibiotic certification, insulin certification, and color additives are certified and paid for by the industry.

Senator NELSON. How can the objective of rational prescribing be achieved unless the question of relative efficacy is considered, especially in view of the thousands of drugs in the marketplace. Previously we were talking about the Darvon case, but there are lots of others.

How does the physician make an election as to what the best mild analgesic is unless there are some relative efficacy studies and the information is available?

Dr. EDWARDS. I think your point is well taken. I think this is an area that we have to get into much more than we have been in the past. Obviously, this indirectly influences many of our decisions today. We certainly cannot totally ignore the relative efficacy question when we are evaluating any new drug. But as you know, we do not have the authority, at least I believe I am correct, in keeping from the market any drug that is considered to be safe and efficacious, but compared to what is another question, and I think that very frankly, we are the only reliable source which the practicing physician should be able to look to to obtain some of this relative efficacy type information.

Senator NELSON. Is there any sound reason for permitting the introduction into the marketplace of a drug if there is another drug in the marketplace that is just as good and there is no proof that this one is better? Is there really any rational reason for permitting it to be marketed?

Dr. EDWARDS. I think this is probably the reason that, and some people disagree with me, is probably the reason that we have some 20,000 drugs on the market today when maybe half or fewer would be enough.

No. I do not think there is any rational justification for it. On the other hand, you know better than I, I am sure, that industry spokesmen would disagree with this position.

Mr. GORDON. Mr. Chairman, I would like to read from a statement that Dr. Walter Modell made before the Kefauver committee way back in 1961 in which he says:

Occasionally molecular manipulation does bring about a significant advance, but usually a far more substantial change is needed for a real improvement.

But simply because a drug is new, it is not necessarily better than those already available, safer or even just as good. Often it is even less effective and sometimes more hazardous than the parent drug.

Now, this is the important part, I think.

But they also do harm by their very existence in the drug market. I take the stand that as a general principle everything that adds to the difficulty in dealing with and understanding drugs also makes drugs more dangerous. Thus, the excessive number of needless drugs constitutes a present danger. We can make the useful drugs both less dangerous and more efficient by weeding out the useless, the ineffective and the duplicates, and by so doing, make it possible for the physician to learn in depth about the potent drugs he will prescribe for his patients. We must add only those new drugs that really add something more than their mere presence.

How do you feel about that particular statement by Dr. Modell?

Dr. EDWARDS. In general, I certainly would agree with him. Unfortunately, we lived for several decades in which this basic principle was not either appreciated or was not observed, and I think it is going to take us some time to put some rationality back, if I can use that word, back into the drug scene, and it is a difficult problem and one that I really sincerely believe that we are slowly coming to grips with, but it is going to take some time.

Mr. GORDON. Has your agency adopted any measures to give technical assistance to small business enterprises? What I have in mind is to assist small firms in meeting FDA requirements, as, for example, when a patent expires, or to assist small firms to start producing drugs so as to make them available on a more competitive basis? Have you done anything along these lines?

Dr. EDWARDS. Dr. Simmons can speak to that in just a moment. We certainly are making every effort possible to assist the manufacturer, small and large, in coming to grips with some of our requirements. We do not have a specific body or unit within the Agency that deals only with this particular problem.

I would only say that I wish we had, but again in the allocation of rather scarce resources we have not felt justified in developing a unit such as this. But I think it makes some sense.

Would you want to add anything to that?

Dr. SIMMONS. No.

Senator NELSON. Has the number of inspectors that you have to inspect plants increased, decreased, or remained the same in the past half dozen years?

Dr. EDWARDS. It has gone down. We have fewer inspectors today than we had 5 years ago.

Senator NELSON. Do you happen to have the figures with you?

Dr. EDWARDS. No, but I can certainly provide them for you.

Mr. Goodrich points out that while our total resources have gone up, the additional resources are in other programs. They are in some of the Public Health Service programs that we now have, such as the Shellfish Sanitation program and the Milk Sanitation program, but in terms of the actual number of inspectors that we have in our food and drug program the number has actually gone down.

I can provide you with those specific figures, Mr. Chairman.

Senator NELSON. I would like to have them for the record.

(The subsequent information was received and follows:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
Rockville, Md., January 29, 1971.

HON. GAYLORD NELSON,
*Chairman, Monopoly Subcommittee,
Select Committee on Small Business,
U.S. Senate,
Washington, D.C.*

DEAR SENATOR NELSON: During the testimony by Charles C. Edwards, M.D., Commissioner of Food and Drugs, before your Subcommittee on January 18, 1971, it was requested that FDA furnish, for the record, the number of inspectors employed by FDA over the previous six years. This information is as follows:

INSPECTORS

	Domestic inspectors	Import inspectors ¹
Year:		
1965.....	756	49
1966.....	693	47
1967.....	718	49
1968.....	628	43
1969.....	590	42
1970.....	577	38

¹ Import inspectors perform import work only.

Thank you for your interest in our consumer protection activities. Please let us know if we can be of further assistance.

Sincerely yours,

M. J. RYAN,
Director, Office of Legislative Services.

Senator NELSON. Is there any sound reason for the Department of Defense having its inspectors and the Veterans' Administration making plant inspections? Would it not make more sense if all the inspectors of all the plants were in one place, the Food and Drug Administration?

Dr. EDWARDS. I think without any question it is a waste of resources, it is a waste of money to have this triple duplication by these three agencies. It really is the responsibility of the Food and Drug Administration to assure the American public, be it the Federal public or the private public, that drugs are in fact safe and efficacious and to have two other agencies involved in this is utter nonsense.

I would like to have the resources that they spend for this particular project allocated to Food and Drug Administration.

Senator NELSON. Maybe we can help you.

Mr. GORDON. Dr. Edwards, millions and millions of dollars are being spent by the public on long acting drugs. These are sold under many names like spansules, sustained action tablets, extenso tablets and others. The Government has spent considerable funds on these drugs also. We have had testimony that these long-acting dosage forms are unreliable, do not do what they purport to do and can be dangerous.

Does the FDA have substantial evidence of the efficacy and reliability of these drugs?

Dr. EDWARDS. If I might, I would like to have Dr. Simmons speak to that particular question.

Dr. SIMMONS. This problem we are well aware of, Mr. Gordon. It is a very difficult field and we know that many people who have

submitted evidence to us for efficacy of these compounds have been unable to show it and we have turned them down. There are a few, though, who have been able to pass our requirements and have a reliable product on the market, but there are very few.

The majority of those currently on the market have not provided adequate evidence to the task and under the drug efficacy study of NAS-NRC we are requiring that they provide such evidence. It is a very difficult field and we would agree with your statement that in general they appear to be quite unreliable.

Mr. GORDON. Now, with respect to advertising? Are you planning to include in your requirements that when a firm advertises a particular drug which has been rated "probably" or "possibly effective" by the NAS-NRC, that that statement will appear in the advertisement?

Dr. EDWARDS. Yes. We have published our original Federal Register document indicating that we were going to require this, I think it was in October, and we will be republishing again indicating that we will require of the manufacturer that the National Academy of Sciences classification be included in any promotional information on the drug.

There are several drawbacks to this because, for instance, a particular drug can be advertised as long as reference is not made to the particular claim that was declared possibly or probably effective or ineffective and, in that case, the advertisement does not have to contain the rating by the National Academy of Sciences. But all of the drugs are going to be required to do this. Mr. Goodrich, would you want to add anything to that?

Mr. GOODRICH. No, other than that we did receive comments, about 20 in number, covering a great many pages and as you can imagine most of them came from the pharmaceutical manufacturers, the proprietary association and drug companies, challenging both the legal basis for such a requirement and the factual justification for it.

We were satisfied of the legal basis when we first published. We are still satisfied. We are in the process of working out a final document on it.

Mr. GORDON. Consider this situation: claims have been made in the past, that is, before the NAS-NRC reports were published. These claims have been inculcated to a large extent upon the minds of physicians. As I understand it, from what you said, the firms can still advertise but as long as they do not advertise the claims again, they do not have to put in the rating of the NAS-NRC, is that correct?

Dr. EDWARDS. If they use an acceptable label, one that is acceptable to the Food and Drug Administration, then, of course, this in effect is what we are trying to accomplish, that is, to make more meaningful the labeling on these particular drugs, so if they clean their labeling up and remove less than effective claims, the NAS-NRC rating need not be included. Mr. Goodrich, am I correct in that?

Mr. GOODRICH. Yes. What he has in mind is that if an ad is made for a drug that had some claims rated "effective," some "possibly effective," some "probably effective," and some "ineffective" and the only claim advertised is the one for which the drug was found effective, you need not have the possibly effective, the ineffective and the other claims in there with the disclaimer. We are striving to the end

point where only effective claims are used but the point of the regulation is that any time a claim rated other than effective is used in promotion during this interim period of implementation, that is the 6- and 12-month period, there must be an appropriate qualification of that claim.

Now, the other point you are addressing is, of course, an important point. Where the prescribing profile of the drug is basically changed, should there be some method of communicating to the physician?

The answer, of course, has to be yes. But whether it should be in that ad which covers only effective claims, we do not think so. There should be other mechanisms of communicating the new prescribing profile for, let us say, the sulfonamides or even the tetracyclines.

Dr. EDWARDS. This will be, as I mentioned earlier this morning, all in a document that we intend to publish as soon as this is complete on all of the drugs that were considered by the National Academy of Sciences and their particular recommendation.

Senator NELSON. Thank you very much, Dr. Edwards. We appreciate your taking time to come.

The hearing will resume in this room at 10 a.m., tomorrow, with the Comptroller General.

(Whereupon, at 11:35 a.m., the hearing was recessed, to reconvene at 10 a.m., Tuesday, January 19, 1971.)

(Upon the direction of the chairman, information pertaining to the hearings follows:)

[Press release dated Jan. 14, 1971]

NEWS OF ELI LILLY & Co.

Senator Gaylord Nelson has attacked the medical value of Darvon® (propoxyphene hydrochloride, Lilly) and criticized government agencies for buying it in a low dosage form he contends is "ineffective."

The Senator quoted the National Academy of Science/National Research Council finding that the "32 mg. dose has often been found indistinguishable from placebo." He added that experts believe there is "no particular reason to use it (Darvon) routinely in preference to (other analgesics)."

The Lilly Company makes the following reply:

The smaller dose (32 mg.) of Darvon® (propoxyphene hydrochloride, Lilly) is made for special situations. It gives flexibility of dosage, enabling the physician to tailor the amount to the needs of the individual patient. Some patients find the 32 mg. dose quite adequate, although a 65 mg. strength is most frequently used. In short, Darvon is effective in the way physicians use it.

The fact that some investigators failed to show a difference between 32 mg. of Darvon and a placebo, or "sugar pill", is not surprising. All analgesics give similar results at their lower ranges of effectiveness. Thus a placebo often performs as well as a single aspirin tablet. This does not mean that the aspirin tablet is a placebo. It merely shows that analgesia research, being based on subjective evidence, is not at all that precise at the lower ranges of dosage.

As for the view that Darvon should not be prescribed "routinely" in preference to other analgesics, we agree. No analgesic should be prescribed except after consideration of the particular needs of the particular patient.

[From the New York Times, Dec. 21, 1970]

MANY DOCTORS IGNORE U.S. LIST OF HAZARDOUS OR USELESS DRUGS

(By David A. Andelman)

A list of 369 drug products considered ineffective or hazardous by the Food and Drug Administration apparently is being ignored by a large number of doctors and their patients across the country. Some doctors go so far as to say they consider the Federal agency's action in issuing the list unethical.

Reports from 18 cities, one month after the list was issued, also indicate that most people are unaware of the list's existence and are continuing to rely on the advice of private physicians on which drugs to take.

"In the end I think the average patient relies more on the opinions of his physician than on public releases by F.D.A.," said Dr. William A. Limberger, president of the Pennsylvania Medical Association. "However, this at times injudicious release by F.D.A. does not enhance confidence in the medical profession."

SOME WITHDRAWN

Last week, the agency released a list of 173 drugs which had also appeared on its previous list of 369. This time the F.D.A. said the 173 drugs had been withdrawn from the market over the last two and one half years.

The original list of 369, which received wider circulation nationally than last week's release, did not distinguish between drug products still being sold and those the F.D.A. had withdrawn from the market. The new list was made available, on request, to newspapers and interested individuals and organizations.

Many doctors, pharmacists and hospital administrators who were interviewed were irate that they had not been informed of the F.D.A.'s list. Many had never heard of it. Most of these were in areas where newspapers did not carry the full list, including such major cities as Los Angeles, Detroit and Baltimore.

In Detroit, a spokesman for a drug store chain said that F.D.A. announcements often had the reverse effect of that intended.

"DON'T TRUST F.D.A."

"Quite often, as soon as the F.D.A. comes out with a list of drugs they've banned, we get a run on them," said Mel Richards, operating manager for the Michigan Revco Drug Chain with 21 branches in the Detroit area. "People get attached to certain drugs, and they don't want to give them up. Really, it shows that people don't trust the F.D.A. Neither do I."

"I think people are just getting used to them crying wolf," said Wallace Nelson, head pharmacist at Harold Meyer Drug Stores in Tacoma, Wash.

In Oregon, the only newspaper in the state to publish the list was The Eugene Register-Guard in Eugene. An official of the Lane County Medical Society, which covers the city and environs, did not receive any calls from physicians, patients or hospitals as a result of the publication.

In Akron, Ohio, The Akron Beacon Journal published the full list, and in nearby Wooster, Dr. James Robertson, senior clinician at Wooster Clinic, reflected the concern of many of his colleagues in other cities that the publication of the F.D.A. list in the form it took bordered on the unethical.

"BREACH OF ETHICS"

"I had to read it in the newspapers," said Dr. Robertson. "I think any agency that goes to the public forum for its endorsement is [involved in] a breach of professional confidence and ethics."

But the reaction of most individuals who had seen the list was to continue to rely on the judgment of their physicians.

Dr. Eugene Upanaveage, a pharmacist at Green's Pharmacy in Philadelphia, said a typical reaction of many of his customers was "My doctor told me this [item] is the best." He said his store had not stopped carrying the items listed. "Most of the physicians think the F.D.A. is 'side-effect conscious,'" he said.

More concern was expressed in the survey over one drug that did not appear on the F.D.A.'s list—the oral diabetic drug tolbutamide, marketed by the Upjohn Company under the trade name Orinase. It is taken orally and widely used by diabetics as an alternative to insulin, which requires injection.

The F.D.A., as well as the American Medical Association and the American Diabetics Association, said in October they concurred with findings of a study that cast serious doubt on the value of Orinase. At that time, F.D.A. urged caution in its use.

Dr. John M. Rumsey of San Diego, who has many diabetic patients, said, "Most [diabetics] continued to thumb their nose at the Government and continued to use it, if their doctors felt there was no danger to them."

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

TUESDAY, JANUARY 19, 1971

**U.S. SENATE,
SUBCOMMITTEE ON MONOPOLY OF THE
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C.**

The subcommittee met, pursuant to recess, at 10:05 a.m., in room 1318, New Senate Office Building, Senator Gaylord Nelson (chairman of the subcommittee) presiding.

Present: Senator Nelson.

Also present: Benjamin Gordon, staff economist; and Elaine C. Dye, clerical assistant.

Senator NELSON. Our witness this morning is Mr. Elmer Staats, Comptroller General of the United States.

Mr. Staats, the committee is pleased to have you here this morning. I see you have name identification cards on the table so the reporter will know everyone.

You may present your statement, Mr. Staats, however you desire. If you wish to extemporize from it or add to it at any time, feel free to do so and if any of your associates have any comments to make as you go along, that is perfectly permissible.

STATEMENT OF HON. ELMER B. STAATS, COMPTROLLER GENERAL OF THE UNITED STATES; ACCOMPANIED BY GREGORY AHART, DEPUTY DIRECTOR, CIVIL DIVISION; DEAN CROWTHER, ASSISTANT DIRECTOR, CIVIL DIVISION; AND PAUL SHNITZER, ASSISTANT GENERAL COUNSEL

Mr. STAATS. Thank you very much, Mr. Chairman. Perhaps it would be well to identify my colleagues here at the table so if they care to add anything or you care to break in on any part of our statement for questions, we will be happy to try to respond.

To my immediate left is Mr. Gregory Ahart, who is the Deputy Director of our Civil Division. To his left, Mr. Dean Crowther, Assistant Director of the Civil Division. To my right is Mr. Paul Shnitzer, from our General Counsel's Office, Assistant General Counsel.

Mr. Chairman, as you requested, we have planned in our statement today to discuss the efficacy, the economy, and rationality of the drug procurement activities of the Federal Government. Specifici-

cally, you asked that we discuss the methods of procurement, the degree of competition obtained, participation by small business and the use of section 1498 of title 28 of the United States Code to procure drugs covered by patents.

Our discussion today will focus upon the systems through which the Federal Government directly procures drugs from manufacturers and other suppliers. We would like to mention, however, that since our last appearance before this subcommittee in May 1967, we have conducted reviews of and issued reports on other aspects of the Government's drug-related activities. We have attached as appendix A to my statement, digests of these reports for your information.¹

There is a growing involvement by the Federal Government in drug procurement, encompassing its substantial role both as a direct provider of medical care and treatment to certain classes of persons and as a supporter of federally financed programs which include the provision of drugs for eligible beneficiaries. During the 3 fiscal years 1967 through 1969, the total estimated Federal expenditures for drugs increased from \$514 to \$975 million. A substantial portion of these expenditures were indirect in that they consisted of the Federal share of the costs of drugs provided to beneficiaries under the medicare and medicaid and certain other programs. Drug costs under the medicare and medicaid programs, for example, increased from an estimated \$350 million in fiscal year 1967 to \$750 million in fiscal year 1969.

Although the major portion of Federal drug expenditures is indirect, the expenditures for direct procurements have increased from \$161 million in fiscal year 1967 to \$203 million in fiscal year 1969.

Three Federal agencies account for most of the direct drug procurement—the Defense Personnel Support Center, an activity under the Defense Supply Agency; the Public Health Service of the Department of Health, Education, and Welfare; and the Veterans' Administration. Each of these agencies operates its own drug supply system.

The Defense Personnel Support Center centrally manages about 1,100 drug items and in fiscal year 1969 procured an estimated \$103 million in drugs. The Public Health Service centrally manages about 600 drug items and in fiscal year 1969 spent an estimated \$6 million for drugs, about 86 percent of which were obtained under contractual arrangements made by the Veterans' Administration. The Veterans' Administration centrally manages about 450 drug items and centrally procured an estimated \$25 million in drugs in fiscal year 1969.

The Veterans' Administration also administers Federal supply schedule contracts under which Federal agencies can satisfy their drug requirements through direct purchase from drug manufacturers. Purchases under these contracts for fiscal year 1969 were estimated at \$56 million.

In addition to drug procurements which are centrally managed or administered, medical facilities of each of the three agencies can, in certain circumstances, locally procure their drug needs.

¹ See information beginning at p. 8051.

Previous testimony before this subcommittee has highlighted the drug procurement system as an activity supporting physicians' decisions on the most appropriate drug therapy for their patients. Such a system has as its base the professional selection of drugs and, in support of that selection, a complementary supply activity.

The objective of Government drug procurement should be to obtain at fair and reasonable prices, and in a timely manner, the proper and needed quantities of drugs that are of a satisfactory quality.

Specifically, we believe that a drug procurement system should provide for:

A selection process which emphasizes drug quality, safety, and efficacy and gives appropriate consideration to drug cost.

Comprehensive and accurate drug usage data to facilitate the selection of the most appropriate and economical method of supply with appropriate corresponding restrictions on all other available supply sources.

The development of product specifications which insure that drugs are capable of producing the desired therapeutic effect while encouraging the widest possible competition and lowest possible cost.

Effective negotiation as the alternative contracting method in instances where competitive procurement is not possible; and

Inspection and testing to establish manufacturer responsibility and capability to produce quality drugs.

We have surveyed Federal drug procurement systems in the light of these criteria and would like to briefly describe our observations.

I would like to emphasize that these observations are based on preliminary studies of the systems involved and cannot be considered as a complete review of such systems. Our work is continuing, however, and we will undoubtedly have more observations and suggestions to offer at a later time.

With respect to the drug selection process, we obtained information at the local level for five Federal medical facilities. Each of the facilities visited has established its own system for judging which drugs are appropriate for use. Each system is under the administration of a central group, the name of which varies but may commonly be referred to as the pharmacy and therapeutics—the P and T Committee.

The P and T Committee's membership generally consists of the directors of the various professional services of the medical facility and the chief pharmacist who acts as secretary. Some committees also have special nonvoting members, such as supply specialists and nursing personnel, whose functions range from that of observer to advisor in their areas of expertise.

A principal function of the P and T Committee is to administer the system for evaluating and selecting from among numerous drugs those considered most useful in patient care. The committee's selections are reflected in a continuously revised compilation of drugs approved for use within the medical facility—the station formulary. In carrying out this function, the P and T Committees generally receive some assistance from headquarters level in the form of policy guidelines, regulations, and information published by various pro-

fessional medical service groups. Agency policy statements and regulations, where available, are generally limited to setting out the scope and authority of the P and T Committees. Headquarters may provide recall and adverse reaction information about specific drugs, and furnish data on the commercial availability and prices of drugs. However, the selection of drugs for inclusion in the station formulary is reserved to the P and T Committees. At military hospitals, the hospital commander is responsible for approval or disapproval of drugs recommended by P and T Committees.

Most of the information on specific drugs which is made available to members of the P and T Committees in their consideration of changes to the station formulary comes from two sources; professional journals and the drug manufacturers.

Senator NELSON. May I interrupt a moment, Mr. Staats? How did you reach that conclusion?

Mr. STAATS. On the basis of our reviews at a number of locations where our staff visited the facilities themselves. There were, what, seven?

Mr. AHART. Five.

Mr. STAATS. Five; and I believe this is confirmed also by interviews with headquarters personnel here in the VA and in the Defense Personnel Support Center.

Senator NELSON. This is the pharmacy and therapeutics committee of Veterans hospitals?

Mr. STAATS. The VA facilities, say, for example.

Senator NELSON. And military hospitals?

Mr. STAATS. That would be an example, right. We can supply you a list of the facilities we visited, if you like.

Senator NELSON. If you would.

(The information referred to follows:)

HOSPITALS AND CLINICS VISITED

1. Walson Army Hospital, Fort Dix, New Jersey
2. Philadelphia Naval Hospital, Phila., Pa.
3. Veterans Administration Hospital, Washington, D.C.
4. U.S. Public Health Service Outpatient Clinic, Washington, D.C.
5. Veterans Administration Hospital, Hines, Illinois

Senator NELSON. As I understand it, a number of those physicians are coming out of private practice into military and Veterans facilities and then go back to private practice. Is that right?

Mr. STAATS. These would be medical personnel at the facility.

Senator NELSON. Yes, and a substantial number of them are not permanent physicians at these facilities.

Mr. STAATS. You are quite correct.

Senator NELSON. They come out of civilian practice or out of medical school, go into the military or into Veterans hospitals, serve their period of time, and go back to their medical practice, is that not correct?

Mr. STAATS. That would be correct.

Senator NELSON. And most of the testimony we have had on the prescribing practices of the physician indicated that the detail man is a very significant factor in influencing the selection of the drug. Then drug advertising, as well as professional journals, ranked behind the detail man.

When you say professional journals here, which ones are you referring to?

Mr. STAATS. Well, these would be the medical journals. I would have to turn to my colleagues here for the specific journal based on the studies. Our work was done on the Walson Army Hospital, Fort Dix, N.J., the Philadelphia Naval Hospital, in Philadelphia; the Veterans' Administration Hospital here in Washington; and the U.S. Public Health Service outpatient clinic here in Washington; and the Veterans' Administration Hospital in Hines, Ill. These are the five facilities we visited in developing our data on this point.

Senator NELSON. Are there not representatives of the drug manufacturers detailing these drugs at each one of these facilities?

Mr. STAATS. Yes. Our next sentence here so indicates. "The drug companies supply most of their information to individual physicians through sales representatives." These are the detail men that you just referred to; and by direct mail advertising.

Senator NELSON. Your conclusion is that most of the information for the pharmacy and therapeutics committee comes from professional journals and drug manufacturers. In drug manufacturers, you are including detail men as a means of promotion?

Mr. STAATS. Yes.

Senator NELSON. Among the professional journals, was the Medical Letter listed as a source of information by the personnel you have talked with?

Mr. STAATS. I cannot answer that personally.

Mr. CROWTHER. The professional journals, especially societies like the American Medical Association, are probably the ones that are most relied upon. But there is a wide number of journals that they receive, including the one you mentioned, Senator.

Senator NELSON. You talked with members of the pharmacy and therapeutics committee, I take it?

Mr. CROWTHER. Yes.

Senator NELSON. To determine what considerations went into their judgment on the selection of drugs for that institution?

Mr. CROWTHER. That is correct.

Senator NELSON. Did all of them, or some of them, or any of them name the Medical Letter as a regular source of information in selecting drugs?

Mr. CROWTHER. It was not specifically pointed out to us as such. There are a great number of journals that are available to P and T Committees, including that particular journal that you mentioned.

Senator NELSON. I am rather puzzled as to how they use the journals in selecting drugs. There are 1,100 items on the Defense Supply Agency's list of drugs. The journals do not just list these drugs and compare them, but run articles on drugs by distinguished authorities. How would they use the journals in the selection of this list? I cannot imagine them saying that in "our decisionmaking process we are going to check articles in the journals."

Mr. CROWTHER. Well, there is no question about the fact that there is a great deal of reliance placed upon the information received from the drug manufacturers' detail men. There is information available in the journals, however, that will comment on a

specific drug and there may be a writeup on some of the clinical tests made of it including the adverse reactions that have been received—but that is not to say that every drug is listed or is written up in each of the journals or in any of the journals, as a matter of fact. There is some information in the journals that is relied upon and that is the information that was passed along to us.

Senator NELSON. Well, quite obviously, of course, if you select a therapeutics committee—if it is a good therapeutics committee—you have professional men on the committee who come to it with expertise in their field.

Mr. CROWTHER. Right.

Senator NELSON. So you could have a good formulary based upon the knowledge of the distinguished group of experts who study the literature and have the latest information available on drugs.

Mr. CROWTHER. That is correct.

Senator NELSON. This sentence, though, says that most of the information on specific drugs which is made available to members of the P and T Committees in their consideration of changes to the station formulary comes from two sources, professional journals and the drug manufacturers. In the drug manufacturers' case I assume from the next sentence that the persuasive factor there is the detail man? Is that correct?

Mr. CROWTHER. Yes.

Senator NELSON. So, when you "refer to changes in the station formulary," what precisely are you talking about? Are you talking about additions to the formulary or selection of a particular drug from a class of drugs available for a specific purpose? Is that what we are talking about?

Mr. CROWTHER. Well, essentially, it means additions to or deletions from the formulary.

Senator NELSON. But within the formulary there may be several compounds that treat the same problem or there may be the same compounds under 25 names that treat the same problem. Somebody has to select one or two of those out of the 25, do they not?

Mr. CROWTHER. Yes, sir, they do.

Senator NELSON. So, are we not talking about the process of adding to the formulary or selecting the particular brand or whatever that will be in the formulary?

Mr. CROWTHER. Well, the selection of the particular brand that is in the formulary is quite comprehensive. Many of these formularies include literally hundreds of drugs in various dosages and strengths, and various combinations. They are not restrictive in many senses. The P and T Committees of both the Defense Department and the Veterans' Administration are making efforts to be more careful about the drugs that are included on the formularies, but up until now the formularies have been very comprehensive with a long list of drugs that are made available.

So to say that the formulary itself is the selection process between specific drugs may be a little misleading because the individual physicians themselves, of course, reserve the right to make these selections and in the event that a drug is not in the formulary, physicians still reserve their right to prescribe any drug.

The P and T Committee obviously wants to include those drugs in the formulary that will be adequate for the prescribing physicians, and, of course, the P and T Committee is composed generally of the directors of the professional services as well as the chief pharmacist and hopefully they have a complete comprehensive listing.

Senator NELSON. Well, of course, you could have a comprehensive listing by just having one compound that is effective for each one of the problem situations that confronts the physician. On the other hand, you could also have a comprehensive one by having every brand name of all the same compounds that do the same thing, could you not?

Mr. CROWTHER. Yes.

Senator NELSON. That is what you are saying.

Mr. CROWTHER. Yes, sir.

Senator NELSON. You say they have hundreds of drugs on the formulary. For example, if they have an anti-inflammatory drug, you are saying they will have several anti-inflammatories, perhaps versions of the same compound, all doing the same thing, or of different compounds or combinations doing the same thing, with the same therapeutic result. Is that what you are saying?

Mr. CROWTHER. That is correct, yes, sir.

Senator NELSON. Then I just would like to know how the formulary is determined. We had testimony here that I'm sure you are familiar with. In the case of both the Veterans' Administration and Department of Defense (but again the record will speak for itself), and when I raised the question about formularies, the witness said, well, "we cannot tell the doctors at a local hospital what should go on the formulary. They come to us as physicians in practice on their own. They are with us 2, 3, 4 years. They are not going to be dictated to about what particular drug should go on the formulary. Or they come here out of medical school and do not want to be dictated to." I gathered from all the testimony that in the circumstances where you did not have strong leadership at the local level, what you really had was a formulary made up of every drug that most of the doctors suggest they would like to use.

Is that what you found out?

Mr. CROWTHER. Well, essentially, that is the way the drugs get on the formulary. There are exceptions; for example, information received from the Food and Drug Administration on ineffective drugs. These drugs will be removed from the formulary. So the P and T Committee does have some voice, but at the same time, they try to make the formularies as comprehensive as they can to be able to be within the prescribing habits of their physicians.

Now, that is not to suggest there is no peer review at the Veterans' Administration or the Defense Personnel Support Center supported hospitals, because they do concern themselves with the drugs that go into the formulary.

I guess our concern stems from the fact that the formularies are so lengthy. There are just so many drugs included. It raises the question of the need for all the drugs in the formularies.

Mr. GORDON. Amongst the sources of information that you list here you do not include the Food and Drug Administration as a source of information. Is that the way it is supposed to be?

Mr. CROWTHER. Well, they do receive information—more recently—now. They have not been supplied with any substantial amount of information from the Food and Drug Administration until recently. Within the past few months, the Food and Drug Administration is disseminating more information. It is available to these people upon request, but some of it is being disseminated at this point in time.

Until now, essentially the information came from the sources we suggest in the statement, but they do have an input from the Food and Drug Administration and these lists of “ineffective” drugs are now available to each of the Government facilities.

Mr. GORDON. If I recall correctly, I think Dr. Edwards stated yesterday when he appeared before this subcommittee, that the Food and Drug Administration has more information about drugs than anybody else.

Now, do you think that it might be a good idea for the FDA to advise Government agencies which drugs are the best drugs to buy in the various therapeutic categories?

Mr. STAATS. Of course, there is also the Food and Drug Administration's study which Dr. Edwards outlined to the committee yesterday which had been made available to the agencies, but this is a fairly recent date. The agency issuances that I have here are all dated within the past few months, for example. The Food and Drug Administration's listing as you probably know, was dated November 1, 1970. So there has been this input and the appropriate directives have been issued by the Veterans' Administration and the Defense Department and the Public Health Service.

But I believe what you have in mind goes a step further and that is in the actual development of the formulary which would extend beyond the listing which came out of the FDA-NAS study, if I understand you correctly.

Mr. GORDON. Yes. These lists are merely negative. These are drugs that are ineffective and they should not be used. I am thinking of it in a positive way.

Mr. STAATS. I do not know that we can say that we have given our final thought to this point. But I believe our conclusions—and we have talked to Dr. Edwards—would be that there is an opportunity here for the FDA to play a more positive role than they have to date. But this will translate itself into funds and personnel and to establishing working relationships with the procuring agencies.

I do not sense any reluctance or reticence on the part of Dr. Edwards and his people in moving into a more positive role, if I may put it in those terms.

Senator NELSON. Over the past 4 years we have had a number of very distinguished witnesses, well regarded in their respective disciplines from all over the country, express their concern about the continuing education of physicians in all fields. Since these were hearings on drugs, they expressed a concern about continuing education of the physician in the field of drugs, which is particularly difficult, since there has been such a spectacular proliferation of new drugs and molecular modifications of old drugs, and new

combinations and new names, that it is very difficult for anyone to keep abreast of the drugs, what their appropriate use is and whether they are better than old drugs, and so forth.

An important problem, then, is continuing education in the drug field to assure good patient care, and appropriate utilization with the multiplicity of drugs which are available. Another idea is to bring all the expertise of the various disciplines together to establish a formulary, which would include a selection of the best proven drugs for the appropriate treatment of the variety of circumstances for which the drugs are used. It is distressing to anyone who is concerned about the best utilization of drugs, the best care of the patient, and the best practice of medicine, that every time we have any testimony on these formularies, a good percentage of them end up not being formularies at all but just a list of the available drugs that the local practicing physician through his expertise or bias, desired to use. A recent dramatic example is the massive purchasing of Darvon by the Veterans' Administration and the Department of Defense. We cannot find anybody who is considered an expert who wants to come before the committee and justify that purchase, including the purchasers themselves.

I have received letters from doctors who say: "I use Darvon all the time and will be glad to come and testify that it is good," but none of the experts will come and testify that they can justify the use of Darvon, though there may be special cases where Darvon may be used such as in the case of a person who cannot use aspirin, but not as the drug of first choice as a mild analgesic.

What I do not understand is how we are ever going to achieve rational prescribing unless the profession itself insists that the experts on the drugs will establish the formulary, and, further, say to the individual physician, "If you, as a physician practicing in this hospital, desire to use another drug, justify it, not with testimonials but with the appropriate, controlled studies that would warrant departing from the formulary."

All the best men in the profession say that is the best way to accomplish this, but somehow they do not do it.

I think it is a very sad commentary that the profession itself cannot summon up the courage to tackle the question head on. This is becoming a catastrophic situation; this multiplicity of drugs, wasteful spending on them, using them for the wrong purpose and the profession itself defaulting in its responsibilities. If you cannot do it in the Army, or in the Veterans hospitals, then one must despair that it can be done any place in this country.

Please proceed.

Mr. STAATS. Recently, Mr. Chairman, a series of actions impacting on the operation of P and T Committees and the formulary system have been taken or are planned within each of the major Federal drug procurement agencies. For example, each of the agencies has directed the distribution of the Food and Drug Administration's recently published list of "ineffective" drugs to their local medical facilities—this is the one we referred to a minute ago—with the recommendation or requirement that the drugs no longer be used.

Public Health Service has also taken action to more fully develop possible approaches to effective drug utilization reviews, as recommended in the report of the Department of Health, Education, and Welfare's task force on prescription drugs. A research study of the methodology and feasibility of this technique is currently underway.

We believe that the recent actions related to the drug selection process, if properly implemented, should improve control over drug operations at the local level. In implementing such actions we believe that emphasis should be placed on providing physicians employed by the Federal Government with appropriate information concerning available drugs to assist them in making decisions relating to drug therapy.

Senator NELSON. May I interrupt? When you say the Public Health Service has taken action to more fully develop possible approaches to effective drug utilization reviews as you mentioned in the report of the Department of Health, Education, and Welfare's task force on prescription drugs, what action have they taken?

Mr. CROWTHER. The task force, as part of its effort, reviewed the utilization of drugs by various organizations with HEW. It made specific recommendations on supporting research projects to develop and test approaches to drug utilization review and emphasized the importance of supplying physicians with drug information and guidelines for rational prescribing.

For the past few years HEW has been funding a comprehensive drug utilization review study. Also the agency recently issued a directive prohibiting the use of ineffective drugs by any Federal facility under the Department of Health, Education, and Welfare. This ban extends to possibly effective drugs as well as the ineffective drugs.

The directive goes a little further, prohibiting the use of these drugs under any Federal program, which would include Medicare and Medicaid.

Senator NELSON. Of course, a layman could come to the conclusion that you ought to recommend not using a drug that the National Academy of Sciences-National Research Council has said is ineffective. What are they doing about the problem we are discussing?

Mr. CROWTHER. Well, a number of the task force's recommendations could result in greater uses of generic drugs.

If you would like, we could supply the specific information on their recommendations.

Senator NELSON. This is the 1969 report we are referring to of the task force on prescription drugs and I see a total of 25 recommendations.

Mr. CROWTHER. Yes.

Senator NELSON. I would have to refresh my memory by rereading them, but are they taking these 25 recommendations and attempting in some fashion to get them implemented?

Mr. CROWTHER. They are implementing a number of the recommendations.

Senator NELSON. Is there any doubt about the recommendation 9.

The Department of Health, Education, and Welfare should provide expanded support to medical schools, enabling them to include a course in clinical pharmacology as an integral part of the medical curriculum?

Mr. CROWTHER. I really do not have the specifics on the status of implementation on each recommendation. We could obtain it for you, Senator, if you would like for us to.

Senator NELSON. HEW is testifying on February 1. We will write and ask them so that you will not have to duplicate it.

But No. 10 goes directly to some of the problems we have been talking about:

The Department of Health, Education, and Welfare should establish or support a publication providing objective, up-to-date information and guidelines on drug therapy, based on the expert advice of the medical community.

Of course, the Federal Government can do that right now in all of its Federal facilities.

Mr. CROWTHER. That is correct. They have the facilities to do that.

Senator NELSON. I asked, when they were here, why they did not call in the best clinical experts on all these classes of drugs in the United States and set up a formulary and then tell the veterans hospitals and the Army hospitals "this is the formulary, and if you wish to depart from it, you must submit to us your justification." This is a recommendation. I would take it that is what this 1969 recommendation means, but I suspect nothing has been done about it from the witnesses we have had here in the past few weeks.

Mr. CROWTHER. Well, we have not looked into, as I say, the implementation of each recommendation. We have looked at some of them and we certainly could look into any one of the specifics if you would like, but I really do not have the specifics on them now.

Senator NELSON. We will wait until we have the further testimony in February. If we have some questions that develop after that, I suppose you would be perfectly willing to check, if it is within your jurisdiction.

Mr. STAATS. Yes, indeed.

Keeping physicians informed is most important because the physicians' decisions guide the drug selection process. Unless this process is based on the best information available, even an otherwise efficient supply function may be uneconomical.

During our visits to local medical facilities we noted specific actions by P and T Committees which we believe are appropriate for wider application. Examples noted were: (1) The dissemination of information on drug studies including drug costs and (2) dissemination of information on adverse drug reactions.

Once determinations have been made through the selection process of the drugs which will be used, the drug supply activity must operate effectively to furnish the required items in the most economical manner. Requirements for frequently used drugs are generally met through a central stock system which allows for quantity purchases.

Veterans' Administration and the Department of Defense both have reporting systems for identifying drugs for inclusion in their centralized stock systems.

In the Department of Defense, each of the three services has its own system and criteria for reporting, and they vary from each other. One result of this is that defensewide usage of a specific drug does not become known until one of the services recommends a drug

for inclusion in the central stock system. Approval of only one service is needed to add a drug to the central supply system, but all services must concur in removing an item from the system. In fiscal year 1970, 66 drug items were added to the system and action taken to delete or discontinue procuring 106 drug items on a centralized basis.

We believe that under the current reporting systems, drug items that merit consideration for inclusion in the central stock system may not be included in the items identified for review and evaluation. This possibility could be removed and the reporting system improved by the use of standard criteria by the three services.

The Veterans' Administration's primary source of information in its continuing effort to capture data on drug usage outside of its central stock system is a quarterly drug report based on reports from each of its medical facilities. This report is characterized by the Veterans' Administration as an important tool in the management of its drug program and shows all procurements from sources other than central stock. The Veterans' Administration uses this report to identify drugs which qualify for inclusion in the central stock system.

We believe that the Veterans' Administration could make its comprehensive report more useful by requiring more uniform adherence to its regulations on reporting nomenclature and by providing for the compiling of certain summarizations and exception reports which would make the identification of drugs for central stock management much easier.

Also, available data indicates that the Veterans' Administration and the Department of Defense could take advantage of higher quantity drug procurements which could possibly result in lower prices by combining their needs for procurement purposes. For example, the Veterans' Administration contracted for 1,404 units of Lincocin at a unit price of \$22.30—5 days later the Defense Personnel Support Center contracted for 4,464 units of the same drug from the same manufacturer at a unit price of \$19.95. In another instance the Veterans' Administration contracted for 3,000 units of Tylenol at \$6.14 each—about 1 month earlier the Defense Personnel Support Center contracted with the same manufacturer for 10,176 units of the same drug at \$3.28 a unit.

Now, while these cases, Mr. Chairman, both show that the VA was paying higher prices than the Defense Department, this would not necessarily hold in every case, but in these two examples which we cite for illustrative purposes, that happens to be the case.

Senator NELSON. Do you see any justification for a differential, for example, of \$6.14 a unit paid by the Veterans' Administration and \$3.28 paid by Defense Personnel Support Center?

Mr. STAATS. No, sir. That is the purpose of our bringing it out here. We feel that that would not have been necessary if they had shared information and procured this item together.

Senator NELSON. We pointed out here, from a survey that we did almost 4 years ago—1967, that a number of municipalities or non-profit institutions and general hospitals, were procuring the same drug from the same company at dramatically different prices. We

had a number of examples. The response to that is, "well, quantity purchase justifies a reduction in the price." These differences, however, were so dramatic that they could not be justified, and we had a number of instances where the large purchaser paid considerably more than the small purchaser—all of them municipalities or non-profit general hospitals, institutions of one kind or another.

I was looking at a report not yet released—a preliminary study by one of the departments of the Federal Government—and I just want to give you another example which supports the record that we made on this point 3 or 4 years ago.

The data indicates that the State of Texas, for example, paid \$27.72 per 500 for 296,500 tablets of 10 milligram Librium—

so that was \$27.72 per 500 for 296,500 tablets—

while Boston paid \$19.50 per 500 for 25,000 tablets of the same product.

So, they bought less than a tenth as much and paid about \$8 per 500 less than the State of Texas did.

Obviously, there is something wrong with the purchasing methods in one place or the other.

Mr. STAATS. Obviously.

Senator NELSON. Go ahead.

Mr. STAATS. At least 150 drugs, we found, centrally procured by the Defense Personnel Support Center during calendar years 1968 and 1969, were also centrally procured by the Veterans' Administration during fiscal years 1968 and 1969.

Both the Veterans' Administration and the Department of Defense have established required priorities of supply sources to be used by their medical facilities. These priorities reflect a policy of using the most economical supply source available. Such a policy is important because the commercial unit prices of drugs available at the wholesale level are generally higher than prices established under Federal Supply Schedule indefinite quantity contracts which, in turn, are generally higher than definite quantity procurements.

To illustrate this fact, we compared prices listed on the Federal Supply Schedule with the highest prices paid under definite quantity contracts for 68 drug items over a recent 2 year period and found that the schedule prices averaged 63 percent higher. We recognize that procurements under indefinite quantity contracts have inherently higher manufacturers' costs of warehousing and administration which would account for some part of the difference between definite quantity procurements. Also additional warehousing costs are incurred by the Government on procurements for central stock under definite quantity contracts, but considering all these factors, a 63 percent difference seems significant in any event. The average price differential is particularly significant considering the amount of total purchases made under schedule contracts and the fact that many centrally stocked drugs are also available under the schedule contracts.

We see no reason why Federal agencies should independently procure drugs from the same manufacturer and lose the possible price advantages resulting from high quantity purchases. We believe consideration should be given to improving Federal drug procure-

ment practices by providing for an exchange of information between the Department of Defense and the Veterans' Administration as to the estimated annual volume of drugs to be procured in order that consideration can be given to combining quantities of certain drugs for procurement purposes, using the most economical method of procurement for each drug item.

Another key requirement to an efficient supply system is its ability to provide, wherever possible, purchase descriptions or product specifications which permit more than one manufacturer to bid effectively.

Both the Defense Personnel Support Center and the Veterans' Administration establish their own specifications on drugs.

Senator NELSON. Let me ask a question at this point. In your checking have you ever made a determination as to how many personnel are involved in the purchasing of drugs in the Veterans Administration and Defense Supply? What kind of group does that take?

Mr. STAATS. You mean the qualifications and size, et cetera?

Senator NELSON. Yes. What is the cost of a purchasing operation, for example, and how many personnel are involved? What is the cost at the Veterans Administration and the Defense Supply Agency? And what is the overhead cost?

Mr. STAATS. The administrative costs involved?

Senator NELSON. Yes.

Mr. STAATS. I do not believe we have——

Senator NELSON. Could you check that for us?

Mr. STAATS. We will look into it and see if it would be feasible to do it and if so, we will provide it. I see no reason why we could not get that information.

Senator NELSON. Fine.¹

Mr. STAATS. Both agencies require compliance with the applicable standards of the U.S. Pharmacopeia and the National Formulary to which each agency adds its own additional requirements. The professional personnel assigned this responsibility within the Defense Personnel Support Center and the Veterans' Administration are chemists or pharmacists.

The Veterans' Administration develops a specification when the demand for a generic product is sufficient to warrant central management or administration and when no patent exists or the patent has expired. The Veterans' Administration has established specifications for about 100 of its centrally managed drugs procured on a generic basis. In addition, specifications have been developed on 46 drug products administered under Federal Supply Schedule contracts.

The Defense Personnel Support Center establishes a specification or purchase description on every drug item in its central stock system.

Both agencies informed us that they use a number of sources in constructing their specifications. In addition to the monographs of the U.S. Pharmacopeia and National Formulary, other sources for constructing specifications include the Food and Drug Administration, drug manufacturers, the National Institutes of Health, and the American Chemical Society.

¹ The General Accounting Office has informed the staff that this material is being prepared but will not be available before this volume is published.

When a drug is standardized for the military supply system, the manufacturer is contacted and requested to supply sufficient information so that the item's essential characteristics can be prepared.

We explored with Defense Personnel Support Center officials the question of whether, because of the substantial reliance upon information obtained from manufacturers, military specifications or purchase descriptions are restrictive and, in effect, result in a proprietary specification. These officials contend that the specifications and purchase descriptions are constructed in such a manner that any firm knowledgeable in the drug industry could manufacture the drugs. Without a detailed study of this matter, we have no basis upon which to either dispute or validate this contention.

It is clear that the degree of competition obtained in the drug procurement area is less than competition obtained for many other Government supply items. The total dollar value of drug procurements for central stock by the Veterans' Administration and the Defense Personnel Support Center in fiscal year 1970, amounted to about \$94 million. About 7 percent or \$6.4 million of the central stock procurements were made under contracts awarded pursuant to formal advertising procedures. The remainder were made under contracts negotiated with the sole source of supply or under contracts awarded after the solicitation of proposals.

Among the reasons for the limited amount of competitive procurement are, of course, the fact that many drugs are patented products and the fact that legal and administrative requirements must be met in order to obtain Food and Drug Administration approval. Also, many procurements are made by brand name either because only one brand of a particular drug is available or because of the prescribing physicians' preference. For example, about 70 percent of the drug items centrally stocked by the Veterans' Administration have been designated for procurement on a sole source basis in order to obtain specified brand name drugs.

In addition, competitive contract awards account for about 25 percent of the procurements under the Federal Supply Schedules. Most of the other contracts, which are included for the purpose of making manufacturers' product lines available to the Government at prices less than market, are negotiated without the benefit of competition.

The Defense Personnel Support Center sought to increase competition on their centrally managed drug items when, in January 1969, approximately 1,100 firms were invited to indicate their interest in bidding on 401 items, 290 of which were classified as single source. Replies were received from 104 companies. Fourteen companies requested to be added to the bidders list for 35 of the 401 drug items. Two other companies requested to be added to the bidders list for eight drug items not included in the solicitation. The other 88 responding companies either did not produce the item; reaffirmed their interest in supplying the drug items for which they were already on the bidders list; or expressed no interest in supplying any of the products to the Government.

Senator NELSON. May I interrupt? Back on page 11 you state:

We explored with the Defense Personnel Support Center officials the question of whether, because of the substantial reliance upon information obtained from manufacturers, military specifications or purchase descriptions are re-

strictive and, in effect, result in a proprietary specification. These officials contend that the specifications and purchase descriptions are constructed in such a manner that any firm knowledgeable in the drug industry could manufacture the drug.

Well, I think you made a perceptive observation. I have here excerpts from a speech made to the 21st annual meeting of the Defense Supply Association and reprinted in *The Review* for November-December 1968. The speech is by Col. W. V. Breyfogle, Chief, Division of Medical Materiel, Defense Personnel Support Center, Defense Supply Agency, in which he addresses himself to the question you raise in your remarks here. I would like to read them for the record and it seems to me it supports the question you raise.

The first problem that has been bothering us for some time is our inability to procure competitively. The policy of the Department of Defense, as it has been for many years, is that we will obtain competition on our procurements to the maximum extent possible. The major problem in our failure to procure competitively is the nature of the specifications that we are using.

It has been said in the past that our specifications are too restrictive in nature and thereby restrict competition. There is some validity in this statement. Before you can understand why we have a problem in procuring competitively, however, you must understand how items are selected for standardization and stockage in our DSA depot system.

The items that are standardized by the Defense Medical Materiel Board and stocked in the DSA depot system were, for the most part, developed by industry or independent research organizations for use by the civilian medical profession and for sale in the marketplace. These items were presented to the Board for study and the determination was made that they would be stocked for use in our system. Therefore, the specifications that are developed of necessity describe a certain manufacturer's item.

Most of the information used in writing these specifications was furnished by the developer. Therefore, even if we have a, pardon the expression, generic specification, in many cases it merely describes the generic equivalent of a brand name—

which I think is a rather telling comment on the very point you raised.

I ask that this be printed in full in the record at this point.

(The document referred to follows:)

[Reprinted in *The Review*, Nov.-Dec. 1968, pp. 161-162]

**SPEECH DELIVERED AT THE 21ST ANNUAL MEETING OF THE
DEFENSE SUPPLY ASSOCIATION**

(By Col. W. V. Breyfogle, U.S.A., Chief, Division of Medical Materiel,
Defense Personnel Support Center, Defense Supply Agency)

In the time allotted me this afternoon, I thought I would review our procurement program, give you some kind of an estimate of what we expect the program to be this year, and then discuss some of the problems that are paramount in our minds at present and expect to be bothering us for the next few months.

This chart (No. 1) will show the procurement program for the past two fiscal years and the mix by commodity within the total program. You will notice a rather dramatic shift into the Drug commodity during the past fiscal year. We went from 47% of the total in FY 67 to 55% in FY 68. The other commodities stayed relatively the same, with the exception of Surgical Dressings.

The next chart (No. 2) shows our performance for the first quarter of FY 69 against the last fiscal year.

The first problem that has been bothering us for some time is our inability to procure competitively. The policy of the Dept. of Defense, as it has been for many years, is that we will obtain competition on our procurements to the maximum extent possible. The major problem in our failure to procure

competitively is the nature of the specifications that we are using. It has been said in the past that our specifications are too restrictive in nature and thereby restrict competition. There is some validity in this statement. However, before you can understand why we have a problem in procuring competitively you must understand how items are selected for standardization and stockade in our DSA depot system. The items that are standardized by the Defense Medical Materiel Board and stockade in the DSA depot system were, for the most part, developed by industry or independent research organizations for use by the civilian medical profession and for sale in the marketplace. These items were presented to the Board for study and the determination was made that they would be stocked for use in our system. Therefore, the specifications that are developed of necessity describe a certain manufacturer's item. Most of the information used in writing these specifications was furnished by the developer. Therefore, even if we have a, pardon the expression, generic specification, in many cases it merely describes the generic equivalent of a brand name.

The Comptroller General has repeatedly held that specifications of this type are not bad so long as the specifications did not go beyond the minimum essential needs of the government. It must be assumed that as these items are selected for standardization by the Defense Medical Materiel Board, a physician or group of physicians have made the decision that the item being standardized meets the minimum essential needs of the government. Therefore the resulting specification must describe the item being standardized. Once again, the Comptroller General has held that if a specification describes a particular manufacturer's product, and if the product being described does not go beyond the minimum essential needs of the government, then the specification cannot be considered to be unduly restrictive.

In the past few weeks we have been taking a hard look at all of the items we have been procuring non-competitively from only one source. Many of these items are patented; also, a large number of the drug items require either an approved New Drug Application or licensing by the National Institutes of Health prior to manufacture. We have eliminated these three categories and are focusing our attention on those where there is no apparent reason for producers not bidding on these items. We have distributed special procurement forecasts on these items with a letter to everyone on our bidders' list encouraging competition for these items. I encourage every one of you to take a hard look at these and see if there is something on the list that you have the capability to produce.

My next subject is one that has been dear to my heart for a long time. Many times you people have complained about the length of time it takes to make an award after the bids have been opened. For the most part this delay is caused by the fact that we do not pre-qualify bidders. Anyone can get on our bidder's list, or request solicitations as a result of reading the Commerce Business Daily, or even come in to the Center and pick up a copy of a bid. Because we do not pre-qualify bidders, when an individual submits a low responsive offer, and we have no experience as to his capability to produce an acceptable product, we must go through the exhaustive procedure of pre-award samples and surveys. This is the reason you are continually receiving requests for extensions of your bids. I know this bothers you because you must commit production capacity in the extent that you do receive the award. It bothers us, too, because increased procurement leadtime must be covered with inventory and this increases our investment. For several years we have been in the process of developing a system of pre-qualifying bidders, whereby only bids from qualified bidders will be considered, and manufacturers of unknown capability can be qualified outside of the procurement arena. This will allow us to make our awards faster, reduce inventory and be more responsive to your desires.

I would like to bring to your attention another item which will be of much interest. On 16 January 1968, the Defense Supply Agency Contractor Experience List (DSACEL) program was established. The purpose of this program is to assist Contracting Officers in the selection of responsible contractors by identifying firms whose performance under DSA contracts has been less than satisfactory. Contractors included on the DSACEL are not barred from bidding on or submitting proposals for future contracts. Contract performance records of firms included on the DSACEL will be reviewed quarterly. It is the desire of DSA that deficiencies which were the cause of

firms being placed on the list are corrected in a timely manner. Both DPSC and the DCAS offices can recommend to DSA Headquarters firms for inclusion on the DSACEL.

The first step in our goal towards achieving a Qualified Manufacturers List has been completed with the issuance of our standards for Pharmaceutical manufacturers. These have been developed by our people and have been coordinated with the Food & Drug Administration and the Defense Medical Materiel Board.

We intend to use the standards for pre-award surveys until we get all of the defects worked out of them. Then these standards will become the basis for the development of a QML. We expect to develop a completely coordinated plan with the Defense Medical Materiel Board and submit it to our headquarters in Washington in the very near future.

Thank you for your attention. Are there any questions?

(Charts omitted.)

Mr. STAATS. Thank you, Mr. Chairman.

On page 13 of my statement, to resume. Some of the reasons advanced with respect to the absence of competition on a large number of drug items include:

- restrictions imposed by law or regulation, such as patents on New Drug Applications;
- inadequate plant facilities and no desire to make the required investment to upgrade the facilities;
- the lack of qualified personnel to make any drugs; and
- the expense of introducing a new product with no assurance of reasonable return through sustained contract awards.

The advantages of seeking the widest possible competition in drug procurement can be demonstrated by available data from which we identified nine drugs procured over a comparable period of time both competitively and on a sole source basis. The drugs purchased from sole source suppliers by the Veterans' Administration are estimated to be 60 percent higher than the average price obtained after formal advertising or the solicitation of competitive proposals by the Department of Defense. Appendix B of my statement shows the nine drugs and comparative prices.¹ It should be noted that the quantities purchased by the two agencies are different, which may account for some part of the price differences.

This statement and conclusion on the 60 percent applies, of course, only to these nine that we selected. We are not necessarily implying here that the VA did a poor job because, as mentioned previously, we found other cases where the opposite was true.

We see no reason why different Federal agencies, and this is our essential point, Mr. Chairman, should independently procure the same drug in a different manner, and possibly from the same manufacturer, and lose the advantages associated with procurement of larger quantities and, where possible, increase competition.

Without effective competition, there is a question of the Government assuring itself that the prices being obtained are fair and reasonable under negotiated procurements. Public information is available on selected areas of drug pricing—an example would be wholesale prices. In determining whether the negotiated price is the best attainable by the Government, comparison of the bid with these prices reflects reasonableness by inference. Although there is no

¹ See information beginning at p. 8058.

assurance that these prices are reasonable, our survey indicates that these prices serve as the basis for most of the price reasonableness determinations made by the Veterans' Administration and the Defense Personnel Support Center.

Mr. GORDON. Mr. Staats, would you consider this a good test of reasonableness?

Mr. STAATS. We would not think so, no. I am not sure, though, that we are prepared to answer today, at least, exactly what would be a better alternative.

Perhaps my colleagues here would want to comment on this. But we think that they should have gone further than simply the wholesale prices.

Senator NELSON. The wholesale price in the retail marketplace—is that what we are talking about?

Mr. STAATS. I think that is right.

Mr. CROWTHER. Yes, sir.

Senator NELSON. Well, does not all the accumulated evidence on competitive bidding reject the wholesale price as a reasonable standard in any event?

Mr. CROWTHER. As a reasonable standard, yes, sir.

Senator NELSON. Let me cite an example. In the same month that Schering was selling Meticorten in New York City for \$17.90 a hundred to pharmacies, the firm offered to sell it to New York City for \$1.20 a hundred. Schering lowered the price from \$17.90 a hundred to \$1.20 and lost it on a bid at 45 cents from another company.

Now, if you were using their wholesale price, quite obviously it is not reasonable. There are other examples of that.

Mr. CROWTHER. I think both the VA and Defense Personnel Support Center found this to be true and that is one of the reasons in their competitive bidding they have been successful in substantially reducing the prices for central stock.

A problem here, of course, is the amount of procurements that are made under the Federal Supply Schedule where there are indefinite quantities. These contracts are negotiated with specific drug manufacturers without knowledge of the specific quantities of a drug that may be procured.

Senator NELSON. But is it not perfectly obvious that because of the method of promotion and sale in the retail marketplace, the wholesale price cannot be used as a standard of reasonableness for anything, because you may not have any serious competition in the retail marketplace?

Though you may have 25 versions of the same compound manufactured in the country, some of them generic and some of them brand name, the company that dominates the retail marketplace is the company that had the patent and had the doctors prescribing it for 17 years with the brand name. When the patent expires, the doctor continues to prescribe it by the brand name. He does not even know the patent has expired. He generally does not know that the drug can now be bought competitively: there are 20 other brands at half, a third, a tenth, a fiftieth of the price. He continues to write the brand name that he's used for years.

In addition, there are 44 States in which the law says you cannot substitute. So, although there is available to the Defense Supply Agency and to New York City, perhaps 25 versions of the same compound—under generic and brand names—competitive bids are possible. In the retail market, on the other hand, competition does not exist, and that is why the price can be 25 times as much as in the institutional market. Therefore, if you use the wholesale price as a standard, you have no guideline at all.

If the VA and the DSA are using it as a standard, they ought to get rid of it in a hurry because the taxpayers are getting cheated by it.

Mr. CROWTHER. There is no question about the fact that the selection process determines which drug is to be procured, and there are a large number of sole source drugs that are used in all Government facilities. Certainly, that raises the question of competition.

The problem on the wholesale price as a standard, however, is there is not much of an alternative at this point for sole source drugs. They can negotiate with the manufacturer but until we change the selection process, we are in a difficult position to say that there is a better standard to use, with all the defects that exist in the wholesale standard.

Senator NELSON. Well, if it is sole source but available in Europe, the Federal Government can compare the domestic price with the price over there.

Mr. STAATS. That is true.

Senator NELSON. And it has been done a couple of times. If there is anything that will make the seller reasonable in a hurry, it is to buy overseas, if the domestic price is exorbitant. If a drug which is available overseas, meets USP and NF standards, is, for example, one tenth the American price, it seems to me that Defense Supply Agency and the Veterans' Administration ought to say to the American company: "You are the sole source here, but if you are going to charge this price we are going to buy it in Europe."

Some of our witnesses thought this was a good idea, but they had never checked the European prices of the drugs they were buying. It seems to me that that would be the first thing they should do. If the foreign price is dramatically lower than the domestic price, then consideration should be given to purchasing the drug abroad.

Would that not be a reasonable approach? The law provides that the Federal Government is not bound by the exclusive license of the American manufacturer or the patent of the American manufacturer. Is that not correct?

Mr. CROWTHER. The problem with that, of course, is that we are not in much of a position to say that if a patent infringement suit were to follow, the results of the suit may actually reduce the price. We have not had that—

Senator NELSON. No. I am talking about the right of the Federal Government to purchase even though a company is the sole supplier in the United States by license, and nobody else may sell it in the marketplace, or even though a supplier in America has the patent in America. If the same drug is available in another country, the

Federal Government can purchase it, if it desires to do so. Is that not what the law is?

Mr. STAATS. I would like to ask Mr. Shnitzer, our Assistant General Counsel, to respond, if I may.

Mr. SHNITZER. Mr. Chairman, I believe that is a correct statement and I think that there have been some instances where purchases have in fact been made overseas.

Senator NELSON. Yes, We have had testimony here that we paid 12,000 percent more than the European or world price on an item that was sole source in this country. That is, it went into the AID program and the foreign country paid 12,000 percent more than the world price for the same compound.

Mr. SHNITZER. Of course, where the Federal Government purchases something which is under patent here from someone who is not a patent holder or licensee, it is subject to suit in the Court of Claims and there may be a reasonable—

Senator NELSON. If they buy it from a supplier here?

Mr. SHNITZER. If they buy it from a supplier who is not the patent holder or a licensee of the patent holder.

Senator NELSON. This was my question. If it is available in the marketplace in Europe, our Government as purchaser is not bound to buy it from the sole supplier here, is it?

Mr. SHNITZER. Yes, sir. Your position is correct. They are not bound. I am simply pointing out that in determining the difference in cost, you may have also to consider the fact that the Government may be liable to suit in the Court of Claims from the patent holder or the licensee—it would be the patent holder.

Senator NELSON. Not if the law exempts them.

Mr. SHNITZER. The U.S. Government is permitted to make the purchase under 28 U.S.C. 1498. However, the law specifically gives the right to the patent holder to bring an action in the Court of Claims against the United States for recovery of the value, let us say, of the patent.

Senator NELSON. Have there been any such suits?

Mr. SHNITZER. Yes. There have been two suits, one which was settled, the other which is still pending.

Mr. STAATS. Mr. Chairman, I have information here on the settlement of the one case which involved the Norwich Corp. as a patent holder, and the Eaton Laboratories, which is licensee. The Eaton price for 100,000 tablets—this is the drug nitrofurantoin—the Eaton price per 1,000 tablets was \$76.30. The foreign source price per 1,000 was \$18.50.

Senator NELSON. From 76—

Mr. STAATS. \$76.30 versus \$18.50. This is, of course, a very substantial difference. The settlement price in this case was \$192,500, which represents about 2 percent of that difference. So that even though there was a settlement here and a suit brought, in that particular case at least, the Government was much better off.

Senator NELSON. You mean they paid 2 percent of the difference between the \$18.50 and the \$76.30?

Mr. STAATS. It represents 2 percent of the domestic price. The settlement represents 2 percent of the domestic price. But the price

differential between the foreign procurement and domestic procurement was almost 400 percent, you see.

Mr. GORDON. Mr. Staats, does not this really amount to compulsory licensing for governmental purposes?

Mr. SHNITZER. Yes. I think what it amounts to is a taking under eminent domain. The Government takes something. The concept was when the law was enacted, and it was enacted in 1918, that the Government should not be prevented from satisfying its needs because of the possibility of infringement of a patent.

Senator NELSON. I still do not know what the law in the case is. You say they have a right to sue.

Mr. SHNITZER. Yes.

Senator NELSON. But law was established by the case. Did they end up negotiating settlement before judgment?

Mr. SHNITZER. Yes. The parties arrived at a settlement. A consent judgment. The court did not render an opinion in the case. It simply was a settlement.

Senator NELSON. If the Government settled for 2 percent they must have had some suspicions they were not going to do too well if they went to judgments, did they not?

Mr. SHNITZER. I believe this was a reasonable conclusion.

Senator NELSON. No established law, then? No decision of any Federal circuit court?

Mr. SHNITZER. There is no decision of the Court of Claims with respect to the purchase of foreign drugs or the purchase of drugs of a foreign country.

Senator NELSON. Considering the differential, which I have seen any number of times in checking the foreign prices, would it not be advisable for the Government to be sued so that it could be settled as to what the law is rather than continuing to buy sole source here at these exorbitant prices?

Mr. SHNITZER. I should make it clear, Mr. Chairman, there have been a large number of suits. I was limiting myself to consideration of suits with respect to drugs purchased in Europe. Now, there have been a lot of others.

Senator NELSON. Have any of the suits against the Federal Government or any department gone to judgment?

Mr. SHNITZER. Yes.

Senator NELSON. And how did they come out?

Mr. SHNITZER. A large number have gone to judgment. In many instances the plaintiff—complainant was paid.

Senator NELSON. Paid what?

Mr. SHNITZER. He was paid an amount which the court determined was proper under the statute. The concept, of course, is to compensate him reasonably for the use of his patent. In terms of percentages, I have not made a complete study of this, but it looks to me as though it would not be uncommon to expect that the settlement or that the judgment would represent something around 5 or 10 percent of the purchase price.

Senator NELSON. You mean 5 or 10 percent of the differential between the price that the exclusive licensee was selling for in this country versus the price in Europe? Is that what you are saying?

Mr. SHNITZER. No. I think in this case I am talking about 5 or 10 percent of the price which would have been paid initially to the patent holder or to his licensee.

Senator NELSON. Is that not what I said?

Mr. SHNITZER. Possibly you did. It was not my interpretation.

Senator NELSON. I want to be clear in my own mind. Are you saying that if the price of this product were \$100 in the United States, and \$50 in Europe, in these lawsuits the exclusive licensee in this country, would be paid 5 or 10 percent of that differential, which is \$50.

Mr. SHNITZER. No. I am saying of the hundred. In other words, he would be paid—again, as I say, this is a subjective determination. I have not made any analysis of the amounts recovered by the plaintiffs and I am sure it would vary in this—

Senator NELSON. Five or 10—

Mr. SHNITZER (continuing). Percent of the \$100.

Senator NELSON. Of the \$100.

Mr. SHNITZER. Yes.

Senator NELSON. Which would amount to a relatively small percentage of the differential.

Mr. SHNITZER. Yes, sir; in the sample—in the illustration you gave.

Senator NELSON. In the illustration I gave at 10 percent, he would get paid \$10.

Mr. SHNITZER. Yes.

Senator NELSON. Is that right?

Mr. SHNITZER. Yes, sir.

Senator NELSON. So, the Government would save \$40, is that correct?

Mr. SHNITZER. I would say so.

Senator NELSON. You ought to try it more often.

Mr. STAATS. Mr. Chairman, we have been talking about negotiated procurements where patents are involved but in the area where patents are not involved, where the patent has expired or no patent is held, we also have some uncertainty as to the application of the truth-in-negotiation law, that is, Public Law 87-653, because that law exempts any item where there is a catalogue price which is offered in substantial quantities to the public.

The law has a cutoff of \$100,000 currently but here again, is an area where the law has not been finally settled as to the extent to which the Government would be entitled to have information on the supplier's costs.

The truth-in-negotiations law, as you undoubtedly know, went to the situation of negotiated contracts in excess of \$100,000 where the Government as a part of the negotiation could require the contractor to supply his costs, his known costs.

Now, that has not been applied in the case of procurement of drugs irrespective of the patent question because of the fact that they do have catalogue prices and these drugs are offered in substantial quantities to the public.

I thought I should bring this point out because here is an area of substantial negotiated procurement where the 1962 legislation apparently—I say apparently, because it has not been fully tested—does not apply.

Senator NELSON. Well, do I understand you correctly that the General Accounting Office has authority under the present law to examine all negotiated contracts for drugs and medicines and to require price and cost information from the suppliers who are supplying medicines?

Mr. SHNITZER. Sir, there is a statute which was enacted in 1951 which says in effect that any negotiated contract awarded pursuant to either the Federal Property Act or the Armed Services Procurement Act, which would cover the two major acts, has to contain a provision which gives the General Accounting Office access to the books, documents, papers and records of the contractor or his subcontractors which relate to the contract.

However, in terms of the cost and pricing data, there is the Minshall bill, which would provide access to the cost actually incurred in order to verify the accuracy and currency and completeness of the data provided. However, of course, if the contract were exempt from the provisions of the Truth-In-Negotiations Act in the first place, then this latter provision would not have any application.

Mr. STAATS. This is the one I was referring to a minute ago.

Senator NELSON. But the purchasers of drugs are not exempt, are they?

Mr. SHNITZER. Well, if the price is based on current catalogue prices and these are items which are sold in substantial quantities to the general public, this is a basis for exempting that procurement from the Truth-In-Negotiations Act.

However, this would not have any effect on our other right to examine the books, documents, papers and records of the contractor or his subcontractors with respect to transactions under the contract.

Mr. STAATS. What Mr. Shnitzer is saying, Mr. Chairman, in other words, is that even though we had access to the records pertaining to the contract, neither we nor the procurement agency, VA or Defense, for example, would have the right to insist that the supplier furnish the Government with their current known costs of production.

Mr. SHNITZER. In the negotiation of the contract.

Mr. STAATS. At the time of the negotiation of the contract. After the contract is negotiated, obviously then we do have authority with respect to all the pertinent records pertaining to that contract, but still we could not go behind the supplier's statement of what his costs are in the contract entered into by the Government.

Senator NELSON. What good is it, then?

Mr. SHNITZER. I think it is very good for the purpose of determining what costs the contractor actually incurred in the performance of the contract as compared to the contract price. We can do that.

Senator NELSON. Are you referring to the costs the seller in a negotiated contract incurred as a consequence of the negotiations? Is that what you are saying?

Mr. SHNITZER. No. What I am saying is, and we do have a case which ultimately went up as far as the Supreme Court, is that under our 1951 authority, the contract is required to include a provision which gives the GAO the right to examine records of costs, direct and indirect, generated in the performance of that contract. So if a contract is awarded to company A and it comes within the purview

of this—it is a negotiated contract for, let us assume, \$100,000—we would have a right then to go back and examine the records of company A—the cost records, direct and indirect, to determine how much it cost him to perform that contract and, of course, that would be—

Senator NELSON. You are not talking about production costs?

Mr. SHNITZER. We are talking about production costs, we are talking about direct costs and indirect costs incurred in the performance of the contract; yes.

Senator NELSON. But did I understand that there is still another provision of the statute that when these are published prices, you cannot go back?

Mr. SHNITZER. No. This is a separate statute. There are two statutes. One statute relates to the Truth-In-Negotiations Act, Public Law 87-653. Most of these contracts, I believe would be exempt, at least, many of them would be exempt, from the provisions of Truth-In-Negotiations Act because the price is based on catalogue price, and so on.

However, regardless of whether the prices are based on catalogue prices, regardless of the application of Truth-In-Negotiations Act, we still have a provision in the contract, so long as it is negotiated, which gives us access to the contractor's records.

Senator NELSON. But access in order to determine his cost of production?

Mr. SHNITZER. Yes, sir.

Mr. STAATS. The distinction—

Senator NELSON. I thought you said that that was not the case. You are saying that this provision requires that in negotiated contracts the supplier must agree that you may examine all of his production costs before or after?

Mr. SHNITZER. After.

Mr. STAATS. After. And this is the essential point.

Senator NELSON. But he still has to supply you the cost of production figures.

Mr. STAATS. That is right. After the contract award, Mr. Chairman, whereas the Truth-In-Negotiations Act laws goes to the negotiation itself, and here is the question of the exemption that Mr. Shnitzer and I have referred to.

Senator NELSON. Well, now, the largest number of purchases by the Veterans' Administration and the Defense Department are repeat purchases. That is, every year the purchase of certain antibiotics and certain analgesics, are repeated. I would suppose such is the case for 90 odd percent of such drugs.

Has any one of these agencies ever requested the GAO to post-audit the negotiated contract for costs?

Mr. STAATS. The answer, I guess, is no. We could do it on our own. To be candid we could do this on our own after the award of the contract.

Senator NELSON. Well, in view of your examination of the purchasing practices of the various agencies, do you think it would be a valuable service to do some of this kind of checking on negotiated contracts, at least the big ones?

Mr. STAATS. This is something we have had some discussion on, Mr. Chairman.

Senator NELSON. Do you have any present plans to go ahead and explore this?

Mr. AHART. Mr. Chairman, as the Comptroller General mentioned, we are continuing our work in examining drug procurement systems and as part of that work we will be giving consideration to utilizing the authority which we have under the provision of the 1951 act which Mr. Shnitzer mentioned, and actually examine the costs of certain of the drug manufacturers.

We have not decided how far we are going to go on this and the final plans are indefinite, but this will be given consideration as part of this continuing work and I am sure some of it will be done.

Senator NELSON. As the Comptroller General's statement demonstrates, there has been a dramatic increase in the taxpayers' expenditures for drugs—direct and indirect purchasing—in the period 1967 to date, going up by \$400 million, from, I believe your figure was \$514 million, to \$975 million. I believe that was the figure—almost a \$400 million increase in a 2- or 3-year period.

I realize it may be a very complicated matter, but it would seem to me that all companies ought to be served notice that the GAO is going to utilize this statute. I think that we ought to take a look at some of those costs.

Nobody has ever been able to get their manufacturing costs. But when you see them selling drugs at \$17.90 a hundred to the pharmacies and offering to sell at \$1.20 in the same month and same city to an institutional buyer you have some idea of what the costs might be.

I think it would be a service to the taxpayer to take a look at that and I am glad you have it under consideration.

Mr. STAATS. Thank you, Mr. Chairman. Would you like for me to continue?

Senator NELSON. Yes, please.

Mr. STAATS. At the bottom of page 14 we refer to small business participation.

Competition through formally advertised procurements seems to have a decided effect on the participation of drug manufacturers classified as small business. When drug supply contracts are awarded competitively, small business is often able to effectively compete. For example, in fiscal year 1970 more than half of the dollar volume of the Veterans' Administration's formally advertised procurements of centrally stocked drugs were awarded to drug manufacturers classified as small business concerns. Only 3 percent of the negotiated procurements for centrally stocked drugs were awarded to small business concerns. Since negotiated procurements constituted more than 96 percent of the total, small business received only about 4 percent of the total procurements of centrally stocked drugs.

During fiscal year 1970 the Defense Personnel Support Center initiated 1,076 procurement actions, each having a value of \$10,000 or more, with domestic drug manufacturers. Small business was involved in 137 of these actions—representing about 7 percent of the total procurement dollars of about \$71.6 million. For contracts amounting to \$19 million awarded under advertised procedures or negotiated with competition by the Defense Personnel Support Center during fiscal year 1970, small business received about 17 percent of the dollar volume or a total of \$3.3 million.

Senator NELSON. What is the rationale given by the purchasing agency for such a high percentage of purchases made on a negotiated basis?

Mr. CROWTHER. This goes back to the sole-source manufacturers. So many brand names are selected by the prescribing physicians that it leaves very little for competition.

Senator NELSON. Certainly nowhere near 96 percent is sole source unless you use the brand name and call that a sole source.

Mr. CROWTHER. In some cases that has occurred, sir.

Senator NELSON. Well, that puzzles me. If you take the various therapeutic categories, there are relatively few in which there is only one drug for the treatment of a particular ailment, unless you are saying as Colonel Breyfogle suggested, that specifications have been drawn up that only a brand-name manufacturer can fulfill. That would, therefore, become a sole source.

Mr. CROWTHER. Well—

Senator NELSON. I do not understand that.

Mr. CROWTHER. In the Defense Personnel Support Center, for all of their drugs in central supply they write specifications and put them out for competitive bids, if possible. They do not receive a great deal of competition, but at least, they go out for competitive bids on most drugs they stock centrally.

The Veterans' Administration writes specifications only on those drugs that are outside of a patent. Either the patent has expired or there is no patent. Drugs with specifications constitute a small number of the total drugs managed or administered by the Veterans' Administration.

Senator NELSON. When you say the Defense Supply Agency writes specifications, what do you mean by that? All you have to do is ask for a drug by its generic name and say that it must meet USP or NF standards. Are there any more requirements than that?

Mr. CROWTHER. Well, quite often—

Senator NELSON. Well, aside from the fact you want certain milligrams dosage and certain dosage forms, what is the complication about the specifications?

Mr. CROWTHER. This is quality control more than anything else.

Senator NELSON. USP standards.

Mr. CROWTHER. They go a little tighter than USP standards in several circumstances, tightening even the manufacturer's standards in several circumstances. The Defense Department itself goes in and inspects the plants and does batch testing of drugs.

Senator NELSON. Does the Defense Department have certain standards that have been published that are different on potency, for example, than USP?

Mr. CROWTHER. Well, it is not the potency as much as the procedures, the mechanisms of how the drug is manufactured in order to get consistency throughout the drugs, throughout each batch. They are concerned with the precision with which the drug is manufactured.

They are satisfied with the potency and its therapeutic value but they want to make certain that they obtain that potency and therapeutic value, so they are very concerned in writing the specifications to—

Senator NELSON. What standards do they use for potency?

Mr. CROWTHER. Well, the mechanisms with which the drug is prepared. I think the answer is that they specify such things as how long a drug compound must run in the centrifuge and at what temperatures. Also they require that the processes be tested to be certain that the compounds fall within certain tolerance levels. They are also concerned that each drug and the related manufacturing process meet the specifications. So, I think the answer—

Senator NELSON. I am very puzzled about that. You are talking about the disintegration rate?

Mr. CROWTHER. Yes, sir; that is part of it.

Senator NELSON. Now, the USP and NF have a disintegration rate. You mean to say that the Defense Department has experts who have decided on a different standard? I am not objecting, if it is better, but I would like to see the proof.

Mr. CROWTHER. Well, I cannot say that the specific example is used in each specification. Quite often the specifications refer to the standard that have been published but sometimes they add to those standards to gain consistent quality in the drugs they procure.

Senator NELSON. Has anybody taken a sampling of the drugs they procure and then a sampling that is procured for any good general hospital just using USP standards and determined that one is different or better than the other?

Mr. CROWTHER. Well, I believe the reverse has occurred. The Defense Department has determined that certain batches are unacceptable and they have been rejected because those batches do not meet their standards. There are several tests that each drug must meet and these tests are included in the specifications.

Senator NELSON. That is interesting. The Commissioner of the Food and Drug Administration was here yesterday saying that so far as the generic drugs and the brand name drugs that are in the marketplace are concerned, we have no cause and no evidence to believe that one is any better than the other. That is not an exact quote.

I would be very suspicious myself that what you are describing is what Colonel Breyfogle was referring to, that they set standards that only a certain brand name can meet so there is no competition.

USP will come here and testify that the best known standards in the world are USP standards. Now, you say that the Defense Supply Agency has a better standard. When you have a situation where 96 percent of the contracts are negotiated and the Federal Government is not using the law to check the cost behind those negotiations, I have a suspicion that the taxpayer is getting euchered out of an awful lot of money. I think the Veterans' Administration and the Defense Department ought to appear here with a panel of USP and NF experts and tell us what it is that they are doing that is so beneficial. If they are right, then USP and NF probably ought to adopt their standards and the FDA ought to go along with it.

But when I look at the high percentage of negotiated settlements and the fact that GAO has never been called upon to look at the costs to see if the prices are reasonable, I think there is some reason to be concerned about the possibility of excessive, wasteful expenditure of taxpayers money.

Does this strike you that way? I do not expect you to have the facts about these various standards the military talks about that

have to be so much different that you end up with sole suppliers, while, at the same time, there are other manufacturers in the marketplace.

Mr. AHART. If I may comment, Mr. Chairman, I think I can clarify this a little bit. I think basically, what the Defense Department is doing is establishing the specifications, is adopting the standards which are in the USP.

Senator NELSON. They are what?

Mr. AHART. They are adopting the standards in the USP or NF, but they are adding to that the testing protocols which they are going to use in satisfying themselves that the manufacturer, whether he be a brand name manufacturer or generic name manufacturer, is actually meeting these standards in the production of the drug.

So, as Mr. Crowther pointed out, it is basically the technique which they are using to assure themselves that regardless of the plant from which they get the drug—whether it is a brand-name, big company, small company or whatever—the drug in fact, by following these testing protocols, does meet the standards which have been established.

Now, most of these standards will be the USP or NF standards for drugs which are listed in those two compendiums but it is the testing protocols, the quality control tests which they are going to require to make sure they are getting the product to meet those standards for which they are paying. I do not think it is a question of developing independent standards in most cases, but setting up the regimens, protocols that make sure that the product they get meets these standards.

Senator NELSON. Well, I do not think anybody would object to inspection of plants. In fact, there ought to be much more of it and the FDA ought to have more inspectors to insure quality control so that they are in the position of being able to guarantee to the profession and the public that whatever goes into the marketplace meets appropriate standards as only careful inspection and supervision can guarantee.

And so, if the objective—I assume it is—of the military is to be sure everybody is meeting the standard, that is fine. But I am a little concerned that some artificial barriers may be getting into the specifications so that you end up, as you do here, with 96 percent negotiated and no real assurance that the end product is on the average any better than the product being purchased by New York City or a good general hospital that has a good pharmacy department. The situation, as I see it, is that we have mostly sole source negotiated purchasing. Government financed purchases are rising rapidly, and although we have a statute that permits examination of costs to see whether or not the profit is reasonable, the GAO has never been asked to use it.

That kind of a situation, I would think, raises a very serious problem, besides having within it the seeds of eliminating competition and denying economic opportunities to perfectly qualified producers if abused. I do not say that it is being abused because I do not know anything about it. It could be abused unconsciously. It would eliminate competition and end up with lots of high prices, especially when you do not use the statutes and we do not check

what is going on in Europe and do not exercise the right to buy in Europe.

Those sellers have got it coming and going both ways for them. I think you ought to take a good look at it.

Mr. STAATS. The absence of satisfactory prices from domestic drug manufacturers has led both the Veterans' Administration and the Defense Personnel Support Center to the procurement of certain drugs from foreign sources. However, neither the Veterans' Administration nor the Defense Personnel Support Center are currently making extensive use of foreign sources for their drug procurements.

In recent years the Veterans' Administration has bought only one drug from a foreign source and does not actively solicit foreign bids in its procurements.

The Defense Personnel Support Center furnished this subcommittee with information relative to its foreign procurement of five drug items during 1968 and 1969. During 1970 only one of these items, tetracycline hydrochloride, has been procured from a foreign source. Another of these items has been obtained during 1970 from a domestic manufacturer because the bid by the foreign sources were not considered low after considering the Buy American Act provisions and related policies. The remaining three items were not procured from any source during 1970.

One factor in the small use of foreign sources is the Government's exposure to possible action under section 1498 of title 28, United States Code. This section provides that whenever an invention described in and covered by a patent of the United States is used or manufactured by or for the United States without license of the owner, the owner's remedy shall be by action against the United States in the Court of Claims for the recovery of his reasonable and entire compensation for such use and manufacture.

Since our last report to you on this subject, dated July 12, 1967, in which we explained the background and purpose of section 1498 of title 28, there have been two suits against the Government by drug patent holders for infringement of their patents rights. One of these suits involving purchases of nitrofurantoin was settled by the parties for \$192,500 in September 1969 and the other one involving purchases of meprobamate is still pending.

As an integral part of their drug procurement systems both the Veterans' Administration and the Defense Personnel Support Center have established programs for assuring the capability of Government contractors to supply a drug product of acceptable quality. These programs vary somewhat in their approach but have a common objective.

At the Defense Personnel Support Center the quality assurance program, and I think that is what we have really been talking about here in the last few minutes—includes an evaluation, through preaward surveys of the plant and preaward testing of product samples, of the contractor's ability to supply a specific drug item.

Preaward surveys and preaward samples may be generally required when: (1) The contractor has never before furnished the item being procured; (2) a doubt exists as to the quality control, housekeeping procedures, or financial position of the prospective

contractor; or (3) the item is to be furnished from or manufactured in a different plant.

The Defense Contract Administration Service has about 80 quality assurance representatives, who are either chemists, chemical engineers, or pharmacists, and function as drug inspectors. They perform preaward surveys at the request of the Defense Personnel Support Center and are charged with the responsibility for inspecting and approving all drug items manufactured under Defense contracts. In performing their inspections the quality assurance representatives are required to inspect each drug lot.

During fiscal year 1969 a total of 168 preaward surveys were made—149 of which were performed on domestic manufacturers which were classified as either small or large business. Sixty-two small business firms were subjected to 90 surveys. Forty-seven of these surveys resulted in disqualifications. Twenty-six large businesses were subjected to 59 surveys, 25 of which resulted in disqualifications. Reasons for disqualification included poor quality control; poor housekeeping; sample failure; unacceptable subcontractor; and inadequate capacity.

The Veterans' Administration inspects each contractor plant with regard to its entire operation and for its entire product line.

Senator NELSON. May I interrupt a moment? "Reasons for disqualification included poor quality control; poor housekeeping; sample failure; unacceptable subcontractor and inadequate capacity".

How many of the small businesses who were rejected were based on inadequate capacity?

Mr. STAATS. You will note there, Mr. Chairman, just above there in the same paragraph, 62 small business firms were subjected to 90 surveys and 47 of these resulted in disqualification.

Senator NELSON. Yes, but what were the grounds for disqualification for the 47?

Mr. STAATS. I see your point. Mr. Ahart, I believe, has this.

Mr. AHART. There were—out of the 90 inspections, Mr. Chairman, seven instances where small business was disqualified, where one of the reasons was the inadequate capacity. And for the other side of the coin, out of the 59 inspections of large business there were nine cases where one of the reasons for disqualification was inadequate capacity.

Senator NELSON. Was this inadequate capacity for the particular order the Government was interested in? Is that what you are saying?

Mr. CROWTHER. Or the ability to manufacture that particular drug in some cases. They may not have the line or a specific manufacturing method for a particular drug and in that sense they are disqualified because of lack of capacity.

Senator NELSON. Could you submit for the record a breakdown of the reasons for disqualifications in each of these cases, because the raw figures do not tell very much. What is your definition of a small business?

Mr. STAATS. We took the Defense Department classification of small business here as related to pharmaceutical manufacturers.

Senator NELSON. What is it, 500 employees or less?

Mr. STAATS. No, 750 employees.

Senator NELSON. I could not draw much of a conclusion from the phrase "inadequate capacity or sample failure". Sample failure—does that refer to a sample off the line?

Mr. CROWTHER. Yes, sir; off a particular drug line.

Senator NELSON. And now, what was the sample failure, based on a USP or NF standard or some standard that the military has?

Mr. AHART. This would be the failure of the product, the preaward sample, to meet the standards which have been established in the specifications which as I mentioned are largely drawn from the USP or NF, using the testing protocols which the Defense Department has established in their specification or in the purchase description.

Senator NELSON. When you say inadequate capacity, are you referring to inadequate capacity or inability to make this particular kind of a drug as well as amount?

Mr. AHART. I am not sure we are in a position to give all the circumstances which might give rise to an inadequate capacity determination but I am sure that one of them would be the manufacturer's inability to provide the particular drug in the quantities which the procuring agency requires. It might go to some of the other things which Mr. Crowther mentioned, such as the ability to produce this particular product on the lines which they have available in the plant. It could be either one of those.

I think we would be happy to submit for the record in as much detail as we can, the various kinds of things which come under this category as well as the other reasons for disqualification of these plants.

(The subsequent information was received and follows:)

DEFENSE PREAWARD SURVEYS OF DOMESTIC DRUG MANUFACTURERS CLASSIFIED AS LARGE OR SMALL BUSINESS,
FISCAL YEAR 1969

	Preaward surveys		
	Large	Small	Total
Manufacturers surveyed	26	62	88
Results of survey:			
Qualified	34	43	77
Disqualified	25	47	72
Total	59	90	149
Reasons by survey applicable to—			
Disqualification by survey	Large	Small	Total
Quality control	2	7	9
Quality control and housekeeping	6	27	33
Quality control, and product sample	1	1	1
Quality control, housekeeping, and capacity	1	2	3
Quality control, housekeeping, and subcontractor	1	1	1
Quality control, subcontractor, and capacity	1	1	1
Product sample	3	—	3
Product sample and subcontractor	3	—	3
Product sample and capacity	1	—	1
Subcontractor	2	5	7
Capacity	7	3	10
	25	47	72

An examination of 21 preaward survey or product sample reports listed the following specific explanations for disqualification by area:

<i>Area of disqualification</i>	<i>Specific reasons cited</i>
Quality control-----	Inadequate inspection program. Inadequate production records. Inadequate testing or testing program. Inadequacies in packaging. Inadequacies in written quality control procedures. Unauthorized people having access to label room. No program for maintenance and calibration of scales.
Housekeeping-----	Spillages not immediately removed from production area. Uncovered trash bins in bottle packaging area. Trash barrel emptied too close to production line. No program for periodic employee medical examinations.
Product sample-----	Unsanitary raw material containers. Container, container caps, or container labeling did not comply with purchase description requirement. Product failed specification requirements such as hardness test, storage test, color test, consistency, material defects, solubility test, etc.
Unacceptable subcontractor-----	Subcontractor was not required to issue adequate inspection instructions.
Capacity-----	Unsatisfactory production capability—no production plan; inadequate test equipment; plant fully utilized for current and future production; employees on strike. Inability to meet required delivery schedule—no production plan; time required to correct quality control deficiencies would jeopardize delivery; plant has insufficient capacity to meet the delivery schedule; plant has a bad performance record; firm had not obtained a commitment for glass. Unsatisfactory performance record—delinquencies on past contracts; production problems in manufacturing specification item. Unsatisfactory plant facilities and equipment—firm did not have necessary punches and dies; on-hand equipment fully committed to other orders.

NOTE. The above schedules do not reflect the relative seriousness of the deficiencies. The preaward survey is an evaluation of the proposed contractor's capability to perform. Each deficiency reported is evaluated as to its effect on the proposed award. The contracting officer must weigh all of the information and advisory recommendations supplied to him in selecting a contractor.

Senator NELSON. It raises several questions, I would suppose: Are the standards being used sound, and then if they are sound, are the same companies putting the same drug into the retail marketplace? Is there any exchange of this information between the Defense Supply people and the Food and Drug Administration?

Mr. AHART. I understand that there is no routine mechanism by which the Defense Department's inspection results get to the Food and Drug Administration or to the Veterans' Administration, as

the case may be. Certainly, it would be a good idea and I understand that Dr. Edwards expressed the opinion that FDA should eventually get into the position where they can give this kind of assurance to everybody in the country for any drugs which do not reach the marketplace.

I think certainly, as you indicated, this is a good objective for the Federal Government to strive to.

Senator NELSON. So, for example, here you have sample failure, but you say that the central procurement is using USP or NF standards.

If there is a sample failure and that supplier is rejected on the grounds that the product did not meet USP or NF standards, then would it not be critically important that the Defense Department notify the FDA forthwith? Otherwise those drugs are going into the marketplace not meeting USP and NF standards and nobody knows it.

Mr. AHART. I think this would be valuable information to the FDA and if it is in the Government's hands I think it should be made available. I understand there is no routine mechanism to make all inspection data available now. As to whether there is provision for exception reporting where the case seems to be particularly bad, I think we would have to check on that and see what has been done.

Senator NELSON. I think you were at the top of page 18 or bottom of page 17.

Mr. STAATS. Bottom of page 17. Let me reread that one sentence, Mr. Chairman. The VA inspects each contractor plant with regard to its entire product line. This is done prior to the contractor being awarded any contracts so that the Veterans' Administration can be assured that the supplier is suitable for any of the products it may offer to the Government. These initial contractor plant inspections represent about 60 percent of all inspections.

The remaining inspections are reinspections on a cycle basis. All inspections evaluate such areas of contractor operations as the adequacy of quality control, test facilities, and sanitation.

All plant inspections are made by two Veterans' Administration pharmacists.

During fiscal year 1970, the two pharmacists performed 134 inspections at 122 contractors' plants. The inspections resulted in 37 disapprovals, the most common reason being the lack of following adequate quality control procedures. Veterans' Administration does not utilize military inspections of domestic plants except as a supplement to its own inspection. Veterans' Administration does rely upon Department of Defense inspections of foreign plants.

The Food and Drug Administration performs testing of selected drug samples for the Veterans' Administration. Brand-name drug items which are centrally stocked are tested on a sample basis once a year. Each order of generic drug items which are centrally managed is tested.

Drug items under Federal Supply Schedule contracts administered by the Veterans' Administration are rarely tested except that the products of any new contractor under schedule contracts are tested.

A compilation of testing reports received by the Veterans' Admin-

istration from the Food and Drug Administration for 1970 through December 29th shows a total of 784 tests made—254 brand-name and 530 generic. The total rejections were 29 for a rate of 3.7 percent. All rejections were on generic drug items.

The Department of Defense and the Veterans' Administration exchange inspection information only upon specific request. The Department of Defense previously supplied the Veterans' Administration with a list of plants inspected by it but this practice was discontinued about 2 years ago. At present there is no routine exchange of inspection information.

Senator NELSON. Have you any explanation for that?

Mr. STAATS. Pardon?

Senator NELSON. Any explanation for that?

Mr. STAATS. I do not have an explanation for it.

Mr. CROWTHER. No, sir; we really have not examined further into it. We have not examined into the reasons why it has not been kept up.

Mr. STAATS. We will be glad to check into that further and supply any further information we could for the record, if you like. We really have not had a chance to pursue it that far.

(The subsequent information was received and follows:)

DEFENSE PERSONNEL SUPPORT CENTER LISTING OF MANUFACTURERS SUBJECTED TO PREAWARD SURVEYS SUPPLIED TO VETERANS ADMINISTRATION REASON FOR DISCONTINUANCE

We were informed by Defense Personnel Support Center personnel that the information which they prepared had a potential for misinterpretation and for this reason they discontinued the practice of routinely furnishing it to VA. Defense inspects a manufacturer to evaluate his ability to supply a specified drug item. When disqualified, the manufacturer was declared unsuitable for that drug item only and not for the rest of his product line. However, the listing previously furnished to VA did not disclose either the disqualified product or the reasons for disqualification, which may have been unique to Defense Personnel Support Center requirements, such as inability to meet Defense packaging standards.

Currently, Defense Support Center supplies Federal agencies including VA with data obtained on pre-award surveys upon specific request.

Senator NELSON. The FDA is inspecting, the Veterans' Administration is independently inspecting, and the Defense Supply Agency is independently inspecting. It would seem to me that we need some clearing house for the results of the inspections, do we not?

Mr. STAATS. That is essentially what we are suggesting in our next paragraph here.

We believe that consideration should be given to establishing appropriate guidelines to facilitate the routine exchange of contractor inspection and product testing information among Government agencies involved with the control or procurement of drug products. Also, we believe that consideration should be given to the possibility of eventually turning over the entire responsibility to the Food and Drug Administration for drug contractor plant inspections and product testing including testing of contract quality control procedures in order to satisfy each procuring agency's requirements and take the greatest advantage of the food and drug inspection system that has been established.

This concludes our formal statement, Mr. Chairman, but we are suggesting in this last paragraph essentially that the Food and Drug Administration be considered as the type of clearing house to which you refer.

Senator NELSON. That is, that the results of all inspections of other agencies be routinely referred to the Food and Drug Administration.

Mr. STAATS. And that can serve as a central repository of this type of information.

Senator NELSON. How many plant inspectors does the VA have?

Mr. AHART. They have two pharmacists basically, that do the inspection of the plants, Mr. Chairman. They also, as I think the Comptroller General pointed out, draw upon the facilities of the FDA to do the product testing for them. So, it would be the two VA inspectors plus whatever use they make of the Food and Drug Administration facilities.

Senator NELSON. I take it the Veterans' Administration's inspections are not general. They are aimed only at a specific contractor who proposes to supply them, is that it?

Mr. AHART. They make an initial inspection of a plant for every prospective contractor and they also reinspect existing contractors from time to time. I am not sure what that cycle is. I think it is somewhere around 3 to 5 years.

Senator NELSON. How many inspectors does DOD have?

Mr. AHART. I am not sure we have the breakdown on that. As the Comptroller General mentioned, they have got about 80 people involved in the testing and inspection functions.

As to how many of these actually perform the plant inspections as opposed to performing the drug testing functions, I do not think we have that split.

Senator NELSON. Then, with three agencies inspecting and practically no exchange of information, there is no way of one agency knowing whether the other agency may have recently inspected the plant they propose to inspect now, is that right?

Mr. AHART. That is correct, Mr. Chairman.

Mr. GORDON. On page 9 you stated that the VA and DOD should combine their purchases of drugs which they both buy. Do you see any objections to including other Government agencies like the Public Health Service?

Mr. STAATS. No. We would not see any objection to that. The Public Health Service currently buys, as I understand, about half of their drugs through the VA system but we would not see any objection, certainly.

The volume in the case of PHS is significantly less but that does not really detract from the conclusion that it would be probably a good idea.

Mr. GORDON. The States and municipalities are having great difficulty in getting enough funds to provide necessary services. Now, the figures that we have show that the States and municipalities pay considerably more for drugs than either the VA or DOD. Is that your understanding, also?

Mr. STAATS. I do not have any figures as to the total volume of State and local government drug procurement. The subject is one that needs a lot of study.

There are some legal questions involved. The subject of the Federal Government's facilities being used by State and local governments has come under some discussion in the Commission on Government Procurement which as you know, is just getting underway with its study. And the expectation is that the Commission will come to the Congress with some recommendations as to how the Federal Government's facilities for procurement could be used by State and local governments, particularly where there is grant-in-aid money involved and, of course, grant-in-aid funds are very substantial, as you know, running more than \$25 billion a year.

The GSA, the General Services Administration, has already taken steps in this direction, which appear very promising. So, in principle, I would see no reason why this would not be a profitable line of study, even if it meant that it would have to ask Congress for some legislation to overcome some legal problems that would be involved with Federal Government using its funds, you might say, in advance to procure stocks and then reselling them to States and local governments.

Mr. GORDON. It could be done in another way. For example, a State can request the Federal purchaser to order drugs for the State. That is all the Federal Government has to do. The drugs could be sent directly to the State, which would pay the manufacturer directly. It would be just a question of the Federal Government ordering on behalf of the State or municipality.

Are there any legal objections to that particular method?

Mr. SHNITZER. I think, Mr. Gordon, that there may be some substantial question about it. We note that there are some specific statutes which authorize in a given instance an agency of the Federal Government to make procurements on behalf of local governments. The Federal Highway Act, 23 U.S.C. 308(b), is an instance. Our feeling is that if it is necessary for the statute to include such a provision, we believe that there may be a good reason for having some doubt about whether or not absent such a specific provision that it could be done because it may be regarded as utilizing a government facility for something other than the purposes intended by Congress.

Senator NELSON. I think part of the shared taxes program we are talking about.

Mr. SHNITZER. It could very well be.

Senator NELSON. Thank you very much, Mr. Staats, for a very informative and valuable presentation to the committee. If we have some further questions that occur to us after we examine the records, I take it we can submit the questions and you will supply the answers for the record.

Mr. STAATS. We will be very happy to respond.

Senator NELSON. Our next hearing will be on February 1, with the AID and Public Health Service as witnesses.

(Thereupon, at 12:10 p.m., the hearing was recessed, to reconvene on Monday, February 1, 1971.)

(The complete prepared statement and appendixes submitted by Mr. Staats follows:)

United States General Accounting Office
Washington, D.C. 20548

For Release on Delivery
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STATEMENT OF
ELMER B. STAATS, COMPTROLLER GENERAL OF THE UNITED STATES
BEFORE THE
MONOPOLY SUBCOMMITTEE
SELECT COMMITTEE ON SMALL BUSINESS
UNITED STATES SENATE
ON
DRUG PROCUREMENT SYSTEMS OF FEDERAL AGENCIES

Mr. Chairman and Members of the Subcommittee, I am pleased to appear here today in response to your request to discuss the drug procurement systems of Federal agencies.

As you requested, we plan to discuss the efficacy, economy, and rationality in the drug procurement activities of the Federal Government. Specifically you asked that we discuss the methods of procurement, the degree of competition obtained, participation by small business and the use of section 1498, of title 28 of the United States Code to procure drugs covered by patents.

Our discussion today will focus upon the systems through which the Federal Government directly procures drugs from manufacturers and other suppliers. We would like to mention, however, that since our last appearance before this Subcommittee in May 1967, we have conducted reviews of and issued reports on other aspects of the Government's drug-related

activities. We have attached as Appendix A to my statement digests of these reports for your information.

There is a growing involvement by the Federal Government in drug procurement, encompassing its substantial role both as a direct provider of medical care and treatment to certain classes of persons and as a supporter of federally financed programs which include the provision of drugs for eligible beneficiaries. During the three fiscal years 1967 through 1969, the total estimated Federal expenditures for drugs increased from \$514 to \$975 million. A substantial portion of these expenditures were indirect in that they consisted of the Federal share of the costs of drugs provided to beneficiaries under the Medicare and Medicaid and certain other programs. Drug costs under the Medicare and Medicaid programs increased from an estimated \$350 million in fiscal year 1967 to \$750 million in fiscal year 1969.

Although the major portion of Federal drug expenditures are indirect, the expenditures for direct procurements have increased from \$161 million in 1967 to \$203 million in fiscal year 1969.

Three Federal agencies account for most of the direct drug procurement--the Defense Personnel Support Center, an activity under the Defense Supply Agency; the Public Health Service of the Department of Health, Education, and Welfare; and the Veterans Administration. Each of these agencies operates its own drug supply system.

The Defense Personnel Support Center centrally manages about 1,100 drug items and in fiscal year 1969 procured an estimated \$103 million in drug. The Public Health Service

centrally manages about 600 drug items and in fiscal year 1969 spent an estimated \$6 million for drugs, about 86 percent of which were obtained under contractual arrangements made by Veterans Administration. The Veterans Administration centrally manages about 450 drug items and centrally procured an estimated \$25 million in drugs in fiscal year 1969.

The Veterans Administration also administers Federal Supply Schedule contracts under which Federal agencies can satisfy their drug requirements through direct purchase from drug manufacturers. Purchases under these contracts for fiscal year 1969 were estimated at \$56 million.

In addition to drug procurements which are centrally managed or administered, medical facilities of each of the three agencies can, in certain circumstances, locally procure their drug needs.

Previous testimony before this Subcommittee has highlighted the drug procurement system as an activity supporting physicians' decisions on the most appropriate drug therapy for their patients. Such a system has as its base the professional selection of drugs and, in support of that selection, a complementary supply activity.

The objective of Government drug procurement should be to obtain at fair and reasonable prices, and in a timely manner, the proper and needed quantities of drugs that are of a satisfactory quality.

Specifically, we believe that a drug procurement system should provide for:

- a selection process which emphasizes drug quality, safety, and efficacy and gives appropriate consideration to drug cost.

- comprehensive and accurate drug usage data to facilitate the selection of the most appropriate and economical method of supply with appropriate corresponding restrictions on all other available supply sources.
- the development of product specifications which insure that drugs are capable of producing the desired therapeutic effect while encouraging the widest possible competition and lowest possible cost.
- effective negotiation as the alternative contracting method in instances where competitive procurement is not possible, and
- inspection and testing to establish manufacturer responsibility and capability to produce quality drugs.

We have surveyed Federal drug procurement systems in the light of these criteria and would like to briefly describe our observations.

I would like to emphasize that these observations are based on preliminary studies of the systems involved and cannot be considered as a complete review of such systems. Our work is continuing, however, and we will undoubtedly have more observations and suggestions to offer at a later time.

Drug selection

With respect to the drug selection process, we obtained information at the local level for five Federal medical facilities. Each of the facilities visited has established its own system for judging which drugs are appropriate for use. Each system is under the administration of a central group, the name of which varies but may commonly be referred to as the Pharmacy and Therapeutics--the P and T--Committee.

The P and T committee's membership generally consists of the directors of the various professional services of the medical facility and the chief pharmacist who acts as secretary.

Some committees also have special non-voting members, such as supply specialists and nursing personnel, whose functions range from that of observer to advisor in their areas of expertise.

A principal function of the P and T committees is to administer the system for evaluating and selecting from among numerous drugs those considered most useful in patient care. The committee's selections are reflected in a continuously revised compilation of drugs approved for use within the medical facility--the station formulary. In carrying out this function, the P and T committees generally receive some assistance from headquarters level in the form of policy guidelines, regulations, and information published by various professional medical service groups. Agency policy statements and regulations, where available, are generally limited to setting out the scope and authority of the P and T committees. Headquarters may provide recall and adverse reaction information about specific drugs, and furnish data on the commercial availability and prices of drugs. However, the selection of drugs for inclusion in the station formulary is reserved to the P and T committees. At military hospitals, the hospital commander is responsible for approval or disapproval of drugs recommended by P and T Committees.

Most of the information on specific drugs which is made available to members of the P and T committees in their consideration of changes to the station formulary comes from two sources; professional journals and the drug manufacturers. The drug companies supply most of their information to individual physicians through sales representatives (detailmen) and by direct mail advertising.

Recently a series of actions impacting upon the operation of P and T committees and the formulary system have been taken or are planned within each of the major Federal drug procurement agencies. For example each of the agencies has directed the distribution of the Food and Drug Administration's recently published list of "ineffective" drugs to their local medical facilities with the recommendation or requirement that the drugs no longer be used.

Public Health Service has also taken action to more fully develop possible approaches to effective drug utilization reviews, as recommended in the report of the Department of Health, Education, and Welfare's Task Force on Prescription Drugs. A research study of the methodology and feasibility of this technique is currently underway.

We believe that the recent actions related to the drug selection process, if properly implemented, should improve control over drug operations at the local level. In implementing such actions we believe that emphasis should be placed on providing physicians employed by the Federal Government with appropriate information concerning available drugs to assist them in making decisions relating to drug therapy.

Keeping physicians informed is most important because the physicians' decisions guide the drug selection process. Unless this process is based on the best information available, even an otherwise efficient supply function may be uneconomical.

During our visits to local medical facilities we noted specific actions by P and T committees which we believe are

appropriate for wider application. Examples noted were (1) the dissemination of information on drug studies including drug costs and (2) dissemination of information on adverse drug reactions.

Procurement and supply system

Once determinations have been made through the selection process of the drugs which will be used, the drug supply activity must operate effectively to furnish the required items in the most economical manner. Requirements for frequently used drugs are generally met through a central stock system which allows for quantity purchases.

Veterans Administration and the Department of Defense both have reporting systems for identifying drugs for inclusion in their centralized stock systems.

In the Department of Defense, each of the three services has its own system and criteria for reporting, and they vary from each other. One result of this is that Defense-wide usage of a specific drug does not become known until one of the services recommends a drug for inclusion in the central stock system. Approval of only one service is needed to add a drug to the central supply system, but all services must concur in removing an item from the system. In fiscal year 1970, 66 drug items were added to the system and action taken to delete or discontinue procuring 106 drug items on a centralized basis.

We believe that under the current reporting systems, drug items that merit consideration for inclusion in the central

stock system may not be included in the items identified for review and evaluation. This possibility could be removed and the reporting system improved by the use of standard criteria by the three services.

The Veterans Administration's primary source of information in its continuing effort to capture data on drug usage outside of its central stock system is a quarterly drug report based on reports from each of its medical facilities. This report is characterized by the Veterans Administration as an important tool in the management of its drug program and shows all procurements from sources other than central stock. The Veterans Administration uses this report to identify drugs which qualify for inclusion in the central stock system.

We believe that the Veterans Administration could make its comprehensive report more useful by requiring more uniform adherence to its regulations on reporting nomenclature and by providing for the compiling of certain summarizations and exception reports which would make the identification of drugs for central stock management much easier.

Also, available data indicates that the Veterans Administration and the Department of Defense could take advantage of higher quantity drug procurements which could possibly result in lower prices by combining their needs for procurement purposes. For example, the Veterans Administration contracted for 1,404 units of Lincocin at a unit price of \$22.30--five days later the Defense Personnel Support Center contracted for 4,464 units of the same drug from the same manufacturer at a unit price of \$19.95. In another instance the Veterans Administration contracted for 3,000 units of Tylenol at \$6.14

each--about one-month earlier the Defense Personnel Support Center contracted with the same manufacturer for 10,176 units of the same drug at \$3.28 a unit.

At least 150 drugs, centrally procured by the Defense Personnel Support Center during calendar years 1968 and 1969, were also centrally procured by the Veterans Administration during fiscal years 1968 and 1969.

Both the Veterans Administration and the Department of Defense have established required priorities of supply sources to be used by their medical facilities. These priorities reflect a policy of using the most economical supply source available. Such a policy is important because the commercial unit prices of drugs available at the wholesale level are generally higher than prices established under Federal Supply Schedule indefinite quantity contracts which, in turn, are generally higher than definite quantity procurements.

To illustrate this fact, we compared prices listed on the Federal Supply Schedule with the highest prices paid under definite quantity contracts for 68 drug items over a recent two year period and found that the Schedule prices averaged 63 percent higher. We recognize that procurements under indefinite quantity contracts have inherently higher manufacturers costs of warehousing and administration which would account for some part of the difference between definite quantity procurements. Also additional warehousing costs are incurred by the Government on procurements for central stock under definite quantity contracts, but considering all these factors, a 63 percent difference seems significant in any event. The average price differential is particularly significant considering the amount of total purchases made under

Schedule contracts and the fact that many centrally stocked drugs are also available under the Schedule contracts.

We see no reason why Federal agencies should independently procure drugs from the same manufacturer and lose the possible price advantages resulting from high quantity purchases. We believe consideration should be given to improving Federal drug procurement practices by providing for an exchange of information between the Department of Defense and the Veterans Administration as to the estimated annual volume of drugs to be procured in order that consideration can be given to combining quantities of certain drugs for procurement purposes, using the most economical method of procurement for each drug item.

Product specifications

Another key requirement to an efficient supply system is its ability to provide, wherever possible, purchase descriptions or product specifications which permit more than one manufacturer to bid effectively.

Both the Defense Personnel Support Center and the Veterans Administration establish their own specifications on drugs. Both agencies require compliance with the applicable standards of the United States Pharmacopeia and the National Formulary to which each agency adds its own additional requirements. The professional personnel assigned this responsibility within the Defense Personnel Support Center and the Veterans Administration are chemists or pharmacists.

The Veterans Administration develops a specification when the demand for a generic product is sufficient to warrant central management or administration and when no patent exists or the patent has expired. The Veterans Administration has established specifications for about 100 of its centrally

managed drugs procured on a generic basis. In addition, specifications have been developed on 46 drug products administered under Federal Supply Schedule contracts.

The Defense Personnel Support Center establishes a specification or purchase description on every drug item in its central stock system.

Both agencies informed us that they use a number of sources in constructing their specifications. In addition to the monographs of the United States Pharmacopeia and National Formulary, other sources for constructing specifications include the Food and Drug Administration, drug manufacturers, the National Institutes of Health, and the American Chemical Society.

When a drug is standardized for the military supply system, the manufacturer is contacted and requested to supply sufficient information so that the item's essential characteristics can be prepared.

We explored with Defense Personnel Support Center officials the question of whether, because of the substantial reliance upon information obtained from manufacturers, military specifications or purchase descriptions are restrictive and, in effect, result in a proprietary specification. These officials contend that the specifications and purchase descriptions are constructed in such a manner that any firm knowledgeable in the drug industry could manufacture the drugs. Without a detailed study of the matter, we have no basis upon which to either dispute or validate this contention.

Competition and negotiation

It is clear that the degree of competition obtained in the drug procurement area is less than competition obtained for many other Government supply items. The total dollar value of drug procurements for central stock by the Veterans Administration and the Defense Personnel Support Center in fiscal year 1970, amounted to about \$94 million. About 7 percent or \$6.4 million of the central stock procurements were made under contracts awarded pursuant to formal advertising procedures. The remainder were made under contracts negotiated with the sole source of supply or under contracts awarded after the solicitation of proposals.

Among the reasons for the limited amount of competitive procurement are of course, the fact that many drugs are patented products and the fact that legal and administrative requirements must be met in order to obtain Food and Drug Administration approval. Also, many procurements are made by brand-name either because only one brand of a particular drug is available or because of the prescribing physicians' preference. For example, about 70 percent of the drug items centrally stocked by the Veterans Administration have been designated for procurement on a sole-source basis in order to obtain specified brand-name drugs.

In addition, competitive contract awards account for about 25 percent of the procurements under the Federal Supply Schedules. Most of the other contracts, which are included for the

purpose of making manufacturers' product lines available to the Government at prices less than market, are negotiated without the benefit of competition.

The Defense Personnel Support Center sought to increase competition on their centrally managed drug items when, in January 1969, approximately 1,000 firms were invited to indicate their interest in bidding on 401 items, 290 of which were classified as single-source. Replies were received from 104 companies. Fourteen companies requested to be added to the bidders list for 35 of the 401 drug items. Two other companies requested to be added to the bidders list for eight drug items not included in the solicitation. The other 88 responding companies either did not produce the item; reaffirmed their interest in supplying the drug items for which they were already on the bidders list; or expressed no interest in supplying any of the products to the Government.

Some of the reasons advanced with respect to the absence of competition on a large number of drug items include

- restrictions imposed by law or regulation, such as patents on new drug applications;
- inadequate plant facilities and no desire to make the required investment to upgrade the facilities;
- the lack of qualified personnel to make many drugs;
and
- the expense of introducing a new product with no assurance of reasonable return through sustained contract awards.

The advantages of seeking the widest possible competition in drug procurement can be demonstrated by available data from which we identified 9 drugs procured over a comparable period of time both competitively and on a sole-source basis. The drugs purchased from sole-source suppliers by the Veterans

Administration are estimated to be 60 percent higher than the average price obtained after formal advertising or the solicitation of competitive proposals by the Department of Defense. Appendix B of my statement shows the 9 drugs and comparative prices. It should be noted that the quantities purchased by the two agencies are different which may account for some part of the price differences.

We see no reason why different Federal agencies should independently procure the same drug in a different manner, and possibly from the same manufacturer, and lose the advantages associated with procurement of larger quantities and, where possible, increase competition.

Without effective competition, there is a question of the Government assuring itself that the prices being obtained are fair and reasonable under negotiated procurements. Public information is available on selected areas of drug pricing--an example would be wholesale prices. In determining whether the negotiated price is the best attainable by the Government, comparison of the bid with these prices reflects reasonableness by inference. Although there is no assurance that these prices are reasonable, our survey indicates that these prices serve as the basis for most of the price reasonableness determinations made by the Veterans Administration and the Defense Personnel Support Center.

Small business participation

Competition through formally advertised procurements seems to have a decided effect on the participation of drug manufacturers classified as small business. When drug supply contracts are awarded competitively, small business is often able to effectively compete. For example, in fiscal year 1970 more than half of the dollar volume of the Veterans Administration's formally advertised procurements of centrally

stocked drugs were awarded to drug manufacturers classified as small business concerns. Only 3 percent of the negotiated procurements for centrally stocked drugs were awarded to small business concerns. Since negotiated procurements constituted more than 96 percent of the total, small business received only about 4 percent of the total procurements of centrally stocked drugs.

During fiscal year 1970 the Defense Personnel Support Center initiated 1,076 procurement actions, each having a value of \$10,000 or more, with domestic drug manufacturers. Small business was involved in 137 of these actions--representing about 7 percent of the total procurement dollars of about \$71.6 million. For contracts amounting to \$19 million awarded under advertised procedures or negotiated with competition by the Defense Personnel Support Center during fiscal year 1970, small business received about 17 percent of the dollar volume or a total of \$3.3 million.

Drug Procurements From Foreign Sources

The absence of satisfactory prices from domestic drug manufacturers has led both the Veterans Administration and the Defense Personnel Support Center to the procurement of certain drugs from foreign sources. However, neither the Veterans Administration nor the Defense Personnel Support Center are currently making extensive use of foreign sources for their drug procurements.

In recent years the Veterans Administration has bought only one drug from a foreign source and does not actively solicit foreign bids in its procurements.

The Defense Personnel Support Center furnished this Subcommittee with information relative to its foreign procurement of five drug items during 1968 and 1969. During 1970 only one

of these items, tetracycline hydrochloride, has been procured from a foreign source. Another of these items has been obtained during 1970 from a domestic manufacturer because the bid by the foreign sources were not considered low after considering the Buy American Act provisions and related policies. The remaining three items were not procured from any source during 1970.

One factor in the small use of foreign sources is the Government's exposure to possible action under section 1498 of title 28, United States Code. This section provides that whenever an invention described in and covered by a patent of the United States is used or manufactured by or for the United States without license of the owner, the owner's remedy shall be by action against the United States in the Court of Claims for the recovery of his reasonable and entire compensation for such use and manufacture.

Since our last report to you on this subject, dated July 12, 1967, in which we explained the background and purpose of section 1498 of title 28, there have been two suits against the Government by drug patent holders for infringement of their patents rights. One of these suits involving purchases of nitrofurantoin was settled by the parties for \$192,500 in September 1969 and the other one involving purchases of meprobamate is still pending.

Federal inspection and testing programs

An an integral part of their drug procurement systems both the Veterans Administration and the Defense Personnel Support Center have established programs for assuring the capability of Government contractors to supply a drug product of acceptable quality. These programs vary somewhat in their approach but have a common objective.

The quality assurance program at the Defense Personnel Support Center includes an evaluation, through pre-award surveys of the plant and pre-award testing of product samples, of the contractor's ability to supply a specific drug item.

Pre-award surveys and pre-award samples may be generally required when (1) the contractor has never before furnished the item being procured; (2) a doubt exists as to the quality control, housekeeping procedures, or financial position of the prospective contractor; or (3) the item is to be furnished from or manufactured in a different plant.

The Defense Contract Administration Service has about 80 quality assurance representatives, who are either chemists, chemical engineers, or pharmacists, and function as drug inspectors. They perform pre-award surveys at the request of the Defense Personnel Support Center and are charged with the responsibility for inspecting and approving all drug items manufactured under Defense contracts. In performing their inspections the quality assurance representatives are required to inspect each drug lot.

During fiscal year 1969 a total of 168 pre-award surveys were made--149 of which were performed on domestic manufacturers which were classified as either small or large business. Sixty-two small business firms were subjected to 90 surveys. Forty-seven of these surveys resulted in disqualifications. Twenty-six large businesses were subjected to 59 surveys, 25 of which resulted in disqualifications. Reasons for disqualification included poor quality control; poor housekeeping; sample failure; unacceptable subcontractor; and inadequate capacity.

The Veterans Administration inspects each contractor plant with regard to its entire operation and for its entire

product line. This is done prior to the contractor being awarded any contracts so that the Veterans Administration can be assured that the supplier is suitable for any of the products it may offer to the Government. These initial contractor plant inspections represent about 60 percent of all inspections.

The remaining inspections are reinspections on a cycle basis. All inspections evaluate such areas of contractor operations as the adequacy of quality control, test facilities, and sanitation.

All plant inspections are made by two Veterans Administration pharmacists.

During fiscal year 1970, the two pharmacists performed 134 inspections at 122 contractor's plants. The inspections resulted in 37 disapprovals, the most common reason being the lack of following adequate quality control procedures. Veterans Administration does not utilize military inspections of domestic plants except as a supplement to its own inspection. Veterans Administration does rely upon Department of Defense inspections of foreign plants.

The Food and Drug Administration performs testing of selected drug samples for the Veterans Administration. Brand-name drug items which are centrally stocked are tested on a sample basis once a year. Each order of generic drug items which are centrally managed is tested.

Drug items under Federal Supply Service Contracts administered by the Veterans Administration are rarely tested except that the products of any new contractor under Schedule contracts are tested.

A compilation of testing reports received by the Veterans Administration from the Food and Drug Administration for 1970 through December 29th shows a total of 784 tests made--254 brand-name and 530 generic. The total rejections were 29 for a rate of 3.7 percent. All rejections were on generic drug items.

The Department of Defense and the Veterans Administration exchange inspection information only upon specific request. The Department of Defense previously supplied the Veterans Administration with a list of plants inspected by it but this practice was discontinued about 2 years ago. At present there is no routine exchange of inspection information.

We believe that consideration should be given to establishing appropriate guidelines to facilitate the routine exchange of contractor inspection and product testing information among Government agencies involved with the control or procurement of drug products. Also we believe that consideration should be given to the possibility of eventually turning over the entire responsibility to the Food and Drug Administration for drug contractor plant inspections and product testing including testing of contract quality control procedures in order to satisfy each procuring agency's requirements and take the greatest advantage of the food and drug inspection system that has been established.

Mr. Chairman, this concludes my statement. I shall be happy to answer any questions that you or other members of this Subcommittee may have.

COMPTROLLER GENERAL'S
REPORT TO THE CONGRESS

CONTROLS OVER THE MEDICAID DRUG PROGRAM
IN OHIO NEED IMPROVEMENT
Social and Rehabilitation Service
Department of Health, Education, and
Welfare B-164031(3)

D I G E S T

WHY THE REVIEW WAS MADE

Under Medicaid, the Department of Health, Education, and Welfare (HEW) shares with the States the costs of providing medical care to persons unable to pay. Because Medicaid expenditures for drugs, nationally, amounted to about \$307 million in fiscal year 1969, the General Accounting Office (GAO) reviewed the Medicaid drug program. About \$14 million of that amount was spent in Ohio where GAO made its review.

FINDINGS AND CONCLUSIONS

GAO sought answers to three basic questions:

- Are recipients of drugs eligible under Medicaid?
- Are drugs reasonably priced?
- Are controls over drugs adequate?

On the basis of a statistical sample, GAO estimates that, during the year ended March 31, 1969, the welfare recipients comprising at least 4,300, and possibly as many as 9,300, welfare cases in Ohio were ineligible for Medicaid services, including drugs. That situation is attributable primarily to a need for more timely and accurate determinations of eligibility, on a continuing basis, by the county welfare departments. (See pp. 7 to 11.)

Certain drugs purchased under Ohio's Medicaid program were not reasonably priced because of several factors.

- The State's policy of paying pharmacies for drugs on a cost-plus-a-percentage-of-cost basis is contrary to Federal and HEW policy because it gives the pharmacies an incentive to sell high-cost drugs to obtain a greater profit. GAO noted that 11 other States and the Virgin Islands paid for drugs on that basis. (See pp. 12 and 13.)
- The State's controls were not adequate for ensuring that prices billed to the State conformed to its formula for determining

payment for drugs, that is, cost plus 50 percent. For example, average markups were 159 percent for Lanoxin, 233 percent for milk of magnesia, and 248 percent for digoxin. The State's policy of permitting pharmacies to charge a minimum of \$1 for each prescription increased the difficulty of controlling costs. (See pp. 13 to 20.)

- Nursing homes were not obtaining long-term maintenance drugs in economical quantities, because the State limits to a 30-day supply the drugs prescribed for welfare patients in nursing homes. (See pp. 23 and 24.)

Also there is a need for HEW, in its studies of drug efficacy, to give priority to certain lower cost, frequently used drugs identified by the HEW Task Force on Prescription Drugs as offering potential for considerable savings. (See pp. 20 to 22.)

Ohio's controls over drugs under its Medicaid program were inadequate for either the State or HEW to determine whether (1) drugs obtained by nursing homes were administered to welfare patients and were effective in their treatment, (2) drugs dispensed and billed by pharmacies were actually received by welfare recipients, and (3) only needed drugs were provided to welfare recipients. For example:

- At four of six nursing homes visited, controls were not adequate for ensuring that drugs paid for by the State had been authorized by a physician. (See pp. 26 to 29.)
- At five of 14 pharmacies visited by GAO, controls were not adequate for ensuring that prescriptions were complete as to quantities, dosages, forms, strengths, or dates. (See pp. 29 to 32.)
- The State had not given county welfare departments adequate information for determining whether recipients were receiving only needed drugs. (See pp. 33 and 34.)

RECOMMENDATIONS OR SUGGESTIONS

GAO is recommending that the Secretary of Health, Education, and Welfare:

- Provide assistance to Ohio and other States in revising their drug-payment policies to conform to HEW policy. (See p. 24.)
- Give priority in the conduct of HEW's drug-efficacy studies to those drugs identified by the HEW Task Force on Prescription Drugs as having considerable potential for savings and furnish physicians with information on the results of the studies. (See p. 24.)

- Issue guidelines for utilization reviews of drugs so that the States will have a uniform system for accumulating, analyzing, and reporting data for use by HEW and the States in evaluating this aspect of the Medicaid program. (See p. 34.)
- Monitor the implementation of these guidelines and give assistance to Ohio and other States, as needed. (See p. 34.)

AGENCY ACTIONS AND UNRESOLVED ISSUES

HEW stated:

- that guidelines for payments of reasonable charges for prescribed drugs were expected to be issued in the next several months; Ohio planned to abolish the \$1 minimum for each prescription; and the States not in conformity with HEW regulations on drug prices had adopted, or were working toward adoption of, policies to bring them into conformity. (See pp. 24 and 25.)
- that it agreed that its efficacy studies of brand-name and chemically equivalent drugs should be completed and the results should be given to physicians. HEW, however, must make certain of the safety and effectiveness of all available drugs. GAO believes that giving priority, in HEW's drug-efficacy studies, to relatively low-cost, chemically equivalent drugs would not be inconsistent with HEW's responsibility and could result in significant economies in Medicaid drug costs. (See p. 25.)
- that utilization review guidelines would be issued in the near future; contracts had been awarded to four States for a pilot medical surveillance and utilization review program which was expected to strengthen the ability of States to plan, administer, and monitor the Medicaid program; and, the model system developed through the pilot program would be made available for adoption by all participating States. (See p. 35.)
- that it planned to institute a closer monitoring and liaison program in each regional office to bring about a closer relationship with State agencies and to include more frequent visits and detailed reviews of State Medicaid operations. (See p. 35.)

MATTERS FOR CONSIDERATION BY THE CONGRESS

GAO is sending this report to the Congress because of congressional interest in the Medicaid program. The report should be useful to the Congress in considering legislative changes to the program.

COMPTROLLER GENERAL'S
REPORT TO THE CONGRESS

OPPORTUNITIES FOR BETTER SERVICE AND
ECONOMIES THROUGH STANDARDIZATION OF
PHARMACY ITEMS AND CONSOLIDATION OF BULK
COMPOUNDING FACILITIES
Veterans Administration B-133044

D I G E S T

WHY THE REVIEW WAS MADE

The General Accounting Office (GAO) reviewed certain operations of the Veterans Administration (VA) pharmacies in the Los Angeles, Chicago, and New York metropolitan areas to determine whether the economies and improved pharmacy service realized from pharmacy bulk compounding operations could be increased by greater standardization of drugs and medicals for patient treatment and by consolidation of such pharmacy activities at centralized facilities.

FINDINGS AND CONCLUSIONS

- Although each VA station where GAO made its review had a therapeutic agent committee, only the stations in the Los Angeles area had formed an interstation therapeutic agent committee to increase the standardization of medications commonly used for patient treatment and had established a centralized facility for the bulk compounding of drugs.

GAO believes that there are opportunities for reducing the costs of drugs used by VA stations in metropolitan areas by the establishment of interstation therapeutic agent and pharmacy committees and centralized bulk compounding and purchasing facilities.

On the basis of the Los Angeles experience, GAO believes also that a centralized facility would contribute to improved patient care by providing needed medications not commercially available, more assurance of the quality of drugs compounded, and better support for research and training activities.

It is GAO's opinion that the use of interstation committees to encourage coordination and cooperation in pharmacy operations has applicability in many metropolitan areas, such as Boston, Chicago, New York, Philadelphia, and San Francisco, each of which has several VA medical facilities.

RECOMMENDATIONS OR SUGGESTIONS

GAO is recommending that the Administrator of Veterans Affairs require the formation of interstation therapeutic agent and pharmacy committees in geographical areas which have several VA medical facilities.

Appendix A

GAO is recommending also that the committees, when established, and with the encouragement and assistance of the VA Central Office, study the feasibility of establishing centralized bulk compounding and purchasing operations within their respective geographical areas.

AGENCY ACTIONS AND UNRESOLVED ISSUES

VA stated that it concurred in GAO's recommendations and would establish such interstation committees.

MATTERS FOR CONSIDERATION BY THE CONGRESS

GAO is reporting this matter to inform the Congress of the action planned by VA to provide better medical service to veterans and to effect economies in the pharmacy program.

GENERAL ACCOUNTING OFFICE
REPORT TO THE SECRETARY OF
HEALTH, EDUCATION, AND WELFARE

OPPORTUNITIES FOR ECONOMIES
IN DRUG PROCUREMENT IN
INDIAN HEALTH PROGRAM
B-164031(2)

D I G E S T

WHY THE REVIEW WAS MADE

The Division of Indian Health (DIH), of the Health Services and Mental Health Administration has the responsibility for providing health services to Indians and to Alaska natives.

Previous reports issued by the General Accounting Office (GAO) on drug purchases by Federal and State agencies with Federal funds showed that there were opportunities for reducing drug costs by revising procurement procedures.

Since there appeared to be a similar opportunity for economies in the program providing health care to Indian beneficiaries, GAO reviewed the drug procurement policies and practices of DIH. In fiscal year 1968, the DIH purchased \$2.7 million worth of drugs for the benefit of Indians.

FINDINGS AND CONCLUSIONS

GAO found that DIH could realize economies by making several improvements in its management of drug procurement.

Opportunities exist for savings if DIH places greater emphasis on the benefits of centralized and competitive buying through the Public Health Service (PHS) supply center or through Veterans Administration (VA) supply depots. GAO believes that the volume of drug products purchased by field installations directly from manufacturers and local wholesale establishments--which is approaching \$1 million a year--can be reduced. (See p. 5.)

DIH has not adopted a system for determining which drug products are, or could be, commonly used at field installations. GAO believes that there is a need for considering the benefits to be derived from the establishment of a program-wide drug formulary which together with better information on drug usage by field installations would help in determining the drugs that could be procured centrally on a competitive basis and generally at lower prices than for drugs purchased directly by field installations. (See p. 6 and p. 9.)

Tear Sheet

Drug pricing methods in some contracts with private pharmacies which furnish prescriptions to Indian beneficiaries were based on cost-plus-percentage-of-cost features that GAO believes are not conducive to economical drug purchasing. This pricing method may encourage the dispensing of higher cost drug products than may be needed to meet the requirements of prescriptions because the amount of markup by a pharmacy is contingent upon its acquisition cost of the drugs. (See p. 12.)

In some locations, recurring or repetitive-type prescriptions for Indian patients treated outside DIH facilities have not been filled by Indian health pharmacies. Present policy established by the DIH central office permits, but does not require, that this method of furnishing needed medications be used to achieve the benefit of lower cost than obtainable from private pharmacies. (See p. 16.)

RECOMMENDATIONS OR SUGGESTIONS

GAO recommends that action be taken to strengthen controls over drug procurement by requiring officials responsible for administering the Indian health program to

- maximize the use of centralized and competitive buying of drugs by purchasing them through the PHS supply center or VA supply depots.
- establish a program-wide system, and consider adoption of a program-wide drug formulary, to determine which drug products are, or could be, commonly used by field installations and could be purchased at lower prices through the supply depots.
- revise pricing methods in contracts with private pharmacies by requiring that the reimbursement to the pharmacies be based on actual acquisition cost of the drug plus a fixed professional fee; and
- use DIH pharmacies, whenever feasible, to fill recurring or repetitive-type prescriptions.

During the review, GAO discussed its findings with DIH officials who indicated that consideration would be given to the above recommendations.

APPENDIX B

COMPARISON OF DRUG PROCUREMENTS
VA SOLE-SOURCE PROCUREMENT VS DPSC COMPETITIVE PROCUREMENTSSUMMARY

Total Actual VA Amount	\$1,421,459
Total Potential VA Amount Using DPSC Average Unit Price At VA Quantity	<u>887,185</u>
Total Difference in VA Actual Amount and VA Potential Amount	<u>\$534,274</u>
Total Percentage Difference	60%

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 8059

APPENDIX B

COMPARISON OF DRUG PROCUREMENTS VA SOLE SOURCE PROCUREMENT VS DPSC COMPETITIVE PROCUREMENTS

Date of Contract	Procurement Method	Quantity Purchased		Unit Price		Amount of Contract	
		VA	DPSC	VA	DPSC	VA	DPSC
<u>GLYCERYL GUAIACOLATE SYRUP</u> <u>650-064-8765</u>							
1-17-68	Negotiated	40,824		\$.35		\$14,288	
5-29-68	Negotiated	16,224		.35		5,678	
7-29-68	Negotiated	14,256		.35		4,940	
10-25-68	Negotiated	6,312		.35		2,209	
12- 9-68	Negotiated	24,456		.35		8,560	
1-30-69	Negotiated	25,200		.35		8,820	
4- 2-69	Negotiated	45,912		.35		16,069	
6- 3-69	Negotiated	77,712		.35		27,199	
4-10-68	Negotiated ^a		120,304		\$.32		\$54,497
7- 3-68	Negotiated ^a		123,840		.28		34,675
8-15-68	Formal Advertised		174,528		.25		42,759
8-15-68	Option ^b		87,264		.25		21,380
2- 5-69	Formal Advertised		197,568		.22		43,084
4-25-69	Formal Advertised		345,600		.18		60,760
5-21-69	Formal Advertised		175,680		.21		36,014
6- 2-69	Negotiated ^a		376,320		.16		59,241
Total		250,896	1,601,104			\$87,763	\$352,410
Average Unit Price				\$.35	\$.22		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$55,197	
Difference in VA Amount and VA Potential						\$32,566	
Percentage Difference							59%

GLYCERYL GUAIACOLATE SYRUP 6505-079-6269

11-13-67	Negotiated	1,032		\$11.99		\$12,374	
12-11-67	Negotiated	864		11.99		10,359	
2-16-68	Negotiated	1,456		11.99		17,457	
5- 1-68	Negotiated	1,680		11.99		20,143	
7-29-68	Negotiated	760		11.99		9,112	
1-30-69	Negotiated	156		11.99		1,870	
4- 2-69	Negotiated	1,272		11.99		15,251	
2- 6-68	Negotiated ^a		3,000		\$11.14		\$33,420
3-29-68	Negotiated ^a		5,200		10.86		56,446
7- 3-68	Negotiated ^a		7,424		7.33		54,414
7- 3-68	Option ^b		3,712		7.33		26,355
7-16-68	Negotiated ^a		5,132		7.75		39,773
Total		7,220	24,468			\$86,568	\$210,408
Average Unit Price				\$11.99	\$ 8.60		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$62,092	
Difference in VA Amount and VA Potential						24,476	
Percentage Difference							39%

^a Competition solicited - one or more bids received
^b Option exercised under preceding contract

APPENDIX B

COMPARISON OF DRUG PROCUREMENTS
VA SOLE-SOURCE PROCUREMENT VS DPSC COMPETITIVE PROCUREMENTS

Date of Contract	Procurement Method	Quantity Purchased		Unit Price		Amount of Contract	
		VA	DPSC	VA	DPSC	VA	DPSC
<u>TRIAMCINOLONE ACETONIDE</u>							
<u>CREAM, USP</u>							
<u>6505-682-8194</u>							
10-23-68	Negotiated	3,312		\$1.25		\$4,140	
1-23-68	Negotiated ^a		16,780		\$1.04		17,451
1-23-68	Option ^b		10,320		1.04		10,733
6-13-68	Negotiated ^a		49,752		.90		44,237
3- 5-69	Negotiated ^a		58,752		.86		50,527
3-28-69	Option ^b		73,440		.86		63,158
3-28-69	Option ^b		43,968		.86		37,812
8-28-69	Formal Advertised		53,760		.81		43,546
Total		3,312	306,772			\$4,140	\$267,464
Average Unit Price				\$1.25	\$.87		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$ 2,881	
Difference in VA Amount and VA Potential						\$ 1,259	
Percentage Difference							44%

<u>ACETAMINOPHEN TABLETS, NF</u>							
<u>6505-985-7301</u>							
8-29-67	Negotiated	1,656		\$9.31		\$15,417	
11-8-67	Negotiated	1,632		9.31		15,194	
12-11-67	Negotiated	1,440		9.31		13,406	
2-16-68	Negotiated	854		9.31		7,951	
5-24-68	Negotiated	2,160		6.14		13,262	
9-11-68	Negotiated	2,712		6.14		16,652	
10-29-68	Negotiated	2,568		6.14		15,768	
2-13-69	Negotiated	3,000		6.14		18,420	
3-21-69	Negotiated	6,456		6.14		39,640	
6-13-68	Negotiated ^a		3,792		4.45		\$16,874
8-19-68	Negotiated ^a		3,552		4.20		14,918
10-15-68	Negotiated ^a		5,760		3.45		19,872
1- 9-69	Formal Advertised		10,176		3.28		33,377
2-17-69	Option ^b		5,088		3.28		16,689
9- 9-69	Formal Advertised		6,816		2.90		19,766
10-10-69	Negotiated ^a		6,624		2.75		18,216
Total		22,478	41,808			\$155,710	139,712
Average Unit Price				\$6.93	\$3.34		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$75,077	
Difference in VA Amount and VA Potential						\$80,633	
Percentage Difference							107%

^a Competition solicited - one or more bids received^b Option exercised under preceding contract

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 8061

APPENDIX B

COMPARISON OF DRUG PROCUREMENTS VA SOLE-SOURCE PROCUREMENT VS DPSC COMPETITIVE PROCUREMENTS

Date of Contract	Procurement Method	Quantity Purchased		Unit Price		Amount of Contract	
		VA	DPSC	VA	DPSC	VA	DPSC
<u>AMPICILLIN CAPSULES</u> <u>6505-770-8343</u>							
7-14-67	Negotiated	5,400		\$12.48		\$ 67,392	
8-31-67	Negotiated	9,600		12.48		119,808	
10-13-67	Negotiated	11,400		9.97		113,658	
12- 7-67	Negotiated	16,800		9.97		167,496	
5-23-68	Negotiated	17,568		9.77		171,639	
7-23-68	Negotiated	15,168		9.19		139,394	
1- 9-68	Negotiated ^a		4,800		\$ 9.62		\$ 46,176
1- 9-68	Negotiated ^a		9,600		9.45		90,720
3- 6-68	Negotiated ^a		24,000		9.24		221,736
4-23-68	Negotiated ^a		22,752		8.86		201,559
4-23-68	Option ^b		11,376		8.86		100,780
9-25-68	Negotiated ^a		26,112		7.18		187,484
11-14-68	Option ^b		52,224		7.18		374,968
4-23-69	Formal Advertised		31,128		5.95		185,212
7-22-69	Formal Advertised		23,346		5.40		126,068
10-21-69	Formal Advertised		26,784		5.23		140,054
Total		75,936	232,122			\$779,387	\$1,674,757
Average Unit Price				\$10.26	\$ 7.22		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$ 548,258	
Difference in VA Amount and VA Potential						\$ 231,129	
Percentage Difference							42%

^a Competition solicited - one or more bids received

^b Option exercised under preceding contract

APPENDIX B

COMPARISON OF DRUG PROCUREMENTS
VA SOLE-SOURCE PROCUREMENT VS DPSC COMPETITIVE PROCUREMENTS

Date of Contract	Procurement Method	Quantity Purchased		Unit Price		Amount of Contract	
Contract	Method	VA	DPSC	VA	DPSC	VA	DPSC
<u>PSYLLIUM HYDROPHILIC</u>							
<u>MUCILOID WITH DEXTROSE</u>							
<u>6505-050-4567</u>							
9-14-67	Negotiated	2,880		\$1.52		\$4,378	
10-13-67	Negotiated	10,800		1.52		16,416	
12- 8-67	Negotiated	11,520		1.52		17,510	
2-19-68	Negotiated	12,432		1.52		18,896	
5- 9-68	Negotiated	14,640		1.52		22,253	
7-31-68	Negotiated	12,768		1.52		19,407	
9-18-68	Negotiated	18,184		1.52		27,640	
10-29-68	Negotiated	4,560		1.52		6,931	
2-18-69	Negotiated	22,320		1.52		87,905	
11-15-68	Negotiated ^a		71,040		\$.85		\$60,029
2-12-69	Option ^b		106,560		.85		90,043
12- 8-69	Negotiated ^a		35,136		.87		30,709
Total		110,104	212,736			\$221,336	\$180,781
Average Unit Price				\$1.52	\$.85		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						93,588	
Difference in VA Amount and VA Potential						\$ 127,748	
Percentage Difference						136%	

<u>KAOLIN MIXTURE WITH PECTIN</u>							
<u>6505-299-9678</u>							
8-11-67	Negotiated	756		\$5.50		\$4,158	
1-17-68	Negotiated	756		5.50		4,158	
9-24-68	Negotiated	750		5.50		4,125	
12-12-68	Negotiated	750		5.50		4,125	
4- 1-69	Negotiated	1,510		5.30		8,003	
1-19-68	Formal Advertised		22,162		\$2.30		\$50,973
Total		4,522	22,162			\$24,569	\$ 50,973
Average Unit Price				\$5.43	\$2.30		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$10,401	
Difference in VA Amount and VA Potential						\$ 14,168	
Percentage Difference						136%	

^a Competition solicited - one or more bids received^b Option exercised under preceding contract

COMPARISON OF DRUG PROCUREMENTS
VA SOLE-SOURCE PROCUREMENT VS COMPETITIVE PROCUREMENTS APPENDIX B

Date of Contract	Procurement Method	Quantity Purchased		Unit Price		Amount of Contract	
		VA	DPSC	VA	DPSC	VA	DPSC
DIBUCAINE OINTMENT							
6505-299-9535							
10-16-67	Negotiated	12,480		\$.22		\$2,746	
12-11-67	Negotiated	12,000		.22		2,640	
5-22-68	Negotiated	7,956		.22		1,750	
9- 6-68	Negotiated	6,708		.22		1,476	
10-24-68	Negotiated	8,400		.22		1,848	
12- 5-68	Negotiated	6,480		.22		1,426	
3-26-69	Negotiated	21,612		.22		4,755	
2-27-68	Formal Advertised		157,896		.14		\$21,316
3-14-68	Formal Advertised ^c		157,896		.14		21,316
Total		75,636	315,792			\$16,641	\$42,632
Average Unit Price				\$.22	\$.14		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$10,589	
Difference in VA Amount and VA Potential						\$ 6,052	
Percentage Difference						57%	

ISOPROTERENOL HYDROCHLORIDEINHALATION, USP6505-299-9661

9- 1-67	Negotiated	11,232		\$.67		\$7,525	
10-13-67	Negotiated	1,440		.67		965	
12-11-67	Negotiated	12,096		.67		8,104	
5- 8-68	Negotiated	10,656		.67		7,140	
9-24-68	Negotiated	11,376		.67		7,622	
12- 9-68	Negotiated	8,496		.67		5,692	
2-27-69	Negotiated	12,384		.67		8,297	
1- 3-68	Formal Advertised		54,864		\$.45		\$24,415
1- 3-68	Option ^b		27,432		.45		12,207
4-16-68	Negotiated ^a		46,224		.41		18,859
12-18-69	Negotiated ^a		28,944		.41		11,867
Total		67,680	157,464			\$45,345	\$67,348
Average Unit Price				\$.67	\$.43		
Potential VA Amount Using DPSC Average Unit Price at VA Quantity						\$29,102	
Difference in VA Amount and VA Potential						\$16,243	
Percentage Difference						56%	

^a Competition solicited - one or more bids received^b Option exercised under preceding contract^c Set aside for small business

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

MONDAY, FEBRUARY 1, 1971

U.S. SENATE,
SUBCOMMITTEE ON MONOPOLY OF THE
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C.

The subcommittee met, pursuant to recess, at 10:05 a.m., in room 1318, New Senate Office Building, Senator Gaylord Nelson (chairman of the subcommittee) presiding.

Present: Senator Nelson.

Also present: Benjamin Gordon, Staff Economist; Elaine C. Dye, Clerical Assistant; and Keith A. Jones, Minority Counsel.

Senator NELSON. Our first witness this morning is Governor Lane Dwinell, assistant administrator for administration, Agency for International Development, Department of State.

Governor, the committee is pleased to have you back again. Your statement will be printed in full in the record. You may present it however you desire. Would you please identify your associates for the reporter, so we will have the record straight.

STATEMENT OF GOV. LANE DWINELL, ASSISTANT ADMINISTRATOR FOR ADMINISTRATION, AGENCY FOR INTERNATIONAL DEVELOPMENT, DEPARTMENT OF STATE; ACCOMPANIED BY LESLIE A. GRANT, DEPUTY GENERAL COUNSEL, AID; SEYMOUR BARONDES, CHIEF, COMMODITY ELIGIBILITY AND PRICE BRANCH, OFFICE OF THE CONTROLLER, AID; NATHAN SALANT, ACTING CHIEF, INDUSTRIAL RESOURCES DIVISION, OFFICE OF PROCUREMENT, AID; AND EDWARD E. KUNZE, SPECIAL ASSISTANT FOR SMALL BUSINESS, OFFICE OF PROCUREMENT, AID

Mr. DWINELL. Thank you, Mr. Chairman, for the opportunity to appear again before this committee. I would, as you suggest, present to the committee the several colleagues who are here who may help me in speaking to the program and answering any questions which the committee may have.

On my right is Mr. Nathan Salant, who is the resources policy adviser in the Office of Procurement.

On my left is Mr. Edward E. Kunze, Special Assistant for Small Business, Office of Procurement, and on his left is Mr. Seymour

Barondes who is Chief of the Commodity Eligibility and Price Branch in the Office of the Controller.

I was accompanied also by—I think he will be here—Mr. Leslie Grant, Deputy General Counsel of AID.

In accordance with the request of the committee we have submitted a prepared statement which I am prepared to present to the committee.

Senator NELSON. Go ahead.

Mr. DWINELL (continuing). If that is your desire, Mr. Chairman.

It is our hope that the joint exploration of the new practices adopted by our Agency will make a significant contribution to your continuing review of the pharmaceutical procurement policies of the various agencies of the U.S. Government. We found our appearance before you last August helpful in reevaluation of AID policies and in the formulation of the new eligibility standards for pharmaceuticals that I will discuss today.

First, may I summarize briefly my previous presentation of the mechanisms by which we finance the procurement of pharmaceuticals. Most of the pharmaceutical transactions which AID finances are between private buyers in the aid-recipient countries and private sellers in the U.S. under AID loans made to the developing nations of the free world. These nations repay the loans made to them in dollars under special concessional terms which include repayment of principal over a period of up to 40 years and with interest rates of $3\frac{1}{2}$ percent per annum. The private buyers however must purchase their foreign exchange needs with local currency at the prevailing official rate of exchange. Should they have to borrow this local currency, it would be at the interest rates in effect at the time—possibly 25 percent per annum or more.

To emphasize, the private buyer does not benefit from any special concession insofar as loan terms or interest rates are concerned—he pays full value in local currency for all pharmaceuticals that he buys.

A relatively small proportion of our expenditures for pharmaceuticals—currently about 15 to 20 percent—represent purchases made directly by AID or by other U.S. Government agencies procuring on behalf of AID. These purchases are subject to compliance with the Federal procurement regulations.

AID does not tell the borrower countries or the private buyers in the countries what they should buy. The Agency maintains a schedule which lists all the items which it is prepared to finance. From this list, the importing countries are free to choose what they wish to procure with AID financing. Excluded from this list are such commodities as luxuries of all kinds, items for which the United States is a consistent net importer, dietetic foods, and dangerous or ineffective drugs.

The Foreign Assistance Act establishes a limit on the prices which AID will finance for commodities. Specifically, the act provides in section 604(b) that:

No funds made available under this Act shall be used for the purchase in bulk of any commodities at prices higher than the market prices prevailing in the United States at the time of purchase, adjusted for differences in the cost of transportation to destination, quality, and terms of payment.

Senator NELSON. May I ask a question at this point? How do you determine the market price?

Mr. DWINELL. The market price is determined by a review made by the Commodity Eligibility and Price Branch headed by Mr. Barondes who is present. In the case of pharmaceuticals, as was indicated in our previous appearance before you, Mr. Chairman, we are guided either by published prices or by prices which are submitted to us by the exporter. Intensive review is made. Documentation is required to show what comparable sales may have been. Previous to the new rules which I am about to explain to you with regard to pharmaceuticals themselves, it was determined that the prevailing price would be the price at which at least 51 percent or more of comparable sales were made.

Senator NELSON. What does that mean? Fifty-one percent or more of what?

Mr. DWINELL. Of comparable sales of a given product.

Senator NELSON. The market price would be 51 percent of—

Mr. DWINELL. No. If there are varying prices, we would require that the prevailing price be the price at which at least 51 percent of sales of that commodity had been sold.

Senator NELSON. How do you find that out?

Mr. DWINELL. By investigation, by various means.

Senator NELSON. I am still confused about what the market price is. Do you use published list prices. What is the market price?

Mr. DWINELL. Where there are published prices, yes, Mr. Chairman. Where not, it is required that the exporting company submit price data.

Mr. Barondes, who is in immediate charge of that function, can amplify this point if you would desire.

Senator NELSON. Is this all bulk prices, not finished products?

Mr. DWINELL. Yes, Mr. Chairman. It is all bulk pharmaceuticals. We do not finance any longer—and have not for several years—under our commodity import program—transactions involving pharmaceuticals in finished dosage form.

Senator NELSON. That is what I am puzzled about. Then how do you find out what the market price of the bulk product is?

Mr. DWINELL. Based on—

Senator NELSON. Who is buying it so there is a market price? One drug company buying it from another?

Mr. DWINELL. Quite frequently that is the case. A subsidiary in a lesser developed country which has a loan for commodity imports from AID, may get an export license from the government of that country to import pharmaceuticals from the parent company in the United States.

Senator NELSON. But that does not determine the market price that you are relying upon here.

Mr. DWINELL. Well, Mr. Chairman, it determines the market price in that the exporting company sells the product not only under AID financed sales but it sells to other purchasers around the world. There is a pattern of pricing for those exports which can be determined.

Senator NELSON. Do you check the bulk price of these compounds as sold by other foreign countries in the world market? In

other words, if the compound is being purchased here through the AID program, do you check to find out what the price of that compound is, if it is made in other countries such as France and Germany, Italy, and so forth, and compare their bulk prices with the bulk price in this country?

Mr. DWINELL. No, Mr. Chairman. We are concerned only with the prevailing price for exports from the United States. But might I say, Mr. Chairman, that we are now talking about our old price rules and I am about to present some new rules which have considerably tightened up on these transactions.

Senator NELSON. You were reading from section 604(b) of the act, and the act uses the language "market prices prevailing in the United States." We are just trying to find out how you determine what the market price of a bulk commodity is.

Mr. DWINELL. Mr. Chairman, I attempted to explain that we obtain information from various sources on the prices at which that commodity is sold.

Senator NELSON. In other words, if you are buying a bulk compound do you require them to show you their books on the prices that they have charged for this product to any buyer, any place?

Mr. DWINELL. Yes, we do.

Senator NELSON. Do you ever take a look at a situation in which a supplier of compounds also produces a finished product and then bids to the Department of Defense or New York City at a price dramatically lower than what they charge in the retail market? Do you understand what I am talking about? They make a drug that is marketed under their brand name in the retail market. Then they bid to the Defense Department or to a big city buyer or hospital which constitute a relatively competitive marketplace. This is unlike the retail market where their brand name may dominate because that is the name that is widely prescribed and best known. However, when the firm offers competitive bids to the Department of Defense or Veterans' Administration, New York City or a big general hospital, its price will end up one-half—perhaps one-fifteenth of what it is charging in the retail market.

Do you ever examine that structure to find out—

Mr. DWINELL. Mr. Chairman, you are talking now about domestic sales?

Senator NELSON. Right.

Mr. DWINELL. We are financing export business and the sales prices which we review and with which we are concerned are based on the best information we can get as to prevailing export prices.

Senator NELSON. If there is one producer of a compound and just one price set by the one producer, you do not go beyond that. You do not look to see what that same compound is being sold for in the European market by another producer?

Mr. DWINELL. Under our new rules, Mr. Chairman, which I am to explain to you later on in my statement, we look at domestic produced pharmaceuticals which may be pharmacologically equivalent, generically equivalent, if you will, and we also under the revised rules take into account the world price.

Senator NELSON. Under the new rules you take into account the world price?

Mr. DWINELL. We do, sir.

Senator NELSON. Go ahead.

Mr. DWINELL. As was indicated at the earlier hearing, we have had pricing problems under our general price rules with the pharmaceutical industry. Relatively more claims have been issued for overcharges in pharmaceutical transactions as a result of our postaudit review than for any other commodity we finance.

Mr. GORDON. Why is that? Why the drug industry? Why do you have more problems with the drug industry than with any other industry?

Mr. DWINELL. Because it is a unique industry, unique in that it has—pricing policies quite different from those of many other industries.

Also, I might say that of all the pharmaceuticals that we finance, a large percentage is rather standard, highly competitive pharmaceuticals where we have very little problem with pricing. We have had problems, as was brought out in the previous hearing, with regard to certain patented items. It is to try to control the pricing in that area that we have instituted these new rules which I am about to explain to the committee.

Relatively more claims, as I have indicated, have been issued for overcharges than for any other commodity we finance. Now, this review is a continuous process and more claims on past transactions will be issued if warranted. Details on our claims and refunds received were submitted to the committee previously.

As I have said, pharmaceuticals are products of an industry which is unique in its character and pricing practices. We have, therefore, established for this industry specific pricing rules to govern the eligibility of pharmaceuticals for AID financing. These were published in the Federal Register of December 31, 1970. They are contained in an appendix to this statement.

(The appendix referred to follows:)

APPENDIX—DEPARTMENT OF STATE, AGENCY FOR INTERNATIONAL DEVELOPMENT

NOTICE—DETERMINATION OF COMMODITY ELIGIBILITY FOR BULK PHARMACEUTICAL PRODUCTS

Pursuant to § 604(f) of the Foreign Assistance Act of 1961, as amended by § 301(a) of the Foreign Assistance Act of 1968, AID has stated in § 201.11(k) of Regulation 1, 22 CFR § 201.11(k), that each commodity "shall be approved in writing by AID for each sale transaction as eligible for AID financing." The statutory language in § 604(f) requires AID to approve each commodity "as eligible and suitable for financing."

It is current AID policy not to finance pharmaceutical products in finished dosage form. The Agency has, however, been financing most bulk (i.e. not in finished dosage form) pharmaceutical products. By means of this announcement, AID advises parties who may be interested in participating in sale transactions of bulk pharmaceutical products under AID financing that henceforth AID will apply the following criteria in determining whether, under regulatory and statutory standards, this Agency should find a product described on the Commodity Approval Application, AID Form 11, to be "eligible and suitable" for AID financing:

(1) AID will not finance from an authorized source country a bulk pharmaceutical product at an FAS price which exceeds by more than 10% the FAS price at which the product, by whatever description, is generally available from any other free world country. With respect to a product patented in the U.S., AID will compare FAS prices between the U.S. product and the

identical product available in any free world country, provided such non-U.S. price was established by the patent holder or his licensee.

(2) AID will not finance from an authorized source country a bulk pharmaceutical product at an FAS price which exceeds the lowest FAS price at which the same product, by whatever description, is available from the same source country.

(3) AID will not finance from an authorized source country a bulk pharmaceutical product at a price which exceeds the price at which another lower priced product can be obtained from any free-world source, if there is evidence that the lower-priced product, although of different generic description, is, for the purpose intended, pharmacologically a substantial equivalent to the higher priced product for which AID approval is solicited. Items which AID has determined to be subject to this rule will be indicated in the implementing document issued by AID which authorizes the use of AID funds for the procurement of pharmaceutical products.

(4) AID will not finance a bulk pharmaceutical product at a price which exceeds the lowest price charged by the supplier in any export sale of the item to any country, whether or not such sale has taken place under AID financing. A supplier under this rule may exclude in his calculation of his lowest price, the lowest priced 5% of his sales volume within the most nearly relevant sales period. The "lowest price" shall take into account all sales by the supplier of the product in export, without regard to any trade mark or other differentiation between items which are pharmacologically identical.

(5) With respect to any bulk pharmaceutical product for which AID does grant commodity approval under the foregoing special rules, a supplier shall continue to execute AID Form 282 which binds the supplier to the price tests set forth in Subpart G of AID Regulation 1. Upon post audit, a supplier of any bulk pharmaceutical product shall be held to the price tests set forth in that subpart of the regulation.

AID expressly reserves its right to determine any product unsuitable for AID financing within the meaning of § 604(f) whether or not the price for the product complies with the foregoing special rules.

AID will endeavor to provide a supplier, upon request, preliminary advice as to whether the price, at which the supplier proposes to sell a product in export, will be eligible for approval under the foregoing special rules prior to his entering into a contract to sell. AID will not supply this type of advice unless the supplier provides with his request to AID an indication that the solicitation may reasonably result in an agreement to sell.

AID intends to coordinate its eligibility standards for bulk pharmaceutical products with the Food and Drug Administration and shall attempt to amend on a continuing basis its policy and regulations to reflect new evaluations concerning the safety and efficacy of pharmaceutical products which it finances. AID will continue to supply its Missions and aid-recipient governments with such various information as may become available to AID concerning the safety and efficacy of end-use products manufactured from ingredients eligible for AID financing.

Effective Date: This Notice shall enter into effect upon publication in the "Federal Register."

MAURICE J. WILLIAMS,
Deputy Administrator.

Published December 31, 1970.

Mr. DWINELL. After indicating that it is AID policy not to finance pharmaceutical products in finished dosage form to the private sector, the published notice provides new pricing standards for bulk pharmaceuticals that are substantially as follows:

Rule No. 1 provides that AID will not finance a bulk pharmaceutical product at a price which exceeds by more than 10 percent the price at which the product is generally available from free world countries. In applying this test, we exclude prices of pharmaceuticals sold in violation of U.S. patents.

Senator NELSON. Now, the purpose of this new practice is to avoid that situation in which foreign buyers were purchasing—we have

some examples at 8 and 10 and 12,000 percent higher than the world market price, is that correct?

Mr. DWINELL. The whole thrust of these new regulations is to eliminate those glaring differentials which were brought out at the previous hearing.

Mr. GORDON. May I ask a question here with respect to patents. This paragraph does not seem to distinguish between product patents and process patents. If a U.S. firm has a process patent, perhaps of little importance, will this entitle it to the special treatment you just mentioned concerning prices of pharmaceuticals sold in violation of U.S. patents?

Mr. DWINELL. Yes; we are directed by statutes specifically in that respect.

Mr. GORDON. Well, suppose a drug is developed overseas and is licensed on an exclusive basis to a firm in this country. Examples are Orinase or Lasix. How does that apply in such a case?

Mr. DWINELL. Since that is a legal matter, Mr. Gordon, I wonder if I could ask Mr. Grant to address himself to that question.

Mr. GRANT. Well, Mr. Gordon, what we are doing here is giving effect to the spirit of Section 606(c) of the Foreign Assistance Act. Section 606(c) prohibits AID from expending funds with respect to pharmaceutical products abroad which are produced in violation of a U.S. patent. The section provides that we may not expend funds for any pharmaceutical product manufactured outside the United States if the manufacture of such a product in the United States would involve the use or be covered by an unexpired patent, unless the manufacture is expressly authorized by the owner of the patent.

As you know, there apparently has been some great difficulty with respect to patented U.S. drugs being produced abroad in violation of the patent. Now, Section 606(c) is a provision which the Agency did not ask for. The Congress passed it and it is part of the mandate to us. The AID policy rule which Governor Dwinell just read to you with respect to excluding sales of a pharmaceutical sold abroad in violation of the U.S. patent from the group of sales which AID takes into account in measuring the maximum price AID will finance is simply a way of helping to carry out the purpose of that statute.

Mr. GORDON. Let me give you a specific example. Suppose you have a drug like chlorpromazine sold under the trade name of Thorazine, of which incidentally, the patent has already expired. Before the patent expired, the price to the Canadian Government by the developer was a little over \$2. The developer who is in France licensed an American company on an exclusive basis and the American company charged about \$32 to the American Government.

Now, in considering the prices, would you consider only the American price of \$32 or would you consider the price overseas of somewhere around \$2 even though the patent holder was a foreigner?

Mr. GRANT. Well, are you postulating a situation, Mr. Gordon, where the sale abroad is in violation of a U.S. patent?

Mr. GORDON. No.

Mr. GRANT. If you are not, then we are not talking about that situation. The statute does not talk about it and our price rule does not talk about it.

Mr. GORDON. Well, which price would you count, the \$2 price or the \$32 price in the United States?

Mr. GRANT. What we are now concerned with, as I say, is a situation in which as far as this rule is concerned, we say we will not finance a bulk pharmaceutical product from the United States at a price more than 10 percent higher than the price at which it is generally available in free world countries. And in calculating what that price is—the price at which it is generally available from free world countries—we do not count those sales abroad which would violate a U.S. patent.

If they would not violate a U.S. patent they become part of the basket of prices by which we would determine the price at which it is generally available in free world countries.

Mr. GORDON. Thank you.

Mr. DWINELL. To continue, Mr. Chairman, as an example of how this rule operates, the drug tetracycline, certified by FDA, is available from many sources, both U.S. and non-U.S. The world market price for this item ranges between \$25 and \$35 a kilogram (about 2.2 pounds). Most applications that we have received for the proposed sales of this drug have been at a price of \$100 a kilogram or more. All such applications are rejected under this rule.

Rule No. 2 states that AID will not finance a bulk pharmaceutical product at a price which exceeds the lowest price at which the same product, by whatever description, is available from the same source country.

This standard establishes clearly that we do not pay premium prices for a brand name drug if the same drug is available under its generic description at a lower price. It is particularly applicable to drugs in the "public domain" such as vitamins, penicillins and certain antihistamines all of which are available from many sources if bought by generic description. As a specific example, a leading antihistamine is sold under its brand name at \$100 per kilogram. The same drug is available at about \$30 to \$35 per kilogram if bought by generic description. Under this rule, AID finances the drug at the lower price only.

Under Rule No. 3 AID will not finance a bulk pharmaceutical product at a price which exceeds the price of another product if there is evidence that the lower-priced product, although of different generic description, is, for the purpose intended, pharmacologically a substantial equivalent to the higher-priced product.

Under the criteria of standard (3) we have declared at the present time 14 drugs ineligible for financing. Two additional drugs have been declared unsuitable for financing within the meaning of Section 604(f) of the Foreign Assistance Act because there are equally effective lower cost drugs available for the purposes intended. These 16 drugs are listed in my statement.

Senator NELSON. You say they are ineligible for further financing. When did they go on the ineligible list?

Mr. DWINELL. As of December 31, 1970.

Senator NELSON. And is that because of the price?

Mr. DWINELL. Yes, Mr. Chairman. As I point out later, it is for price reasons only, because we certainly have no findings as to any inadequacy of those drugs.

Senator NELSON. In other words, there are equivalent drugs that are cheaper?

Mr. DWINELL. This means that AID would finance these drugs if they were offered for sale at the lower prices prevailing for their generic pharmacological equivalents. We just do not anticipate that this will be done.

Senator NELSON. You mean they would be eligible for consideration if they reduced their price to the competitive price of the equivalent drug. Is that what you are saying?

Mr. DWINELL. That is what I am saying.

Now, I will read that list, Mr. Chairman, which will demonstrate the fact that I am not an expert in this field.

Senator NELSON. I have read the list.

(The list of drugs follows:)

<i>Generic name</i>	<i>Brand name</i>
Chlortetracycline.....	Aureomycin
Doxycycline.....	Vibramycin
Methacycline HCL.....	Rondomycin
Demethylchlortetracycline.....	Ledermycin, Declomycin
Rolitetraeycline.....	Bristacin, Syntetrin, Valacycline
Oxytetracycline.....	Terramycin
Chlorcyclizine.....	Histantine
Cyproheptadine HCL.....	Periactin
Dexchlorpheniramine Maleate.....	Polaramine
Triamcinolone.....	Aristocort, Ledercort, Kenacort
Dexamethasone.....	Decadron
Paramethasone.....	Haldron
Betamethasone.....	Celestone, Valisone
Methylprednisolone.....	Medaprin, Medrol
Propoxyphene.....	Darvon
Ethoheptazine.....	Zactane, Zactirin, Equagesi

Mr. DWINELL. The first six drugs that I listed are tetracyclines for use in treating infectious diseases. The next three are antihistamines for use in treating allergic conditions. The following five are corticosteroids important in the treatment of rheumatic diseases. The last two items are analgesics—pain killers.

The merits of most of the listed drugs were discussed at earlier hearings of the committee. The testimony at the hearings and the findings of the NAS-NRC, along with information obtained from such expert sources as the Medical Letter, offer substantial expert opinion that lower-cost drugs which are equally effective, are readily available for the indications ascribed to the 16 ineligible drugs.

I should like to offer some examples:

Experts say that tetracycline HCL is the drug of choice among all the tetracyclines. Although tetracycline HCL is available here and abroad at about \$30 to \$35 a kilogram, we have been asked to finance various other forms of tetracyclines at prices ranging from \$100 to \$2,250 a kilogram.

Senator NELSON. Did you previously buy tetracycline HCL at the \$2,250 price per kilogram?

Mr. DWINELL. Other forms.

Senator NELSON. Or other forms?

Mr. DWINELL. Yes. At higher prices.

Senator NELSON. As I understand this—if you were to purchase tetracycline HCL, it could not then, under your new rule, exceed by more than 10 percent of the price at which it is available in the foreign marketplace, is that correct?

Mr. DWINELL. That would be one criterion of the four.

The drug of choice for corticosteroids is prednisone and here, too, the difference in prices are equally striking. Prednisone sells for \$550 to \$600 a kilogram. We have received and denied requests to finance triamcinolone, one of the drugs in this category, at prices over \$30,000 a kilogram and betamethasone, another drug in this category, at a price of \$30,980 a kilogram.

I would indicate and emphasize, Mr. Chairman, that we have received but we have denied requests to finance at those prices.

The same price situation prevails in the antihistamines. An effective drug in this category is chlorpheniramine maleate, which is available at about \$30 to \$35 a kilogram. One of the variations of this drug is dexchlorpheniramine maleate, which sells for \$650 per kilogram and which according to expert opinion is not superior to the lower priced drug.

In all these cases, we finance only the lower priced drugs.

Under new rule No. 4 AID will not finance a bulk pharmaceutical product at a price which exceeds the lowest price charged by the supplier in any export sales. The lowest priced 5 percent of his sales volume may be excluded by the supplier in the calculation of his price under this rule.

That is for the reason that certain isolated distressed or special situation sales could be excluded if they did not exceed the 5 percent.

Now, under our previous pricing standards, we would not finance pharmaceuticals whose prices exceeded the prices generally charged. Under this test, and this is a point that I referred to earlier, under this test the eligible price was generally interpreted to be the price that would cover at least 51 percent by volume of the sales of the item. This test provides adequate protection for most commodities whose price variations fall within a relatively narrow range.

Pharmaceuticals, as we have indicated, are different. We found that prices for many pharmaceutical items differed from one importing country to another by as much as 10 to 1. We could ascribe the wide difference in price to a number of factors such as patent restrictions, supplier-importer affiliations, and differing competitive conditions from one country to another.

A striking example is the price of trihexyphenidyl hydrochloride which ranged from about \$303 to \$1,800 per kilogram. Under rule No. 4, the price of this item could not exceed the lower of the two prices.

The new eligibility standards, which became effective on December 31, 1970, are particularly significant for two reasons:

(1) They provide a new and more stringent eligibility test for pharmaceuticals.

(2) They create a practicable procedure for applying to pharmaceuticals the authority for product prequalification contained in Section 604(f) of the Foreign Assistance Act of 1968. In other words, Mr. Chairman, we can now apply our price tests before rather than after delivery.

Formulation of the new standards with their more stringent criteria enables us to continue to finance pharmaceuticals with some assurance that the interests of all parties in procuring essential and suitable items at reasonable costs are safeguarded. With this assurance, we are continuing to finance pharmaceuticals—products of American industry that are considered vital to health and population control programs supported by AID.

I wish to make it clear that AID does not find fault with any of the drugs we discuss today except for their prices. We ourselves do not evaluate the relative efficacy of drugs or the cost-benefit ratio of one drug compared to another since we have no special expertise in this area. Rather we rely on the advice and guidance of recognized experts.

It would be helpful to us if there were official cost-benefit studies of drugs which we could consult. In the absence of such studies, we must rely on the best published expert information available from semiofficial or private sources. We will continue to make decisions as to the ineligibility of specific drugs whenever experts indicate excessively high prices for drugs for which equally satisfactory lower cost substitutes are available.

The Agency also has under review a relatively new problem in the pharmaceutical area—the status of drugs declared “possibly effective” by the FDA as a result of NAS-NRC findings. These are drugs for which there is little evidence that they are effective for any of their claimed indications. Drugs in this category have not been taken off the U.S. market. We note, however, that the Surgeon General has announced a policy for HEW that no Federal funds be expended for purchasing drug products classified “possibly effective.” By memorandum of December 11, 1970, all department agencies of the HEW were so notified.

Our Agency now is reviewing the action that it should take to complement actions of other U.S. Government agencies, such as HEW, to bar the financing of any bulk ingredient which is virtually synonymous with a dosage brand designated as “possibly effective” by the NAS-NRC.

The work we have done on pricing standards for pharmaceuticals since the hearings of last August provides a foundation for future activities that may encourage increased participation in our programs by the small business community. I would like to be a little more specific on this point. All 16 drugs which have been referred to and which have been declared ineligible under our new price rules are the exclusive products of large companies. The lower priced drugs of choice that are logical replacements are generally made by small business firms. These small business firms now have increased prospects that their products will be considered for purchase by importers.

As a second example, we already have evidence that at least one large company finds it unattractive to sell some of its products at

generic prices to meet our new limitations. These companies may withdraw certain brand items from AID programs and thereby open the door to small business firms.

We in AID would be pleased to have greater participation by American small business in our programs. We have assisted and will continue to assist our small business firms to share in AID financed export opportunities within the limits of our authority and to the extent consistent with our statutory obligations and basic objectives of the foreign aid program.

We recognize, for example, that most small business firms do not have representation throughout the world. They need an independent and inexpensive means of learning which foreign importers are buying the products they are interested in selling. To fill this need, we publish the details of proposed AID-financed purchases in our release called AID financed export opportunities. These are available without charge to American small business.

Also available free are our procurement information bulletins which provide general information on programs in specific countries together with the names and addresses of importers, by categories of commodities imported. Both releases are useful tools to small business firms interested in exports.

A second way in which we help small business firms is by making information on their products available to prospective purchasers. We maintain in all our missions in the field commercial libraries that are widely consulted by importers. U.S. small business firms are encouraged and urged to make their products known to importers by sending to these libraries or directly to named importers copies of their brochures, catalogs, descriptive literature, and price lists.

Still another area of aid to small business covers such activities as counseling and consultations on a person-to-person basis, work shops, appearances before trade associations and businessmen's forums, resolutions of specific problems that may be encountered and both general and specific guidance on trading under the foreign aid program.

Since the role of AID is primarily that of a financing agency, our emphasis is logically directed toward assuring that U.S. small business is informed of sales opportunities that arise out of our programs. However, we are also concerned with obstacles to small business participation in our programs and try to remove these obstacles when feasible.

I think our new price standards will serve not only to promote better procurement but will also aid those small pharmaceutical firms that seriously wish to participate as suppliers in AID programs.

To be successful, such firms must promote their products actively, perhaps even to the extent of embarking on joint enterprises with pharmaceutical laboratories in lower income countries. We are ready to work with small firms that demonstrate this kind of interest and to help resolve any problems that are generated by unnecessary or unwarranted AID requirements or regulations.

Mr. Chairman, this concludes my prepared statement. If you have any further questions on the pricing of pharmaceuticals, my associates and I will endeavor to answer them.

Mr. JONES. Governor, do you have any idea what dollar volume

would have been effected if your guidelines had been in effect throughout fiscal year 1970?

Mr. DWINELL. Well, if you look at it on the basis of AID dollars given for AID financing, there would be no effect because if these pharmaceuticals had not been procured, the borrowing governments would have used the funds, issued export licenses, for other purposes.

If you are asking what is the difference between the old prices and the new, I am not sure whether or not we have made any estimates on that. It would be relatively small because the volume in these items is quite small.

Mr. BARONDES. It is almost impossible to estimate. We do know that 16 drugs which have been declared ineligible comprised approximately a million dollars a year in our procurement program. If these rules had been in effect earlier it is doubtful whether any of these drugs would have been financed. We probably would not have spent the million dollars on the 16 drugs but we would have spent it on cheaper drugs, or spent it on iron and steel or any other product, tractors or whatnot.

We do know that at least 50 percent of our procurement has been in what you might call public domain items, items which are generally available, which we have financed very often at world market prices or even below world prices.

Then you have that other group of drugs which are the patented drugs where we anticipate very substantial cuts on specific drugs. Many of the companies may withdraw these drugs from the AID-financed market. So it is hard to say exactly what we would save. Obviously we would save something.

Mr. JONES. So you have roughly a million dollars' worth of financing with respect to these 16 drugs?

Mr. BARONDES. That is right.

Mr. JONES. Would you have any idea what percentage difference there would be between the prices of these drugs and the drugs which might have been alternatively purchased?

Mr. BARONDES. Well, in some cases, it may be only a few percent. As you have seen from the testimony, in other cases it is several thousand percent. As I said, I do not know what they would buy, what the importing countries would buy if the suppliers would not reduce their prices on these 16 to the eligible prices. I would guess, frankly, that these drugs are just going to be out of the program.

Mr. JONES. So it is not inconceivable that this new program could free perhaps half a million dollars for additional drug purchases. In other words, you could be supplying more drugs at lower cost to the countries which participate in these AID programs.

Mr. BARONDES. I would not want to give a precise figure but obviously the purpose of this whole approach is to save money. So I presume there will be savings.

Senator NELSON. On page 9 you state:

We do not evaluate the relative efficacy of drugs or the cost-benefit ratio of one drug compared to another since we have no special expertise in this area.

Dr. Edwards said that:

We at FDA have a responsibility to do what we can to assure that the federal purchasers are fully informed about the products they buy.

That was his testimony at page 9022 of the transcript. Then he also said:

I think that very frankly we are the only reliable source which the practicing physician should be able to look to to obtain some of this relative efficacy type information.

In your program of purchasing drugs why don't you consult with FDA for advice?

Mr. DWINELL. We do, Mr. Chairman. I think the thrust of what we were saying on page 9 is that we rely on all of the best evidence that we can get, from FDA, from the Medical Letter, from other sources.

Senator NELSON. Is that a new policy?

Mr. DWINELL. No, we always have.

Senator NELSON. That puzzles me because if it were your old policy, how did you end up buying a long list of drugs for which there was an equivalent drug just as effective?

Mr. DWINELL. Well, may I say—

Senator NELSON. And much cheaper.

Mr. DWINELL. We were not concerned at that time with the relation to efficacy. The expert advice that I am referring to was as to efficacy, not as to price, because following the general guidelines of the Foreign Assistance Act which directs our Agency to follow as closely as possible the normal standard practices of trade, it had been our practice to finance pharmaceuticals, as I have already pointed out, at what were determined to be prevailing prices, even if those prices seemed to be excessively high prices.

We took that to be the general policy and we are directed to follow—to encourage normal business trade practice as a financing agency.

Mr. BARONDES. I think even to this day I have yet to see a study by the FDA which speaks of the relative efficacy of the drugs. For example, for expert information on the relative efficacy of triamcinolone and prednisone, we have to rely on the Medical Letter. We have discussed relative efficacy in terms of price. As to the statement of the FDA that they will—they should keep us fully informed, I am not certain now whether they are talking to the subject of efficacy and safety or whether they are also talking to the question of relative efficacy in terms of one drug as against the other and its relationship to the price.

Senator NELSON. But you did decide that 14 drugs would not be purchased because, as I understand it, there were equivalent tetracyclines, for example, in six cases, at a much lower price. Is that the reason?

Mr. DWINELL. That is correct, Mr. Chairman. And this is a special rule, as has been indicated, that has been put in for the financing of pharmaceuticals.

Senator NELSON. How did you happen to select this grouping of drugs?

Mr. DWINELL. As I understand it, those are drugs which we had financed before or been requested to finance for which we have determined that there are pharmacological equivalents by generic description at lower prices. This does not mean that this is an

all-inclusive list as far as any future action by our Agency is concerned. These were simply those that we had been requested to finance or had financed in the past.

Senator NELSON. So that I will understand fully what the policy is respecting this aspect of your authorizing or making AID funds available for purchases, will it be the practice to check for whatever available scientific information there is from the FDA or the Medical Letter or other sources respecting the relative efficacy of two or more drugs sold for a specific therapeutic purpose and that if the price of one of them or two of them is excessive, you simply will list them along with these other drugs that you have listed here?

Mr. DWINELL. That is correct, Mr. Chairman. And the thrust of our point on page 9 was certainly no reflection on the FDA or any other agency. We were simply pointing out that in pursuit of our objective which you have just mentioned, we want to have all the best information that is available and that we have had to rely on semiprivate sources.

Senator NELSON. Who furnishes you the list of drugs that are to be funded? The foreign government itself?

Mr. DWINELL. I would ask Mr. Salant.

Mr. SALANT. We do not require the borrowing country to submit a list of the specific drugs to be imported under a commercial import program. We have a list by schedule B numbers of commodities that are eligible for financing if desired by the cooperating country. We exclude from this list those pharmaceuticals that have been determined to be ineligible for one or more reasons, either because they were withdrawn from the market by FDA or because under these present rules they are determined to be excessively high in price, or because they happen to be fixed combination drugs or for some other reason which has been determined to be a factor of eligibility.

But within the broad range of pharmaceuticals that are eligible, the importing country and their importers, may select any drugs without coming to us for specific approval.

I am talking now of the commercial import program, sir.

Senator NELSON. So this is not a program in which AID money is involved?

Mr. SALANT. AID money is involved to the extent that it provides the foreign exchange used to purchase the drugs. The importers put up the local currency equivalent for that foreign exchange.

There are two programs, Mr. Chairman, one in which we are very much concerned with the specific drugs to be financed. This is in our technical assistance projects and in our direct aid for health program activities. But in addition there is the program in which we finance imports for resale and it is in that latter category where we do not designate the specific pharmaceuticals that may or may not be purchased.

Senator NELSON. But you still use AID money to pay the local manufacturer?

Mr. SALANT. We use AID money to finance the export sale.

Senator NELSON. Does it become a loan?

Mr. SALANT. It is a loan to the country.

Senator NELSON. But this is for the commercial market in that foreign country?

Mr. SALANT. That is correct.

Senator NELSON. So in that case, if they are ordering some very expensive drug, it does not come under the rules we are talking about?

Mr. SALANT. It does come under these rules at the present time. These rules definitely apply in all such instances.

Senator NELSON. As I recall, about 80 percent of the AID financed drug sales in foreign countries are sales really from American manufacturers to their own subsidiaries in the foreign country. Is that not correct?

Mr. SALANT. I do not recall the exact figures. I think that is approximately correct. About that amount would represent sales from parent to affiliates or to subsidiaries.

Senator NELSON. Just as a policy matter, what is the need for the Federal Government through its AID program to finance these exports from an American manufacturer to its own wholly owned foreign subsidiary? If a firm has a subsidiary in a foreign country, won't it supply whatever drugs they want or they need?

Mr. SALANT. No. Not necessarily. I think perhaps we had better view this as two independent companies that may have some relationship but the company abroad is subject to the rules of the country in which it operates. It can obtain foreign exchange only in accordance with the rules that exist in that particular country. It must import as any private firm in that country imports in the sense that it may need to get an import license. It would have to buy foreign exchange. It would have to adhere to all the laws and regulations of the country in which it is located.

Furthermore, at the present time we rarely have a situation of a wholly owned subsidiary operating abroad. In almost all instances it is a joint venture operation with the U.S. firm holding up to 50 percent of the control in the company, but with most countries requiring that at least 51 percent of the enterprise be owned by nationals of that country.

Thus, regardless of affiliation, we actually have two separate companies dealing with each other under contractual arrangements which tie them together from the standpoint of purchasing and possibly from the standpoint of the product that is produced.

Mr. GORDON. Mr. Salant, may I interrupt you for a second.

Mr. SALANT. Certainly.

Mr. GORDON. When you mentioned 51 percent being owned or that has to be owned by the foreign—

Mr. SALANT. By nationals of the country.

Mr. GORDON. That is from now on, isn't that correct?

Mr. SALANT. No. It has been in effect for a good long period of time.

Mr. GORDON. But isn't it correct that most of the subsidiaries of American parent companies are wholly owned by the American companies?

Mr. SALANT. You are talking about the pharmaceutical field only?

Mr. GORDON. Yes.

Mr. SALANT. I honestly do not know. Perhaps Mr. Kunze—no. I do not have information on that. I can only say that current laws for most of the low-income countries in which we have programs prescribe that new ventures must be owned at least to the extent of 51 percent by local nationals. I would assume that there is a carryover in some of these countries of old firms. But this does not change the fact, Mr. Gordon, that they must still operate in accordance with the laws of the country, that they do not have foreign exchange on their own, that they have to go through the regular procedure of obtaining licenses and of purchasing with their local currency of foreign exchange for any imports.

Senator NELSON. I think that it is important that AID is modifying its rules. I am not sure how well they will work, but I think it is an important step in the right direction which needs to be monitored very closely. Quite obviously, this was a very delightful, cozy, profitable arrangement for everybody except the poor consumer in the aided country and the American taxpayer. Here you have a situation in which the subsidiary was ordering drugs made by the parent company—obviously as many sole source or brand name type drugs as possible—so that we have in the testimony, as you know, examples where they were paying 500, 2,000, and 12,000 percent more than the world market price. So everybody was a winner except the poor consumer because when it went into the retail marketplace at that inflated cost figure, the American company made a huge profit right off the bat and the foreign country got a 40-year loan at $3\frac{1}{2}$ percent.

Mr. SALANT. Excuse me, sir. That was the country that got the loan, not the company.

Senator NELSON. Yes. Everybody was a winner except the poor foreign consumer and the American taxpayer, under that previous arrangement. I am glad to see that you have modified the policy and I certainly think it is important that you continue to monitor it very carefully because it appeared to be quite unfair to the consumer in those countries and to the American taxpayer as well.

So I think it would be of some value to review this in a year to see just how well the policy is working out.

Thank you very much. I appreciate your taking the time to come this morning.

Mr. DWINELL. Thank you, Mr. Chairman.

Senator NELSON. Our next witness is Dr. Jesse L. Steinfeld, Surgeon General, U.S. Public Health Service.

Dr. Steinfeld, the committee is pleased to have you here this morning. First, however, at this point in the record I ask that a brief statement by me be printed in the record with the accompanying letters from Dr. Charles Edwards, Dr. Steinfeld, and the president of the Pharmaceutical Manufacturers Association.

(The information referred to for inclusion in the record at this point follows:)

STATEMENT BY SENATOR GAYLORD NELSON

The President of the Pharmaceutical Manufacturers Association has recently complained to the Executive Branch of the Government as well as to some members of Congress that the new policy of refusing to use public funds for drugs for which there is at present no proof of efficacy, is unfair to the drug industry. His argument is that since the Food and Drug Administration has given the industry additional time—30 days—for “ineffective” drugs and 120 days for “possibly effective” drugs, the United States Government should continue to use these drugs as if they were really effective.

The Kefauver-Harris Amendments to the Food, Drug and Cosmetic Act, which requires that all drugs on the market must have *substantial* evidence that they are effective as well as safe, was enacted in 1962. The drug industry was put on notice at that time. Over eight years have elapsed and the required scientific evidence was not—or could not be—supplied to support the claims for many drugs.

Dr. Charles C. Edwards, Commissioner of the Food and Drug Administration in a recent letter to me stated that:

“In the real sense, the industry failed to mount any effort to provide the necessary evidence of effectiveness. Rather, they continued to request hearings, revise labeling, or otherwise avoid the issue of supplying substantial evidence of effectiveness. No drugs of any economic significance were voluntarily removed from marketing, except in those cases where the matter was resolved in the courts, such as some combination antibiotic products. We, therefore, considered it prudent to publish the decisions we made based on the NAS-NRC review.”

Now the industry's trade association not only is asking for more time to come up with the evidence that such drugs are effective, but also insists that public funds be continued to be spent on them.

In reply to such requests Dr. Jesse L. Steinfeld, the Surgeon General, wrote to the president of the Pharmaceutical Manufacturers Association and I would like to read the last two paragraphs of Dr. Steinfeld's reply, for which I wish to commend him.

“The policy stated in my memorandum is intended to improve patient care in those programs supported with Federal funds. It does not constitute good medical practice to administer drugs that have not been shown to be effective for the purposes for which they are prescribed.

“I do not agree that the Departmental policy is unfair to the drug manufacturing industry as you allege. Even if it were, I would then have to weigh that against the unfairness of giving sick people drugs that have not been shown to be effective. I would have to decide in favor of the sick people.”

SURGEON GENERAL,
PUBLIC HEALTH SERVICE,
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Washington, D.C., January 28, 1971.

Mr. C. JOSEPH STETLER,
*President, Pharmaceutical Manufacturers Association,
Washington, D.C.*

DEAR MR. STETLER: Your letter of January 21, 1971, requests me to modify my memorandum of December 11, 1970 stating Departmental policy about the use of Federal funds to purchase drug products classified as “ineffective” or “possibly effective.” The request is based on your view that the result of the policy will be to effectively remove any “ineffective” or “possibly effective” products from the market. You also state your view that my memorandum is unfair to the drug manufacturing industries.

The policy stated in my memorandum will not effectively remove drugs from the market. It applies only to drugs purchased with Federal dollars and these make up a relatively small volume of the drugs sold in the United States.

The policy stated in my memorandum is intended to improve patient care

in those programs supported with Federal funds. It does not constitute good medical practice to administer drugs that have not been shown to be effective for the purposes for which they are prescribed.

I do not agree that the Departmental policy is unfair to the drug manufacturing industry as you allege. Even if it were, I would then have to weigh that against the unfairness of giving sick people drugs that have not been shown to be effective. I would have to decide in favor of the sick people.

Sincerely yours,

JESSE L. STEINFELD, M.D.,
Surgeon General.

PHARMACEUTICAL MANUFACTURERS ASSOCIATION,
Washington, D.C., January 21, 1971.

JESSE L. STEINFELD, M.D.,
*Surgeon General,
Deputy Assistant Secretary for Health and Scientific Affairs,
Department of Health, Education, and Welfare,
Washington, D.C.*

DEAR DOCTOR STEINFELD: We have reviewed with some concern your memorandum of December 11, 1970 setting forth Departmental procedures concerning the handling of drug products classified as "ineffective" or "possibly effective" by the Food and Drug Administration.

We are concerned because it appears that the Department intends to refuse to pay for drugs so listed by FDA even though:

(a) The decision with respect to some of the products is not final, pending FDA evaluation of further information supporting the product's effectiveness, which has been supplied by the drug's manufacturer.

(b) A "possibly effective" rating, as your memorandum itself notes, may involve only a single claimed indication for the product, while other claims for it have not been ruled out, and new studies are being undertaken.

If drug products now said to be "ineffective" are, when the regulatory process is completed, finally judged to be "effective", then your action will have seriously and irreparably harmed the products in question without justification.

If HEW refuses to honor claims for a drug rated "possibly effective" when the claim in question has not been rejected and studies are being initiated in accordance with regulatory policy, HEW will have denied due process to the manufacturers and will have grossly damaged the product's reputation without even the most tenuous of justifications.

Ironically, Doctor Steinfeld, your actions will have their worst effects on the firms that have acted most responsibly in this matter. The drugs involved here are those for which drug companies have provided the material necessary to obtain an approved New Drug Application; and for which they submitted, in accordance with the Government's requests, information showing the claims being made and the supportive evidence upon which those claims rest. Further, these firms cooperated in every way possible with the panels and staff of the efficacy review committee, and with the staff of the FDA.

The result of your action, if prematurely carried out, will be to effectively remove these products from the market; yet similar or identical competitive products, manufactured by firms that have given this effort *no* cooperation, will be rewarded for their irresponsibility by being permitted to continue on sale.

Your memorandum is extremely unfair to this industry, it seems to us, and goes far beyond the intent of the efficacy review and the Department's legal authority. I therefore request that you modify that memorandum to make clear the Department's intention to honor claims for payment for drugs until their effectiveness status has been finally determined in accordance with established prescribed regulations.

Inasmuch as we understand that the Social Security Administration and the Medical Services Administration intend to implement your policy state-

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ment, I trust that you will take the requested action at the earliest practicable time.

Sincerely yours,

C. JOSEPH STETLER, *President.*

P.S. I am enclosing a PMA release which discusses the FDA list of "ineffective" drugs for your information. (Enclosure: omitted.)

FOOD AND DRUG ADMINISTRATION,
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
Washington, D.C., January 29, 1971.

HON. GAYLORD NELSON,
*Chairman, Subcommittee on Monopoly,
Select Committee on Small Business,
U.S. Senate,
Washington, D.C.*

DEAR SENATOR NELSON: Thank you for your January 26, 1971 request for comment on a letter and press release from C. Joseph Stetler, President, Pharmaceutical Manufacturers Association, concerning the Food and Drug Administration's review of the efficacy of drugs approved between 1938 and 1962.

Congress in 1962 clearly expresses its intent that drugs then on the market, or thereafter introduced, be safe and effective. A grace period of two years was allowed for the industry to submit the scientific evidence to support claims made for drugs on the market at that time.

No real effort to comply with this requirement occurred on the part of members of the Pharmaceutical Manufacturers Association or others. Therefore, it became necessary in 1966 for the FDA to turn to the National Academy of Sciences for assistance in evaluating the effectiveness of drugs approved between 1938 and 1962.

Even after the evaluation of those drugs by the NAS-NRC Drug Efficacy Study Group and in view of their criticism of drug labeling and the quality of evidence submitted in support of effectiveness for label claims, industry resistance continued. Our early actions were challenged in the courts.

In the real sense, the industry failed to mount any effort to provide the necessary evidence of effectiveness. Rather, they continued to request hearings, revise labeling, or otherwise avoid the issue of supplying substantial evidence of effectiveness. No drugs of any economic significance were voluntarily removed from marketing, except in those cases where the matter was resolved in the courts, such as some combination antibiotic products. We, therefore, considered it prudent to publish the decisions we made based on the NAS-NRC review.

I do not view with alarm the disclosure that some drugs, found ineffective for label claims, were not in commercial distribution at the time this list was released. I would be surprised or even alarmed if at the time the list was released, all drugs listed were still being marketed. The Drug Amendments of 1962 plainly put drug manufacturers on notice that substantial evidence for effectiveness claims was required. To this end, we applaud those voluntary actions by responsible manufacturers to remove from marketing products lacking the necessary evidence of effectiveness.

The first *Federal Register* announcements of intention by FDA to initiate proceedings to withdraw approval of the new drug applications or to repeal the antibiotic regulations were published early in 1968. Thus a considerable period has elapsed during which evidence supporting effectiveness claims could have been developed. The time for removal of these ineffective products from the market is now overdue. Action must be taken.

However, I believe it would be inadvisable not to exhaust the scientific method before ruling drugs off the market. If data is submitted supporting effectiveness claims, FDA will take steps to reclassify them if warranted by the evidence. I am convinced that it makes good sense to allow the drug companies to conduct the necessary studies to definitely answer the question whether a drug rated as "possibly" or "probably" effective, is effective or ineffective. Procrastination will not provide the answer, we must see progress.

Public confidence in our Nation's drug supply cannot be achieved while

ineffective drugs remain in our hospitals and neighborhood pharmacies. Public confidence must be built upon the firm foundation of adequate, scientific evidence clearly supporting the effectiveness claimed. The sooner this is accomplished the greater will be the public confidence in the entire medical establishment, be it the drug manufacturer, physician, pharmacist, or the Food and Drug Administration.

We sincerely desire to enlist the support of all members of the medical community to lend their support to the accomplishment of this objective.

Thank you for your interest in our consumer protection activities. Please let us know if we can be of further assistance.

Sincerely yours,

CHARLES C. EDWARDS, M.D.,
Commissioner of Food and Drugs.

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., January 26, 1971.

HON. CHARLES C. EDWARDS,
Commissioner, Food and Drug Administration,
Washington, D.C.

DEAR DR. EDWARDS: I would very much appreciate your comments on the attached letter which I have received from the President of the Pharmaceutical Manufacturers Association.

Kindest personal regards.

Sincerely,

GAYLORD NELSON,
Chairman, Monopoly Subcommittee.

PHARMACEUTICAL MANUFACTURERS ASSOCIATION,
Washington, D.C., January 21, 1971.

HON. GAYLORD NELSON,
Chairman, Monopoly Subcommittee,
Senate Select Small Business Committee,
Old Senate Office Building,
Washington, D.C.

DEAR SENATOR NELSON: In connection with your present series of hearings concerning the Food and Drug Administration's review of the efficacy of medicines marketed between 1938 and 1962, there have been numerous statements in the press and before your Committee which, I think, tend to overstate the situation.

The primary example of this is the list of products made available late in November, 1970, by FDA, in which some 359 products are described as "ineffective." Newsmen and patients quite understandably were led to conclude that several hundred of the drugs their physicians were prescribing are useless.

In fact, as a result of a survey by PMA of its member firms, we can state that fully two-thirds of their products named on the FDA list had been withdrawn from the market before the list was released. Indeed, dozens of them have been off the market for over two years, some have not been offered for sale for a decade or more, others have never been marketed in the United States.

The number in real question, then, is small. For PMA firms, it is ninety-two; and were double counting, due to repetition of multiple forms of the same drug, eliminated, the number of actual products involved would be still smaller.

But there is a more important point than the number of products that are in question. That is the status of such products, in the legal sense. The regulatory procedures involved here permit the manufacturers of products judged "ineffective" to submit additional data in support of their claims, and call for FDA to make an evaluation of that data before issuing a final ruling.

With respect to most of the 92 PMA-firm products in question, we are advised that the manufacturers have submitted additional supportive infor-

mation to FDA. Pending evaluation of that data, the products remain available, and, we believe, will in many cases finally be ruled effective.

Due process requires, it seems to us, that no physician be required to end his use of any of these drugs against his will at this time. We are therefore concerned when we read of the premature elimination of drugs on the November FDA list—and even the elimination of drugs judged “possibly effective” in some instances—from the procurement schedules of Federal agencies. For those products ultimately judged effective, the damage done to them by that premature delisting will have been as unwarranted as it was substantial.

I enclose a copy of a press release which discusses this subject in a little more detail. We would be appreciative if you would make this letter and the release a part of the Subcommittee's printed record at the appropriate place.

Sincerely yours,

C. JOSEPH STETLER, *President.*

Enclosure.
cc: Members of the Monopoly Subcommittee of the Senate Select Small Business Committee.

[Press release]

PMA CHALLENGES PRODUCT LIST ISSUED BY FDA

WASHINGTON, D.C., January 15, 1971.—Two-thirds of the products made by its member companies that were included in a recent list of so-called “ineffective drugs” issued by the U.S. Food and Drug Administration are already off the market, the Pharmaceutical Manufacturers Association announced today.

President C. Joseph Stetler made public an analysis of the list of 359 products distributed recently by the FDA to federal agencies and to the mass communications media.

The list contained prescription and nonprescription drugs and such assorted other products as tooth pastes and mouth washes, all deemed by the FDA to be lacking “substantial evidence of effectiveness” or having “an unfavorable benefit to risk ratio.”

Representing regulatory actions published by the FDA in the Federal Register for the period from January 1968 to the end of 1970, the list has received wide publicity.

“This publicity has had the effect of giving the public the erroneous impression that a new, large-scale action, based on incontrovertible scientific evidence, is being taken against hundreds of products still in use,” Stetler said.

The FDA list was based on an evaluation for effectiveness of drug products by the National Academy of Sciences-National Research Council. The list in some cases represented varied dosage forms and package sizes for the same drug, which reduces considerably the total of 359 items, the PMA noted.

The PMA analysis showed of the 359 items listed, 292 were manufactured by its member companies. Three of the products made by PMA members were never marketed in the United States. Another 25 ceased to be marketed before January 1968, some as long as 20 years ago.

Eliminating those non-available items, a total of 172 products on the FDA list were removed from the market over the past three years. Ninety-two remain on the market.

In the latter category, in virtually all instances the manufacturer is responding to FDA requests to make available more data to demonstrate effectiveness, Stetler said. Some labeling and formulation changes have been and are being made. A few products have become the subject of regulatory or judicial redress.

“We are confident that a great many of these products, which have been used successfully by doctors for many years, will remain in use,” Stetler said.

The analysis showed that four products rated “effective” by the NAS/NRC showed up on the FDA's ineffective list. Forty-three products rated “effective, but”, five found “probably effective”, and 22 deemed “possibly effective” were placed by the FDA in the same category.

Stetler pointed out that of the group of 292 PMA company products, 59 received an “ineffective” rating by the NAS/NRC and another 159 involved the concept of “ineffective as a fixed combination.”

A considerable scientific debate is underway over the entire fixed combination question, with expert opinion on both sides of the issue.

"The way the FDA has translated the often qualified NAS/NRC findings into summary regulatory action against individual products remains the most controversial aspect of the review process", Stetler declared.

Many contested drugs have been voluntarily withdrawn from the market by manufacturers because the required lengthy clinical trials and studies are not feasible, in part because of a shortage of qualified investigators.

While the PMA did not survey non-PMA member companies producing 67 products on the FDA list, a breakdown would probably be similar to that for PMA companies, it was pointed out.

Senator NELSON. Your statement will be printed in full in the record, doctor.

Go ahead and present it however you desire.

STATEMENT OF DR. JESSE L. STEINFELD, SURGEON GENERAL, PUBLIC HEALTH SERVICE, AND DEPUTY ASSISTANT SECRETARY FOR HEALTH AND SCIENTIFIC AFFAIRS, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE; ACCOMPANIED BY WINTON B. RANKIN, SPECIAL ASSISTANT TO THE ASSISTANT SECRETARY FOR HEALTH AND SCIENTIFIC AFFAIRS, HEW; AND ALLEN J. BRANDS, PHARMACY LIAISON REPRESENTATIVE, PHS, HEW

Dr. STEINFELD. Thank you, Senator Nelson.

With me on my left is Mr. Winton Rankin, Special Assistant to the Assistant Secretary for Health, HEW, and on my right is Mr. Allen J. Brands, Pharmacy Liaison Representative of the U.S. Public Health Service.

If I may, I would like to proceed with the statement.

Once more, Mr. Chairman, I am pleased to appear before this committee to discuss the drug procurement activities of our Department.

Our Department has adopted the policy that it will not spend Federal funds for purchasing drug products classified as "ineffective" or "possibly effective" by the Food and Drug Administration. This policy applies to our direct care programs, the contract care programs under the direct care programs, the Federal grant programs and the medicare and medicaid programs for both inpatients and outpatients with the following two exceptions:

(a) Federal funds may be expended to purchase "ineffective" and "possibly effective" drug products for use in the pursuit of approved clinical research projects.

(b) Federal funds may be expended to purchase a "possibly effective" drug product when no alternate means of therapy with drug products in the "probably effective" or "effective" classification is available.

This policy is in full effect now with respect to direct purchases of drugs and we are in the process of making it effective for the reimbursement programs; this latter case takes more time since there are regulations that must be changed and there is the problem of giving adequate notice to numerous individuals and offices that are entitled to seek Federal moneys under the reimbursement programs.

We have already supplied your staff, Mr. Chairman, with a copy of my memorandum of December 11, 1970, stating the departmental

policy. We have another copy here for the information of the committee if you wish it.¹

The Health Services and Mental Health Administration of the Public Health Service has established a committee with members drawn from the several programs that make direct purchases of drugs: Bureau of Prisons; Coast Guard; Division of Emergency Health Services; Federal Health Programs Service; Indian Health Service; and National Institute of Mental Health.

This committee will insure compliance with departmental policy on drug procurement and on drug utilization by:

- a. Developing uniform basic policy on:
 1. Pharmacy and therapeutic committee responsibility.
 2. Drug product admission to formularies.
 3. Drug utilization review committees.
 4. Formulary review.
 5. Nonformulary drug product purchases.
- b. Reviewing a sample of present formularies with respect to:
 1. Duplication of drugs with therapeutic equivalency.
 2. Combination drug products.
 3. Ineffective and possibly effective drugs.
 4. Probably effective drugs when an effective drug is available for the same use.
- c. Monitoring the purchasing of nonformulary drugs.
- d. Approving the selection of drug products to be stocked at the HSMHA Medical Supply Service Center.

In addition to participating in the HSMHA committee, the programs that operate hospitals and clinics have established their own committees to:

- a. Supplement the policy of the HSMHA committee.
- b. Review, monitor and approve station formularies and additions of drug products to formularies.
- c. Review reports of drug utilization review committees.
- d. Review the purchasing and use of nonformulary drugs.
- e. Review present formularies with respect to:
 1. Duplication of drugs with therapeutic equivalency including a cost comparison.
 2. Combination drug products.
 3. Ineffective and possibly effective drug products.
 4. Probably effective drug products when an effective drug of therapeutic equivalency is available.

The reviews and studies of these several groups of experts are now underway. Additionally HSMHA is developing mechanisms to assure that future grants and contracts which are likely to involve the procurement of drugs will require compliance with the departmental policy stated earlier.

Mr. Chairman, your staff has advised me of your interest in the steps our Department has taken and plans to take with respect to the recommendations of the task force on prescription drugs.

The task force was composed of a group of scientists and other experts drawn from within the DHEW. It was assisted by 160 non-

¹ See appendix I, exhibits provided by the Public Health Service, pp. 8233-8422.

government experts. After 20 months of studies covering several broad fields of health and health related activities it submitted a report to the Secretary of HEW on February 7, 1969.

In transmitting the report to the Secretary, the Chairman of the task force, Dr. Philip Randolph Lee, former Assistant Secretary for Health and Scientific Affairs, identified the two most significant findings and recommendations as:

The finding that a drug insurance program under Medicare is needed by the elderly, and would be both economically and medically feasible, and the recommendation that such a program be instituted.

The finding that the once-confusing matter of clinical equivalency is far less complex than had been anticipated, and that as a result of current laboratory and clinical studies—initiated in large part in response to requests by the Task Force—the problem is well on its way to solution.

I am sure you are aware that the present administration is developing health insurance recommendations. These are to be submitted to the Congress at a later date. I am not in a position to discuss details of the recommendations at this time.

With regard to clinical equivalency of drugs, there also has been much work. Food and Drug Commissioner Charles C. Edwards discussed this when he testified here last month.

There are many other recommendations in the report of the task force on prescription drugs that we have found to be worthwhile, and I will speak to a number of them shortly.

First, however, I would like to mention a serious problem that this administration has encountered. The Nation lacked a carefully planned national policy on health. This has severely hampered the exercise of effective Federal leadership in health. Such national health policy as we found seemed to be the end product of bargaining processes covering a period of many years in which ongoing programs were treated as essentially inflexible commitments, and any change or leadership which occurred resulted from the addition of increments to existing programs, or the inauguration of new programs.

We have found it necessary to restudy the role of the Federal Government in the entire health area. Actions with respect to prescription drugs must be considered in the light of all the other health options available to the Federal Government. Decisions about prescription drugs must not be reached in isolation from other health matters such as prevention of illness, health research, and health insurance. Rather, the Government's health program must be considered as a whole, when its separate elements are under review. Out of this process will come a well-organized national approach to health.

Since this review process is still underway, I am sure you will understand why it is not possible for me to make final comment today on every recommendation of the task force. However, I am in a position to outline the significant progress that has occurred.

The task force on prescription drugs made 25 recommendations.

Responsibility for conducting a continuing study of drug costs, average prescription prices, and drug use as suggested in the first and 22d recommendations, was assigned to the Social Security Ad-

ministration which began working on these problems in the summer of 1969.

Senator NELSON. Have any of those studies been completed?

Dr. STEINFELD. One of them has been completed. It is a Prescription Drug Data Summary, dated July 1970, and we have a copy of it here for the committee.

Senator NELSON. Prescription Drug Data Summary.

Dr. STEINFELD. Yes, sir.

Senator NELSON. What was that study about?

Dr. STEINFELD. It was a review of prices and utilization of drugs by ages of patients for the past several years, in hospitals and in outpatient care, by States, types of programs, and indicating the sales in terms of manufacturers, wholesalers, retailers, and so forth. And then it describes the drugs by various categories, whether for the central nervous system, neoplastic disease, infectious disease, et cetera.¹

It is primarily a fiscal summary which would be used along with other information for development of further policy.

Mr. GORDON. May we have a copy?

Senator NELSON. Your statement says "responsibility for conducting a continuing study of drug costs, average prescription prices, and drug use as suggested in the first and 22d recommendations was assigned to the Social Security Administration." Is this their continuing responsibility so far as task force recommendations were concerned?

Dr. STEINFELD. Mr. Chairman, we have a departmental task force working on drug utilization which takes into account drug cost, prescription price and drug use. This comprises people from SRS, SSA, FDA, the various agencies conducting research in health service delivery (the health service research and development activity in HSMHA), and our own office and we attempt to coordinate and correlate through this overall committee.

Senator NELSON. OK. Go ahead.

Dr. STEINFELD. Research on retail drug prices is being conducted through Social Security Administration-supported methodology studies which may permit measurement of the true economic costs associated with operation of prescription departments in community pharmacies. Findings from these studies are expected by the early part of February of this year.

Social Security Administration staff has conducted various studies related to drug product cost. Research includes analyses of drug industry pricing techniques as manifest in pharmaceutical procurement by Federal agencies (AID, DPSC, GSA, OEO, PHS, and VA) and selected local and State governmental units. In addition, studies are underway dealing primarily with economic issues on selected therapeutic categories. These deal with drug classes such as antibiotics, thiazide diuretics, corticosteroids, tranquilizers, oral antidiabetics, as well as Vitamin B₁₂.

Efforts will be made in the future to gather primary data which will permit a comparison to be made of the economic cost of pro-

¹ See pp. 8260-8288

ducing and distributing pharmaceutical products, on the one hand, and market prices on the other.

Mr. GORDON. May I interrupt you there?

Dr. STEINFELD. Certainly.

Mr. GORDON. How are you going to get these costs? Do you have mandatory powers to get it? Do you ask the manufacturers to give it to you? As I understand it, this is rather sensitive information which the drug firms would be very reluctant to give.

Dr. STEINFELD. You are absolutely correct, but we believe that a number of the smaller drug firms which have just gotten into the business of manufacturing generic products will cooperate with us. From the information we obtain on these products, we think we can extrapolate to some extent to some of the larger manufacturers and brand name products. It will be a difficult problem, however.

Mr. GORDON. But you can get a general idea of the manufacturing costs?

Dr. STEINFELD. We think we can from some of the smaller manufacturers producing generic products, yes, sir.

One report, Prescription Drug Data Summary, was published last year. I have just supplied a copy for the committee's information. The 1971 edition will go to press in April. Two other studies are being developed for publication: These reports cover Profits in the Drug Industry, 1959-69 and Comparison of Domestic and Foreign Prescription Drug Prices. We expect another report, Techniques and Problems in Federal Drug Procurement, to become available later this year.

Recommendation No. 4 called for the enactment of legislation requiring that the containers of dispensed prescription drugs be labeled with the identity, strength, and quantity of the product unless the prescriber waived this requirement. The Department's proposed Drug Identification Act of 1969 (S. 3297 in the 91st Congress) included amendments to the Federal Food, Drug, and Cosmetic Act which would have implemented this recommendation fully.

Hearings were held on S. 3297 and related bills on April 28 and 29, 1970, by the Subcommittee on Health of the Senate Committee on Labor and Public Welfare. No further action was taken on this legislation in the 91st Congress. This legislation was last week resubmitted to the Congress by the President.

Encouragement of the wider use of prepackaged dispensing was suggested in recommendation 5. Our Department subscribes wholeheartedly to this recommendation.

The Health Services and Mental Health Administration Supply Service Center has requested bids on both prepackaged and bulk sizes of drugs when purchasing. Most bid solicitations are returned with no bid on the prepackaged sizes, or the cost differentials between the prepackaged and bulk sizes are too great for the prepackaged forms to be economical. The Supply Service, however, purchases 60 items prepackaged, where it is economical.

The National Center for Health Services Research and Development is currently supporting six grants designed to improve the efficiency and effectiveness of community and hospital pharmacist operations in accordance with the 6th recommendation.

These projects cover a wide variety of program interests, such as pharmacy manpower, arrangements for pharmacy services, and utilization and quality of pharmacy services. More specifically, within the past several months the Center has cosponsored with the University of California, San Francisco, a Conference on Pharmacy Manpower. A copy of the summary will be supplied to the committee.¹

Three conclusions emerged from the conference and are being pursued in the National Center at this time. One is the need to describe a clinical role for the pharmacist. A task force was convened by the Center in November 1970 to begin discussions of this topic and related matters. Further, the Center is in the process of identifying locations where the concept of such a clinical role can be tested, and an evaluation can be made of the effectiveness of this role for the pharmacist, as well as its economic feasibility. The Center has been exploring concurrently the potential for developing and testing other models suitable for pharmacy services and is giving attention to a model for a community drug formulary program.

Recommendation 10 suggested that our Department support a publication providing objective, up-to-date information and guidelines on drug therapy based on the expert advice of the medical community. This is being done. The Food and Drug Administration established a publication in February 1970 entitled "Current Drug Information." This publication is intended to communicate to physicians up-to-date and accurate information on matters that may affect the prescribing of drugs. It is sent to 360,000 physicians, 60,000 pharmacies (including hospitals), departments of pharmacology in medical schools, and to all schools of pharmacy.

There have been four such publications issued (oral contraceptives, L-Dopa, lithium carbonate, and sulfonylurea drugs). In each case, physicians were brought up-to-date on the drug's indications, adverse reactions, recommended dosages, precautionary measures to be taken in administering the drug, and reference information.

We have copies for the committee of these publications.²

Mr. GORDON. Can this be done for other classes of drugs? For example, the tetracycline family? The penicillins, corticosteroids?

Dr. STEINFELD. Yes, sir. We plan on doing this irrespective of whether we have a formulary or compendium.

Mr. GORDON. And you will compare, as I understand it, the relative merits—safety and efficacy—of the drugs within each therapeutic category; is that correct?

Dr. STEINFELD. We will review the indications, contraindications, efficacy, safety, uses, all of these things. This, of course, is being done in part in the reworking of the labeling as a result of the NAS-NRC study but where there are classes of compounds to be compared, this is something that we will undertake.

Senator NELSON. How will the FDA's current drug information publication compare with the Medical Letter, for example? Will it do the same thing?

Dr. STEINFELD. It will be distributed to all physicians free of charge as it is now for those who ask, and it will probably restrict

¹ See pp. 8289-8323.

² See pp. 8324-8331.

itself to one subject at a time. It will not be a substitute for the Medical Letter.

Senator NELSON. On page 10, your last sentence is: "The Center has been exploring concurrently the potential for developing and testing other models suitable for pharmacy services and is giving attention to a model for a community drug formulary program."

What does that mean? Are you talking about a formulary that can be used at the local level?

Dr. STEINFELD. Yes, and to be used in a number of pharmacies in an individual community. The easier problem is to work it in individual institutions or groups of institutions such as the Public Health Service or VA hospitals. It would be more difficult when one moves out into a community.

Senator NELSON. That is what I am curious about. How will you do this? What are the mechanics for establishing the formulary? Who is going to use it?

Dr. STEINFELD. Well, I think since it is an R. & D. program, the questions that you raise are the ones that must be answered: Will there be resistance on the part of physicians? How will pharmacists react to it? And so forth.

Mr. Brands, can you amplify on this subject?

Mr. BRANDS. Yes, sir. There has been a study done, I believe, in Virginia. The Medical Society and the Pharmacy Association got together to see if they could work out a formulary; this would be a limited number of drugs, not a total formulary but a limited number of drugs that would be used in practice.

In Delaware they have done the same thing with a few drugs for generic prescribing. This is in Wilmington, Del., where the Medical Society and the Pharmacy Association have gotten together and tried to work out the mechanics so that they can have a formulary and generic prescribing, if you wish, just like they have in the hospitals. It works similarly, except on a larger scale, as it does in the hospitals.

Senator NELSON. Well, all right. Who made up the formulary in Delaware and Virginia? The local medical association, county, and the pharmacists—in association with whom?

Dr. STEINFELD. It was the two together, working together, that worked out the details, what would be included in it.

Senator NELSON. What is the progress on this model for community drug formulary program. It is an R. & D. program. You are going to test this in some parts of the country?

Dr. STEINFELD. We can get you a progress report on the ones—the models that Mr. Brands described. In addition, at Los Angeles County they are attempting to move from Los Angeles County General Hospital into certain communities, San Gabriel Valley just east of the county, in an attempt to see if the formulary used there can be applied in other areas in the Metropolitan Los Angeles area.

(The subsequent information was received and follows:)

A FORMULARY FOR DELAWARE PRACTITIONERS

Discussions at a joint meeting of the Delaware Medical Society and the Delaware Pharmaceutical Society resulted in the formation of an interdisciplinary group of health professionals with responsibility to develop guidelines in the areas of drug prescribing and dispensing and rational drug therapy.

The group is named the Delaware Formulary Advisory Board and has as members four physicians, four pharmacists, one dentist and one osteopath with each member being appointed by the respective Delaware professional society.

The objective of the Board is to devise a method by which quality drugs can be prescribed and dispensed at reasonable cost. The plan calls for a pilot program whereby by mutual agreement selected drugs would be recommended to the health professionals by virtue of their quality and relative reasonable price. To date the pilot study includes seven items.

The program is voluntary. If the prescriber gives permission to use a formulary drug, the dispenser is expected to supply the one suggested by the Board.

The program is to have an educational component for the health practitioners so the objective can be achieved. The education has not been implemented because of the need for funding.

There has been some concern about whether or not this program is in violation of the Sherman Anti-Trust Act.

Enclosed is information on the Board.

1. The Delaware Formulary Advisory Board. A memorandum dated January 19, 1971, from the Medical Society of Delaware.

2. Guidelines for the Creation of a Formulary for Delaware Practitioners.

3. Protocol to be Followed by Delaware Formulary Board in Considering a Product for Listing in the Formulary.

MEDICAL SOCIETY OF DELAWARE,
Wilmington, Del., January 19, 1971.

Re: The Delaware Formulary Advisory Board.

To Whom It May Concern:

The Delaware Formulary Advisory Board was created a couple of years ago by the respective State Associations representing medicine, osteopathy, dentistry and pharmacy. The purpose was to devise a method by which quality drugs could be prescribed and dispensed at reasonable cost. The plan of operation was to create a voluntary and pilot program whereby mutual agreement selected drugs could be recommended to our various professions by virtue of their established quality and relative reasonable price. To date the pilot study includes seven items. If the prescriber gives permission for use of a formulary drug, the dispenser is expected to supply the one suggested by the Board. After a year of active implementation of this program, a study will be undertaken to compare the cost factors.

The Medical Society of Delaware is on record as approving this as a voluntary and pilot program as an experimental means of helping to maintain quality and reduce health costs.

WILLIAM O. LAMOTTE, Jr., M.D.,
President-Elect.

GUIDELINES FOR THE CREATION OF A FORMULARY FOR DELAWARE PRACTITIONERS OF MEDICINE, OSTEOPATHY, DENTISTRY, AND PHARMACY

INTRODUCTION

As members of the health team, physicians, dentists and pharmacists have been traditionally allied by their mutual efforts to provide the best of health care and treatment services to the public.

The advent of modern day drug treatment has brought not only new hope and renewed health to many, but also has underscored the value of the professional bonds among all members of the health team. It is, therefore, logical that those health professions dealing with modern chemotherapy should strive not only for excellence in this care, but also to recognize their obligation to provide this care at a minimum cost to the public.

Recent action by the Federal Government has underscored the general concern of the public in the cost of drugs. It would, therefore, appear that any moves which could be made at the local level to reduce patient drug cost without sacrificing the quality of therapy would be well received by the

public. Naturally, the greater the number of health practitioners who participate in such a program, the greater the ultimate effect on drug costs to the general public.

It is, therefore, the purpose of this proposal to further meet the obligation of all health practitioners to the public, that is excellence of drug care at a minimum of cost.

OBJECTIVES

1. To provide a compilation of drugs by physicians and pharmacists which will ultimately reduce patient costs still maintaining the present-day excellence of drug therapy.
2. To advise, inform and educate practicing health professionals of the professional and economic advantages possible through the utilization of an approved pharmaceutical formulary.
3. To encourage the utilization of a drug formulary by practicing health professionals in the best interests of the patient.
4. To promote the cooperation and coordination between members of the health professions in providing optimal health care services.
5. To meet the obligation of all health practitioners to the public, that is to provide the highest standard of health care services at the lowest possible cost.
6. The successful functioning of the formulary idea is solely dependent upon the voluntary cooperation and support of the individual members of the respective professional organization.

BACKGROUND

Hospitals now operating under the Medicare Program are required to have a Drug List which is prepared by a Pharmacy & Therapeutics Committee of the medical staff or by a like committee. The sole purpose in this requirement of the Federal Medicare Program was to encourage hospitals to develop approved drug lists. These lists usually result in an approximate drug savings of ten percent to the institutions so utilizing them.

These lists are designed to allow the patient to receive the least expensive of a variety of trade name products, all representing the same chemical entity and of proven therapeutic efficacy. This is usually done by the physician writing his order in non-proprietary (generic) terminology. He is assured a quality product in that the Pharmacy & Therapeutics Committee must specifically approve the manufacturer from which the drug is purchased, prior to the pharmacy dispensing a drug ordered on a non-proprietary basis.

The utilization of such a drug list results in a reduction in patient costs by the following ways:

1. Reduction in inventory levels of the various trade names for one drug and the subsequent dispensing of only the one approved, if the prescriber so designates.
2. Purchase of greater quantities since, ideally, one drug will be ordered (one trade name) instead of a number of trade name products of the same drug. Greater quantity purchases will usually result in lower costs.
3. Institution of a bid system where all of the possible companies supplying one drug would compete for the right to be the sole supplier of that drug when the prescriber so designates through the use of non-proprietary terminology.

Systems such as the one just described have been in operation for many years throughout the country in hospitals of all sizes and have resulted in decreased drug costs. The systems have, in most cases, been well received by the treated public and by medical and dental practitioners utilizing them. The extension of such a system to ambulatory patients has been successful in hospital outpatients and could be expected to be successful outside of the hospital setting.

ORGANIZATION OF THE FORMULARY ADVISORY BOARD

1. This body shall be titled the *Formulary Advisory Board*.
2. The chairman of the board shall be a responsible member of the consumer public to be selected by the presidents of the respective professional organizations represented on the committee. He shall serve for two years and be an ex-officio member.

3. The board shall be composed of four physicians who are members of the Medical Society of Delaware, three pharmacists who are members of the Delaware Pharmaceutical Society, one dentist who is a member of the Delaware Dental Society, and one osteopath who is a member of the Delaware Society of Osteopaths. These members will be selected by their respective professional organizations.

4. Each member shall be appointed for a three-year term of office. Initially, members of the board shall be appointed for staggered terms of office of one, two and three years.

5. The presidents of the respective professional organizations or their representatives shall be ex-officio, non-voting members.

6. The secretary shall be a pharmacist. He will be an ex-officio member of the board and will be selected by the Delaware Pharmaceutical Society. The term of office of this member will be two years.

7. An executive committee of the board to be composed of the chairman, the secretary, and a non-pharmacist member of the board to be elected by its members. This committee will be responsible for the preparation of the agenda.

8. The board will meet not less than once per quarter. Emergency meetings may be called as required by the chairman or by the request of a majority of the board members.

FUNCTIONS OF THE BOARD

1. The Formulary Advisory Board evaluates, reviews and approves drugs proposed for addition to the formulary based on criteria as suggested by the purposes of this formulary.

2. Drugs favorably acted up will be alphabetically listed in the formulary based on non-proprietary terminology with the name of the supplier.

3. Requests that a drug be added to or deleted from the formulary may be made in any of the following ways:

(a) A letter stating such submitted by a professional who is a member of one of the health professions represented on the board. This letter should be forwarded to the secretary.

(b) The secretary may bring to the board's attention a drug on which a decision is necessary.

(c) Any member of the board can make such a request.

4. An agenda shall be distributed to the board by the secretary after review by the executive committee at least ten days prior to the next meeting.

5. Revisions in the formulary shall be distributed by the secretary of the board within a time limit specified by the board. This distribution may be through local professional journals, correspondence or any other appropriate method determined by the board.

6. The board shall operate independently and not be subject to the control of any of the organizations represented on it except as by the appointment of members.

7. Minutes of the meetings will be kept by the secretary.

OPERATION OF THE FORMULARY

A. Administration

1. Drugs will be listed in the formulary by non-proprietary name, trade name and manufacturer. A cross-reference trade name non-proprietary name will also be present.

2. Physicians and dentists desiring to order a drug under the Delaware Formulary system may do so by one of two ways:

(a) By prescribing the drug by non-proprietary name utilizing the Formulary Prescription Blank. Medical practitioners desiring their prescription to be considered as falling under the formulary system must check this blank appearing on the prescription order forms:

"OR-----FORMULARY EQUIVALENT".

(b) By designating on a regular prescription blank his desire that the drug dispensed be that approved by the Formulary Board. He could do this by a number of methodologies such as circling the drug, writing "Formulary" on the prescription blank or by any other means so indicated by the Board.

3. Additions to and deletions from the Formulary will be disseminated to all members of the associations represented by periodic mailings.

4. An up-to-date formulary reflecting all additions and deletions will be maintained and provided to all physicians, dentists and pharmacists.

PROTOCOL TO BE FOLLOWED BY DELAWARE FORMULARY IN CONSIDERING A PRODUCT FOR LISTING IN THE FORMULARY

1. All communication between the Board and applicants for listing will be coordinated and centralized through the Formulary Board secretary, or alternatively through the chairman.

2. Applications for listing of a product may be received either unsolicited, or may be solicited by the secretary at the request of the Formulary Board.

3. Upon receipt, applications will generally be reviewed for completeness by the secretary, and he may request any missing or incomplete information from the applicant.

4. In brief summary form, the secretary will proceed to notify the Board members on a weekly basis of applications received. (This will enable any Board member having pertinent information regarding the applicant or his product to bring such information to the attention of the secretary without undue delay.)

5. The secretary will assemble appropriate and sufficient background information regarding the applicant to enable a reasonable judgment to be made as to the qualifications, integrity, and reputation of the applicant. (The amount of information needed here will vary considerably depending upon the circumstances; applicants who have been previously considered or who enjoy well established reputations will require much less information than initial applicants or applicants whose reputations are less well known.)

Towards this end, the secretary may:

(a) review the weekly listings of "Drug Recalls" as released by the FDA, noting any past reference to the applicant or the drug product, and the reasons for any recall or recalls (to indicate nature and severity of any past problems);

(b) consult with the FDA local or District office in which the applicant is geographically located to ascertain applicant's general performance record and compliance with FDA's regulations for Good Manufacturing Practices;

(c) consult with the Defense Personnel Support Center of the Defense Supply Agency (in Philadelphia) to ascertain whether the applicant is on the list of approved bidders of the DPSC;

(d) consult with other government or private (e.g., hospitals) procurement groups or other qualified consultants having knowledge of the applicant or the drug product;

(e) request general—as well as any specific—background information from the applicant as to history of the firm, identification of its offices, nature of its corporate structure, etc.

6. The secretary will complete for review and evaluation by the Formulary Board all information which he assembles and which the applicant supplies.

7. Upon review the Formulary Board may decide to:

(a) approve the product for listing in the Formulary; or

(b) disapprove the product for listing in the Formulary; or

(c) recommend that further information or data be obtained, and defer action pending receipt and evaluation of such additional information. (Such information might include such things as a site visit to the applicant's plant, laboratory testing of the samples supplied, etc.)

COMMUNITY FORMULARY—CHARLOTTESVILLE, VA.

A joint committee of physicians and pharmacists representing the Albemarle County Medical Society and the Charlottesville-Albemarle Pharmaceutical Association was appointed in 1967 to review problems of mutual interest with particular attention to be paid to generic prescribing.

The committee did not intend to prepare a formulary of drugs approved for use, but to prepare a list of drugs that could be prescribed and dispensed generically that would assure a quality product and savings to the patient. Most prescribed drugs were controlled by patents or were in the form of proprietary combinations.

A list of eleven drugs was prepared and approved that would offer a reasonable savings to the patient. These were oral buffered penicillin G, tetracycline; meprobamate; prednisone; dioctyl sodium sulfosuccinate; chloral hydrate; secobarbital; phenobarbital; dextroamphetamine; reserpine; and rauwolfia.

The program was voluntary. The percentage of prescriptions written generically for the drugs on the list increased from 36.4 percent before the study to 49.5 percent six months after the study began.

A report of the Charlottesville program was published in the *New England Journal of Medicine*, June 26, 1969. A copy of the article is enclosed.

[From the *New England Journal of Medicine*, June 26, 1969, pp. 1442-1446]

SPECIAL ARTICLE—A PHYSICIAN-PHARMACIST VOLUNTARY PROGRAM
TO IMPROVE PRESCRIPTION PRACTICES*

(By Calvin M. Kunin, M.D., and J. Walter Dierks, M.B.A.)

Abstract.—A joint resolution prepared by a committee made up of physicians and pharmacists in Charlottesville-Albemarle County, Virginia, dealt with improvements in prescription writing, labeling of prescriptions and the use of generic drugs. Only eleven widely used generically available drugs were found to offer enough of a cost advantage to the patients to warrant inclusion in a list of recommended generic preparations. Nevertheless, it was demonstrated that when these were prescribed, pharmacists passed on savings to the consumer.

Prescribing of recommended generic drugs increased from 36.4 per cent before the study to 59.8 and 49.5 per cent three and six months later. This experience may serve as a prototype for similar voluntary programs and may be extended to a wide variety of drugs to achieve realistic analysis of differential costs of generic and brand-name preparations. If the physician and pharmacist are to use generic drugs, they must also be assured that these agents have a biologic availability equal to that of brand-name preparations.

The generic prescribing of pharmaceuticals is an issue that has gained increasing attention in recent years. The federal Government, since the passage of Medicare, has looked on generic prescribing as one approach toward reducing costs of administering present programs.¹ The problem is complex since it encompasses areas such as patient rights, established prescribing practices, quality and cost control and the economy of the pharmaceutical industry.² The practicing physician is particularly concerned with these problems

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¹ United States Department of Health, Education, and Welfare, Office of the Secretary, Task Force on Prescription Drugs, Third Interim Report, *Coverage of Drugs Under Medicare*, Washington, D.C.: Government Printing Office, December 31, 1968.

² Small Business, Select Committee on Senate, *Competitive Problems in the Drug Industry: Hearings before Subcommittee on Monopoly, 90th Congress, 1st session, on present status of competition in pharmaceutical industry*. Part 3. Washington, D.C.: Government Printing Office, 1968.

since he must have assurance that his generic prescriptions will be filled with a high-quality product and that the savings in cost will be passed on to his patient. The pharmacist is concerned because he is responsible for selection of a generic preparation ensuring both quality and savings to the patient and yet yielding a reasonable income to himself.

A joint committee of physicians and pharmacists, representing the Albemarle (Virginia) County Medical Society and the Charlottesville-Albemarle Pharmaceutical Association, was appointed in September, 1967, to review problems of mutual interest with particular attention to be paid to generic prescribing. It soon became evident that only a few commonly used drugs could be considered. Most agents were still controlled by patents, or were in the form of proprietary combinations. The cost differential of most was minimum in relation to frequency of use of the generic or brand preparations. Eleven drugs that appeared to offer a reasonable price differential to the patient were recommended: penicillin G, oral buffered; tetracycline; meprobamate; prednisone; dioctyl sodium sulfosuccinate; chloral hydrate; secobarbital; phenobarbital; dextroamphetamine; reserpine; and rauwolfia.

The joint resolution was adopted by the Albemarle County Medical Society on May 2, 1968, and a slightly modified version was approved by the Charlottesville-Albemarle Pharmaceutical Association on February 19, 1969. The resolution is as follows:

RESOLUTION

Introduction

The physicians and pharmacists of this region reaffirm their dedication to serve the public by prescribing and providing the very best drugs and biological agents at the lowest possible cost. The increasing complexity of modern day medicine has stimulated a review of problems of mutual concern to physician and pharmacist which affect the public interest. A Committee of these organizations has met to resolve these issues within the framework of the voluntary free enterprise system. Agreement has been reached on the following items:

1. Improvements in prescription writing
2. Labeling of prescriptions
3. The use of generic drugs

Other issues discussed, but not resolved, include fixed fee schedules by pharmacists.

It is hoped that these recommendations will improve the practice of medicine and pharmacy and that communication between physician and pharmacist will continue to be productive.

I. The Prescription Blank

The Committee has agreed to the following principles:

1. Prescription blanks should not be marked with names of pharmacies or appliance dealers (such as optometrists).
2. Prescription blanks shall not be accepted from drug house representatives that are prewritten with brand name drugs. Stamped prescription blanks prepared by physicians for routinely used drugs may, however, be used.
3. Physicians are urged to adopt a prescription form containing information on refill, size labeling, and expiration notices. It is recommended that the form be purchased by physicians from local printers without financial assistance from pharmacists.
4. Multiple prescriptions should not be written on a single blank.

II. Labeling of the Prescription

The Committee recommends that prescriptions given patients be labeled with the name of the drug unless the prescriber specifies otherwise. This practice will be helpful in emergency situations such as poisoning and treatment of acute episodes at the hospital. It is not uncommon for physicians to have patients bring in medicine prescribed by another doctor. It is time consuming and often frustrating to have to call the pharmacy to look up

the prescription number or to guess what the drug might be, from the shape or color of the pill or capsule. The Committee recognizes that in some instances, it may be desirable not to put the drug name on the label. Accordingly, the following procedure is recommended:

All prescriptions will carry the drug name, unless the physician indicates otherwise by checking appropriate space on the prescription form.

III. Generic Drugs

Every drug has at least two names, the brand name, given by the manufacturer, and the generic name which identifies the drug regardless of the source of distribution. A usually more complex chemical name may also be given. Every drug has a generic name, but the brand name is reserved for use by the manufacturer or distributor. Protection by patent laws permits only one manufacturer to market or license distribution by other companies using the generic name. In some instances, prescription of generic name drugs may result in substantial savings to the patient. The physician and pharmacist must, however, be assured that the quality and potency of a generic equivalent drug is as good as that sold by the prime manufacturer.

The Committee has attempted to resolve the problem of providing the patient with the cost advantage of generic equivalent drugs while assuring quality by the following mechanism:

The pharmacists agree that these prescriptions will be honored with quality product from a well recognized manufacturer. This will be accomplished by continued discussion by subcommittees of this association and the Albemarle County Medical Society. In addition, review of the generic drugs currently in use by pharmacies in this community will be undertaken by the pharmacists. They will consult with the committee periodically concerning the best generics that can be purchased at a reasonable price.

A survey of differential costs to the patient using the new system will be conducted at intervals with cooperating pharmacies, and use of the system by physicians will be reviewed periodically to determine the efficacy of the program. Cooperating pharmacists agree to permit members of the Committee to undertake these surveys provided that no individual store or physician is identified.

This report will deal with the effect of this voluntary program on prescription practices in the community.

METHODS

Study Area

The city of Charlottesville is the county seat of Albemarle County, Virginia. The 1968 population of the city and county is estimated at 79,300, with an additional 8000 students at the University of Virginia. Geographically, the county is located in the center of the state, Charlottesville being 120 miles southwest of Washington, D.C., and 72 miles west of Richmond, Virginia. Approximately 100 physicians are engaged in the private practice of medicine in the area. There are 152 full-time attending staff physicians at the University Hospital and 222 house staff and clinical fellows. Ten retail pharmacies serve the community in addition to pharmacies located at the University and Martha Jefferson hospitals.

The Albemarle County Medical Society draws its membership from both the University and the private sector of practice. Monthly meetings are well attended and marked by warm personal friendship among all elements of the medical profession. So-called "town-gown" friction is virtually absent. Officers and committees are well integrated between the two groups. The Charlottesville-Albemarle Pharmaceutical Association is a relatively young organization, representing all retail pharmacies and hospital pharmacists. Meetings are held as the need arises, about three or four times a year, with attendance usually exceeding 75 per cent of the membership.

Postal Survey

Shortly after the resolution was adopted by the Albemarle County Medical Society, copies were mailed to all members together with a postpaid card that queried physicians concerning their plans to use the recommended prescription forms, their opinion of the program and their interest in having it publicized in a suitable medical journal. Identifying signatures were requested on the cards.

Prescription Audit

A total of 3000 prescriptions, divided in groups of 1000, were analyzed during three separate intervals: March 28 to April 25, September 4 to October 15, and November 22 to December 28, 1968. The initial survey covered the period immediately before the passage of the joint resolution, and the latter two at intervals of three and six months after implementation.

Audits were conducted at two retail pharmacies. Store "A" is located in the immediate vicinity of the University. It could be expected that prescriptions being filled at this location would reflect prescription practices of physicians at the University Hospital and clinics, would be filled for patients representing a cross-section of the community and would also represent the prescribing habits of physicians in private practice since the store offered delivery services throughout the area. Store "B" was selected because it was located in the downtown area of the city, close to the local community hospital (Martha Jefferson), represented a survey site less under the influence of University prescribing practices, also offered delivery service throughout the community and drew its clientele from a cross-section of the community. On precoded forms information was then collected on study period, outlet, source of prescription, specific drug, generic or brand name, price and days covered by prescription size. Prescription prices were broken down by "cost per day," the cost of the prescription, the number of tablets or capsules prescribed and the number to be taken daily being used.

RESULTS

Physician-Opinion Survey

Responses to a mail survey of opinions regarding the joint resolution by members of the medical society are shown in Table 1. Replies were more complete from private practitioners than from members of the University staff. Both groups of respondents, however, indicated a positive attitude to the program in wanting to see it published. Physicians in private practice expressed willingness to follow the recommendations regarding prescription writing. The University staff already uses such forms. No formal survey of opinion of pharmacists concerning the resolution was conducted. Interviews indicated enthusiasm among many, and a somewhat more cautious approach by some. The overall attitude of the pharmacists was willingness to survey the generic drugs that they stocked to ensure high quality. A subcommittee of the pharmacists reviewed generic preparations already in stock to determine that they had been obtained from reliable sources.

TABLE 1.—RESPONSE BY MEMBERS OF THE MEDICAL SOCIETY TO A MAIL SURVEY OF OPINIONS REGARDING THE JOINT RESOLUTION

Survey	Private Practitioners		University Staff	
	Number	Percentage	Number	Percentage
Inquiries mailed.....	103	100	217	100
Replies.....	68	66	55	25
Information should be published:				
Agree.....	52	76	40	73
Disagree.....	6	9	4	7
No response.....	10	15	11	20
Agree to use new prescription form:				
Will change.....	43	63		
Already used.....	12	18		
Will not change.....	8	12		
No response.....	5	7		

Audit of Prescriptions

Most prescriptions were written by community physicians. They accounted for the same proportion during each study period (Table 2). Generic and study drug prescriptions contributed less than 10 per cent of the total.

TABLE 2.—AUDIT OF PRESCRIPTIONS BEFORE AND AFTER PASSAGE OF THE JOINT RESOLUTION BY THE MEDICAL SOCIETY (1,000 PRESCRIPTIONS IN EACH AUDIT)

Item of audit	[Percent]		
	Before resolution	3 months after resolution	6 months after resolution
Source of prescriptions:			
Community physicians	76.0	76.8	77.4
University hospital	22.2	21.3	21.6
Attending staff	(13.6)	(12.2)	(15.7)
House officers	(8.6)	(9.1)	(5.9)
Other	1.8	1.9	1.0
All generic prescriptions	6.2	10.4	9.4
Study prescriptions	7.7	9.2	10.5

Analysis of generic versus brand-name prescriptions of study drugs for each period is shown in Table 3. Only one third of these were prescribed generically before the resolution was adopted, but this figure rose to 59.8 per cent in three months and was 49.5 per cent six months later. The decrease in generic prescribing in the third study period may have been due to the promotion of an inexpensive brand of tetracycline (Sumycin). Tetracyclines accounted for half the study prescriptions during this period, which also coincided with the influenza season. There were 53 prescriptions written for tetracycline (brand or generic) during this audit period. Of these, 34 were filled with the inexpensive brand referred to above, 16 were written on a brand-name basis, and 18 were prescribed by the generic name.

TABLE 3.—AUDIT OF PRESCRIPTIONS BEFORE AND AFTER ADOPTION OF THE JOINT RESOLUTION BY THE MEDICAL SOCIETY, ACCORDING TO USE OF STUDY DRUGS

Use of drugs	Before resolution		3 months after resolution		6 months after resolution	
	Number	Percentage	Number	Percentage	Number	Percentage
Study prescriptions:						
Total	77	100.0	92	100.0	105	100.0
By private practitioners	55	71.4	60	65.2	87	82.9
By University staff	22	28.5	32	34.7	18	17.1
Prescribed generically:						
Total	28	36.4	55	59.8	52	49.5
Private practitioners	18	32.7	47	78.3	43	49.5
University staff	10	45.4	8	25.0	9	50.0

A total of 274 prescriptions for the 11 study drugs were filled among the 3000 audited. Of these, 215 (78 per cent) were limited to only four drugs; tetracycline; penicillin G, buffered; meprobamate; and prednisone (Table 4). It can be seen that in each case, the cost of the patient per day, as charged by the pharmacist, was less for the generically prescribed drug. Thus, it is clear that the pharmacists honored their agreement as set forth in the joint resolution.

TABLE 4.—AUDIT OF COST TO PATIENT OF DRUGS PRESCRIBED BY GENERIC OR BRAND NAME BEFORE AND AFTER ADOPTION OF THE JOINT RESOLUTION BY THE MEDICAL SOCIETY

Drug and type of prescriptions	Before resolution		3 months after resolution		6 months after resolution		Total average	
	Number of prescriptions	Average cost to patient per day	Number of prescriptions	Average cost to patient per day	Number of prescriptions	Average cost to patient per day	Number of prescriptions	Average cost to patient per day
Tetracycline:								
Generic	14	\$0.45	31	\$0.49	30	\$0.35	75	\$0.43
Brand name	9	.75	11	.57	23	.50	43	.57
Penicillin G, buffered:								
Generic	9	.25	15	.19	13	.23	37	.22
Brand name	8	.47	8	.54	12	.50	28	.50
Meprobarbital:								
Generic	1	.20	2	.35	2	.21	5	.26
Brand name	9	.29	3	.90	1	.30	13	.43
Prednisone:								
Generic	3	.23	5	.05	4	.08	12	.10
Brand name	2	.38	0	0	0	0	2	.38
Total	55	-----	75	-----	85	-----	215	-----

DISCUSSION

Several points clearly emerge from this study of a voluntary agreement between physicians and pharmacists in Charlottesville-Albemarle County, Virginia. The first is that both groups in the community are willing to act jointly to improve prescription practices. Secondly, the potential for prescribing generic drugs is severely limited by the small number available that would provide an economic advantage to the patient. Efforts by some manufacturers to lower prices of brand-name drugs in competition with other brands and generic drugs must be taken into account. Thirdly, pharmacists, at least among those audited, passed savings in cost to the consumer when generic drugs were prescribed.

It must be emphasized that this experiment was conducted in a relatively small community where "town-gown" friction is minimal and communication is good between various groups. Also, since the study drugs made up only a small proportion of total prescriptions, little local control could be exerted over most drugs. In this sense, very little effect should be expected on the average cost of prescriptions in the community. In addition, the manufacturers of tetracycline and corticosteroids provide such a wide variety of proprietary analogues and fixed dosage combinations that it is difficult for the physician to know the relative efficacy of the generically available patent compound.

Despite these limitations, the following forms of voluntary programs could emerge. First of all, other medical societies and pharmaceutical groups can begin to appoint joint committees to consider this prototype plan for their area. This might extend to regional groups established under Comprehensive Health Planning legislation.³ Secondly, local study groups can consider a voluntary community formulary system, perhaps based on a fee system for prescriptions, using the minimum number of variations of each type of drug. Good advice may be obtained from well informed hospital drug and formulary committees. Thirdly, there must be a clear guarantee that generic drugs are equivalent to brand-name prescriptions, both in capsule or tablet potency and in biologic availability as determined in studies in man. Fourthly, there must be evidence that prescription of an approved generic preparation will result in substantial savings to the consumer.

Finally, one of us (C.M.K.) believes that it would be extremely helpful to the practicing physician if every drug advertisement was required, by voluntary action of medical journals and other media, to indicate the average price of the drug to the pharmacist on the basis of small and large purchases of the preparation, of regional differences and of the cost per day of the recommended doses. This proposal must take into account the wide range in prices offered by manufacturers to their various outlets. The price a state institution, hospital or chain pharmacy pays, for example, is usually considerably less than that charged to a community pharmacy. Visibility of drug pricing would permit the physician to weigh cost advantage with claims made for the wide variety of single agents and combinations offered to him.

The members of the Joint Committee of the Albemarle County Medical Society and the Charlottesville-Albemarle Pharmaceutical Association were as follows: Calvin M. Kunin, M.D., chairman; Jesse Cumbia, M.D.; Richard Morris, M.D.; Edward Cawley, M.D.; John Owen, M.D.; George Minor, M.D. (ex-officio); Armistead P. Booker, M.D. (ex-officio); Sam Crickenberger, Ph.G.; Carson Payne, Ph.G.; James Hubbard, Ph.G.; Jacqueline Young, Ph.G.; and J. R. Ponton, Ph.G. (ex-officio).

Senator NELSON. Do you mean that the hospital is attempting to get local communities to adopt, or physicians to use, the Los Angeles General Hospital formulary?

Dr. STEINFELD. They are exploring what the problems would be associated with the introduction of formulary and generic prescription from communities in the southern California area. It is certainly far easier, to do in a single institution where the physicians are full time. There are many problems associated with trying to

³ Jacobs, A. R., and Froh, R. B. Significance of Public Law 89-749: comprehensive health planning. *New Eng. J. Med.* 279:1314-1318, 1968.

work this out but they, too, as the areas that Mr. Brands described, are experiments with models to see what the problems are in trying to carry it through.

Senator NELSON. One of the obvious among many problems, is that the hospital can procure the drugs for its formulary as a substantial buyer, with the knowledge that the compound will be prescribed. In the retail marketplace, on the other hand, you may prescribe generically and end up with a brand name because the brand name is a popular one and so you have not gained anything.

Dr. STEINFELD. This certainly can occur. There is a problem of education of physicians, education of pharmacists, and a whole series of working relationships that must be carried through.

Senator NELSON. With respect to these two experiments in Virginia and Delaware, were they locally initiated or were they initiated from some other source?

Mr. BRANDS. Those were locally initiated, sir.

Senator NELSON. So here you are talking about initiating a model project yourself; is that it?

Dr. STEINFELD. Well, the Los Angeles County one would be locally initiated, too, but what we try to do is stimulate the communities to initiate such experiments in delivery.

Senator NELSON. How long has that Virginia project been underway?

Mr. BRANDS. As I recall, it was just about 2 years ago when it was started. This was the beginning, the planning stage. Now, how long it has been in operation, this I would have to find out and let you know.

Senator NELSON. You do not have any reports?

Mr. BRANDS. No, sir.

Senator NELSON. Where is it being done in Virginia?

Mr. BRANDS. I believe it is Richmond.

Senator NELSON. In association with the Medical College at Richmond?

Mr. BRANDS. I do not believe the Medical College is involved. It may be as an adviser but the Pharmacy Association and the County Medical Society were the organizers.

Senator NELSON. But you say your role is to induce this kind of experimentation? In what way? How will you do that?

Dr. STEINFELD. Well, there are a number of medical schools or county medical societies interested in the problem in association with pharmacy groups and pharmacists and we, through the Department's interest in the same problem, informed these groups that funds are available for such kinds of experimental programs. In this way I think we can encourage them, help them to complete funding applications, tell them what problems we know about, what problems people who have attempted to do this in the past have encountered.

So it is kind of a mutually reinforcing activity. There are a number of places in the country in addition to those Mr. Brands mentioned which are interested in carrying out experiments of this type.

Senator NELSON. Please proceed.

Dr. STEINFELD. Thank you.

Physician and other professional reaction to the FDA publication has been encouraging. A sizable amount of correspondence has given FDA some measurement of the publication's readership effectiveness. And, nearly 1,000 requests have come in from other health professionals seeking to be placed on the mailing list.

FDA also plans to publish a comprehensive report on all drugs reviewed by NAS-NRC, along with the summary from NAS-NRC on the drug efficacy study. This will supplement the recent FDA publication of the list of drugs found ineffective by NAS-NRC review which has been sent to county and State medical societies, hospitals, and other government agencies, and is available to others who request it.

Senator NELSON. You say FDA also plans to publish a comprehensive report on all drugs reviewed by NAS-NRC. Is that part of their current drug information publication?

Dr. STEINFELD. This would be a separate document, Senator Nelson, which would encompass the total drug efficacy review, a summary plus a list of the various drugs in the various categories. We are planning, at least at this point, to distribute it to all physicians.

Senator NELSON. Will this come out as one big publication?

Dr. STEINFELD. One publication.

Senator NELSON. And what is its purpose?

Dr. STEINFELD. Its purpose is to inform the practicing physician of those drugs which were found ineffective or probably effective, or possibly effective, to inform him of the criteria which were used by the various panels in making these recommendations, and to inform him of the problems the panels encountered as they have submitted their evaluations in their original report to the Commissioner of the FDA. I think it will serve a very useful purpose.

Senator NELSON. This review is not over yet, is it? Will they have a series of publications on this subject?

Dr. STEINFELD. Well, we think the review will be over fairly shortly. We hope to publish the remaining list of drugs in the next few months.

Senator NELSON. So this will cover all the drugs covered by the Kefauver amendments, 1938 to 1962?

Dr. STEINFELD. This will cover the drugs reviewed by the NAS-NRC and be really what we think is a final summary. Of course, new knowledge may result in changes and there would have to be supplements. Perhaps the bulletin that the FDA publishes could be used for that purpose, but it would be an extensive document because of the number of drugs involved.

Senator NELSON. Well, of course, on each one of the drugs that each panel considered, the NAS-NRC made a statement. This will be a more elaborate discussion; is that correct?

Dr. STEINFELD. This will be a summary document which will be written primarily to help the physician to give him the background data which the NAS-NRC used in making its judgments as well as their judgments. It will not be the total mass of material transmitted from the National Academy of Sciences to the FDA. It will be just a summary, hopefully usable and used by the practicing physicians.

Senator NELSON. Go ahead.

Dr. STEINFELD. FDA has for some time been issuing routine publications on adverse drug reactions reported to FDA, general news releases, and, in extreme emergencies, telegrams to county and State medical and pharmacy societies.

This overall goal of communicating with the physician is being developed in a new unit established for this purpose in the FDA's Bureau of Drugs. The Assistant to the Director for Medical Communications is responsible for continual development of communication techniques designed to reach the physician and to promote rational drug therapy.

The Department is taking the approach that continuing education is the best method of bringing about rational drug therapy. As you know very well, most people, especially physicians, resent edicts of "you shall" or "you shall not." We plan to appeal to the logic of the Public Health Service physician by bringing to his attention the results of important published studies on individual drugs and classes of drugs. The information will be conveyed by a short covering statement that summarizes the study or studies with a copy of the published article attached. Copies of the NAS-NRC report and Federal Register material pertaining to the drug may also be included.

Three such statements have been prepared and distributed for the programs in Health Services and Mental Health Administration an amphetamines, mixed dose combination drug products, and on propoxyphene hydrochloride.

I have copies for the committee available here.¹

These statements are designed to bring potential problem areas in drug usage to the attention of physicians and pharmacists in the Public Health Service.

You have already been advised by Commissioner Edwards that the FDA is giving priority to insuring the biological equivalency of drugs sold under the same name. This meets recommendation 14, that present clinical trials to determine the biological equivalency of important chemical equivalents should be continued.

Mr. GORDON. Dr. Steinfeld, may I interrupt a moment?

Do you see any trend in the direction of more rational drug therapy? Actually I have three questions. That is one of the three. Two, is it your opinion that FDA will have to take the lead in bringing this about? And three, would it not be helpful if the Government presented a good example in its usage and purchasing of drugs?

Dr. STEINFELD. First, I do think that we are making progress in rational prescribing. We are making it particularly as a result of the Kefauver amendments and the requirements that drugs shall be proven efficacious as well as safe for use.

I certainly agree that the Government should be a leader in good rational prescribing practices and it is apparent from the hearings which you have been carrying out these past several months that the Government has not always been a leader in this area.

¹ See pp. 8331-8339.

I think what we need is a consortium of universities, certain practicing physicians who are knowledgeable and have carried out adequate controlled clinical trials along with the FDA and possibly NAS-NRC in order to obtain the best kind of drug knowledge available in the country. I do not believe a single Federal organization has within it all the necessary knowledge or expertise to make the kind of judgments that I think we would want to have made for drug prescribing. So we will have to develop this expertise through a continuing interaction such as with the NAS-NRC with its academic physicians and the FDA in carrying out the second role which you described.

This Department and the Congress are providing financial support to FDA for necessary educational and inspection operations. Within this level of support significant improvements in quality control are being instituted and maintained in drug manufacturing and packaging establishments. The following are among the initiatives being taken by FDA:

(1) An Intensified Drug Inspection Program (IDIP) has been quite effective in bringing the need for quality control to the attention of drug industry management. This program involved the assignment of inspectors to selected drug manufacturing establishments on an extended basis to detect and assist in the correction of manufacturing defects. This inspectional surveillance covered all manufacturing steps; that is, the examination of raw materials, formulation mixing, production of dosage forms, and quality control procedures.

(2) Revised good manufacturing practice regulations for the drug industry were published in the Federal Register on January 15, 1971. I have a copy here for the committee's information.¹

(3) The development and dissemination to the drug industry of drug recall case histories has been begun. These cases analyze the causes of drug manufacturing defects and describe the remedial actions taken. They serve as a useful industry information and educational device.

(4) Drug manufacturing and quality control workshops have been held in various sections of the Nation in which over 1,900 drug industry employees participated. Approximately 7,000 key drug industry personnel have also attended showings of the FDA film, "Good Manufacturing Practices."

Recommendation 17 asked for a test of the proposed drug classification system. The system is being tested in a drug utilization review study now underway. A report is due next month.

The Department has developed an appropriate drug coding system as proposed in recommendation 18. It is designed to meet the need for a single, comprehensive nomenclature, and coding system for identifying drug products covered by departmental drug-financing programs and private third-party programs. Use of the code can enable high-speed data handling equipment to process millions of claims and other pieces of drug information with tremendous speed, accuracy, and economy.

¹ See pp. 8339-8347.

The National Drug Code System was developed under the direction of the Nomenclature and Coding Subcommittees of the Task Force on Prescription Drugs and there was close cooperation with representatives of drug manufacturers and distributors, private insurance companies, and government agencies.

Recommendation 18 also suggested that the Department introduce appropriate legislation to require coding of all drugs in interstate commerce. Such legislation was introduced in the 91st Congress, and as mentioned earlier, has now been resubmitted.

The drug code just discussed has been adopted. The Department has published and distributed two editions of the National Drug Code Directory. The second edition, published in June 1970, includes coding data for more than 18,400 drug products marketed by some 265 companies. We have supplied copies of this document earlier to the committee.¹

Many manufacturers have begun to use national drug code identifications in catalogs and promotional material. Some firms have voluntarily placed product identification symbols of the code on tablets and capsules. Use of the code is voluntary, however, and we cannot at this time require it on labeling or on tablets and capsules.

Recommendation 20 requested that the National Center for Health Services Research and Development support pilot research projects looking toward the development of good prescription drug utilization review methods. Shortly after the task force report appeared, the Center supported a comprehensive study of drug utilization review. The study was published in April 1970 in a document entitled "Drug Utilization and Drug Utilization Review and Control." I have a copy here for the information of the committee.²

Since July 1970 the Center has provided consultation to a number of universities and community hospitals and other groups regarding their responsibilities in relation to drug utilization review.

Other studies have been and are being supported not only by the National Center for Health Services Research and Development as suggested in recommendation 20 but also by the Social Security Administration and the Social and Rehabilitation Service of HEW. A number of examples are:

A study at the University of Rochester on patient care research in adverse drug surveillance.

A study at the University of Alabama Medical Center of a hospital pharmacy-based drug communication service.

A study at the University of Kentucky Research Foundation of guidelines for practical hospital unit dose systems.

A study at the University of Mississippi of the pharmacist's role in hospital pharmacy committees.

A study at the University of Pittsburgh of socio-economic analysis of EDP-based drug utilization.

A study at Johns Hopkins University of the development of a methodology for evaluating the drug prescribing patterns of physicians in a given community.

¹ The document, "National Drug Code Directory, 2d Edition," June 1970, has been retained in committee files.

² See pp. 8348-8422.

A study at the University of Arkansas Medical Center Hospital of a proposed intrahospital drug distribution system.

A study at the Los Angeles County General Hospital of drug utilization review with on-line computer capabilities.

A study at the University of California School of Medicine of patterns of influence among pharmacists, physicians, and patients.

A study being conducted in four States—Colorado, Rhode Island, Oklahoma, and West Virginia—by the Medical Services Administration of the Social and Rehabilitation Service, together with staff members and a contractor, Publication Engineers, Inc., to develop model utilization review systems that may be adapted for all States with Medicaid programs.

A study by Touche Ross & Co. on interim requirements for the Medicaid surveillance and utilization review reporting system.

Further, a Drug Utilization Review Committee was established last fall in my office with representatives from FDA, HSMHA, SRS, and SSA to study developments to the present and recommend further steps that should be undertaken by the Department. Recommendations of this Review Committee will be utilized in determining what further measures may be required by our Department.

The complex of drug activities that was assigned to FDA in February 1969 continues to be administered by that agency as suggested in recommendation 21. (Certain reassignments resulting from the formation of the Environmental Protection Agency have no impact upon FDA's drug activities.)

The skills of experts both within and outside the Department of Health, Education, and Welfare are being used to augment the scientific capabilities of the Food and Drug Administration as proposed in recommendation 23. We have participated in and utilized information from many interdepartmental committees and we plan continued use of such groups. Examples include a study group on drug research and study group on medical services, both of which tapped the resources of several segments of the various health agencies within this Department.

Senator NELSON. What was recommendation 23?

Dr. STEINFELD. To use more experts both within the Department and outside in augmenting the scientific capabilities of FDA. The concern is that FDA was carrying out many of its responsibilities without adequate consultation with other experts.

We have recommendation 23, I can read it if you would like.

Senator NELSON. Yes.

Mr. RANKIN. The recommendation is:

Efforts should be strengthened to assure that the skills of experts both within and outside of the Department of Health, Education, and Welfare are used to augment the scientific capabilities of the Food and Drug Administration.

Senator NELSON. Please proceed.

Dr. STEINFELD. Interdepartmental committees have also been used to supplement the scientific capabilities within FDA. An ad hoc committee on toxicological procedures employed experts from the Environmental Protection Agency and the Department of Agriculture as well as industry representatives. Their report is not yet complete.

The Commissioner of Food and Drugs has been delegated authority to establish ad hoc committees to advise him on matters of importance and urgency.

Earlier I thought I could not address recommendation 24 of the task force report which suggested establishment of additional FDA basic and clinical laboratories to augment its research capability. However, on January 27, the President announced the establishment of the National Center for Toxicological Research at the Pine Bluff Arsenal in Arkansas.

The President's budget request for fiscal year 1972 contains an additional \$4 million for the FDA for a long-term program to determine the cumulative effect of chemical additives, and to establish levels of such additives which can be safely tolerated by man. The Pine Bluff facilities will be equipped to make low-dosage studies on large populations of animals, what has been called the mega-mouse experiments in some quarters. The dosages will much more nearly approximate quantities consumed by man. The results of these studies, therefore, should provide much better support for developing consumer protection policies with regard to various kinds of additives. This facility should be an important laboratory addition to our resources for assessing potential hazards to man which may exist or which may develop.

Senator NELSON. Well, that lab is already there.

Dr. STEINFELD. Yes. That lab is engaged in the disposal of the biologic warfare stockpile currently.

Senator NELSON. But there is going to be a series of studies conducted there on food additives and their effects?

Dr. STEINFELD. On food additives and other chemicals, yes, sir. The idea is that as soon as the place is certified to be free of any hazard, both FDA and EPA will begin renovating and constructing the necessary facilities to carry out large scale animal testing.

Senator NELSON. Food additives and what other things?

Dr. STEINFELD. Well, there are other chemicals to which we are exposed which may get into our water supply.

Senator NELSON. Are you talking about herbicides, pesticides?

Dr. STEINFELD. Pesticides and recently the things we find in detergents. I think any of the chemicals to which we are exposed in large measure should certainly be tested. The thing we have not done, Senator Nelson, is compare the interaction of a number of these chemicals and this is one of the real problems. The problem was not NTA alone but NTA picking up methyl mercury or other metals and transporting it where it ordinarily would not go. So the interactions are a big area that still must be studied.

Recommendation 25 proposed a study to reappraise the efficiency of methods now used in our Department to evaluate the safety and effectiveness of pharmaceuticals. In December 1969, the Secretary authorized convening of a study group (HEW study group on research and regulation) to act on this recommendation. This study group was made up of representatives of the Department (OS, NIH, and FDA), industry, higher education, and consumer groups. It met regularly from January to May 1970 and filed a report with the Commissioner of Food and Drugs during June 1970. The report is still under consideration at this time.

Mr. Chairman, I have outlined the status of our actions on 16 of the 25 recommendations of the task force. The remaining recommendations relate to matters currently under study in the administration's development of a coordinated health program for the Nation. As explained earlier, I am not prepared to state departmental or administration policy on these matters at this time.

It is evident that both the legislative and the executive branches are greatly concerned that good drugs be supplied the American people at reasonable prices. The interest and attention of this committee have without doubt been a large factor in the increased attention our Department is giving to its own drug procurement practices.

As indicated in the statement I have just made, and in other testimony you have heard, there are a number of activities being undertaken concurrently within our Department that should increase the effectiveness of Federal dollars used to purchase drugs and serve as an aid to more rational utilization of drugs in medical practice generally.

Some of the more significant developments are the steps FDA is taking to be sure that drugs are effective; improved methods of detecting and reporting adverse effects from drugs; improved communication with physicians on drug questions; the recognition that drug utilization review is an essential tool to insure better therapy at less cost; and the improvement of our management practices in the various components within the Department.

I believe, Mr. Chairman, that we are making significant progress. And I want to thank you for your patience in allowing me to read this very long statement.

Senator NELSON. Thank you, doctor. Do you have any questions, Mr. Gordon?

Mr. GORDON. Dr. Steinfeld, on page one you talk about a Medicare-Medicaid program for inpatients and outpatients—that is, not reimbursing for those drugs which have been found to be ineffective and possibly effective.

Now, how would you be able to monitor these drugs? Isn't it going to be rather difficult because they are on a reimbursement basis?

Dr. STEINFELD. Well, the Social Security Administration and Social and Rehabilitation Service at this point are working with us to try to figure out the best system to implement this decision. It will be difficult to monitor but I think it will be worthwhile and that it will improve patient care.

Mr. GORDON. Are there any figures to indicate how much money will be saved by this new policy—either in direct purchases or as reimbursement? Is it possible to make an estimate?

Dr. STEINFELD. Mr. Gordon, I am not certain at all that any money will be saved. I think the primary result of this decision will be to improve patient care. The physicians who are picking ineffective or possibly effective drugs for various indications will now have to choose either effective or probably effective drugs and they may cost less than, as much as, or even more than, the drugs that are now being used. But this is not a cost reduction device. It is primarily an improvement in the quality of care that we are seeking.

Mr. GORDON. What do you plan to do about the "probably effective" drugs? For example, do you see any reason for using a "probably effective" drug if there is an alternative drug known to be effective?

Dr. STEINFELD. This is a real problem. In the NAS-NRC review they found, as you know, many studies which were really not too well carried out. They were not certain that the drug was really effective for the indication for which it was proposed. So that what we are requiring for the probably effective drugs is that the companies, if they propose to continue manufacturing them, provide use data, good data, which would demonstrate the drug is indeed efficacious for the indication for which it is proposed. They have a year in which to either provide that data or provide protocols showing that the data will be forthcoming.

Now, I can conceive of instances where a patient may be allergic to an effective drug for a particular complaint and that therefore the physician may have to use a probably effective drug. I could conceive of some instances of cost differentials, perhaps, some instances where a physician is convinced that something really does work, and has a great deal more experience with what is called a probably effective drug than with an effective drug, and thus might continue using it—so that I can see instances where probably effective drugs would continue to be used until such time as we have adequate data to determine either that it is effective or it is not.

Mr. GORDON. But they will be used except when you know that an effective drug is available and the patient is not allergic to it, and so forth?

Dr. STEINFELD. Ideally the physician would use the effective drug. I think the panel felt probably effective drugs most likely with some additional information would fall into the effective category. In earlier years the companies did not have to demonstrate effectiveness in the way they do now, so a number of the studies on which approvals were based, we would now fault in terms of present knowledge and present scientific criteria; these will have to be brought up to date or the drugs will then be placed in another category.

Mr. GORDON. Now, the HEW task force report gives as one example of irrational prescribing—this is on page 24 of the task force report—the use of a costly duplicative or "me-to" product when an equally effective but less expensive drug is available. You probably heard this morning that AID will no longer finance such drugs. Dr. Edwards told us when he was here on January 18 that—

The Government as a major purchaser of drugs should and must insist on the least expensive of equivalent drugs and upon rational choices among different drugs which satisfy the same medical needs.

I am quoting him.

What do you plan to do about this form of irrational drug usage and purchasing?

Dr. STEINFELD. You are raising here for the non-Federal direct programs, the whole question of the formulary, which is certainly one of the things we have under intensive consideration as one of the parts of the overall health program which the President will cover in his message, but I do not think I can address that issue now. I think that is the formulary issue.

Mr. GORDON. Are you saying we should have a formulary for Government purchasing?

Dr. STEINFELD. No.

Mr. GORDON. You say it is a formulary issue. What are you saying?

Dr. STEINFELD. I am saying this is one of the things we have under discussion and that I cannot say what the Government's position will be at this point. I am sorry.

Mr. GORDON. Now, Dr. Steinfeld, as you know, neither the USP nor the National Formulary recognizes sustained release preparations as being reliable dosage forms. Expert testimony before our subcommittee has confirmed this view and Dr. Edwards told us on January 18 that the majority of those currently on the market have not provided adequate evidence, and in general, they appear to be quite unreliable.

These are generally expensive drugs on which the Federal Government has been spending considerable funds. Do you think the use of these drugs by the Government is rational?

Dr. STEINFELD. Well, let me tell you what our policy has been. The NAS-NRC did not look at sustained release drugs; they looked at the individual drug in its regular form. So as a matter of policy, the FDA put the sustained release version of any compound in a lower category from the rating given the regular form.

For example, if a drug was "effective," the sustained release one would be rated "probably effective." If it was "probably effective," the sustained release form would be rated "possibly effective," a "possibly effective" would be rated "ineffective" and the manufacturers would then be required to provide us with adequate information showing that in fact the sustained release compound did do what it was supposed to do—provide a concentration over a period of time.

They are, as you pointed out, erratic, difficult to standardize with different people, and I think very likely we would find fewer uses for such compounds. Where they can be shown to work, I can conceive of places where they would be useful—nursing homes, for example. Rather than having somebody distribute drugs four or five times a day, the sustained release compound would be extremely useful, if indeed it works.

So I think there are places where it would be useful but we are going to have to require evidence that indeed they do perform as advertised.

Mr. GORDON. But until they show that they cannot perform, what do you recommend the Government do?

Dr. STEINFELD. We are going to proceed as we have with the classification I just described. We are going to—

Mr. GORDON. Do I understand you recommend the Government not buy such drugs until they are proven to be effective, reliable, et cetera?

Dr. STEINFELD. Mr. Gordon, those which are in the ineffective or possibly effective category we would not buy. Those that are probably effective we could buy now. None of them would be "effective" because all of the sustained release drugs are one category lower in the NAS-NRC scale than the regular dosage forms.

We are going to be purchasing relatively few of these and we certainly will require within the very near future adequate evidence that they indeed do work.

Senator NELSON. The probably effective classification category has 1 year? Is that it?

Dr. STEINFELD. Yes, sir.

Mr. GORDON. Does HEW buy or pay for Peritrate in any of its programs?

Dr. STEINFELD. I cannot answer that.

Do you know, Mr. Brands?

Mr. BRANDS. We had none reported in our list. The purchases may have been so small, however, that it was not recorded. It was not picked up in our search of the purchase orders.

Mr. GORDON. You would not know if you are reimbursing for it, either?

Mr. BRANDS. We would not know if we were reimbursing for it.

Mr. GORDON. Dr. Edward Freis, Senior Medical Investigator at VA Hospital here in Washington, told us that the controlled studies indicated that Peritrate is not effective compared to a placebo. So apparently he regarded that as an ineffective drug.

Would that be in the same class as the other ineffective drugs judged by the National Research Council and you would refuse to reimburse for that drug?

Dr. STEINFELD. I would have to look that one up specifically, Mr. Gordon, but if it fell in those categories, possibly effective, effective, we would refuse.

Mr. GORDON. It was not reviewed by the NAS-NRC?

Dr. STEINFELD. Peritrate was not?

Mr. GORDON. No.

Dr. STEINFELD. We will have to—maybe it was after, developed after 1962.

Mr. GORDON. I think it could have been developed before 1938.

Dr. STEINFELD. Before 1938?

Mr. GORDON. I do not know. It might have been.

One more question. What steps have you taken since you appeared here in August to buy more competitively?

Dr. STEINFELD. I am afraid I did not hear you, I am sorry.

Mr. GORDON. Since your appearance here in August, what steps have you taken to buy drugs on a more competitive basis?

Dr. STEINFELD. Mr. Brands is our purchaser.

Mr. BRANDS. Our steps taken at the HSMHA Supply Service Center at Perry Point, are really the same as they have been—to request bids for the drugs that are purchased other than those that are purchased from the Department of Defense in Philadelphia.

We have 102 companies that are on the bidding list at the Supply Service Center. They do put a notice in the trade journals that they will receive bids from companies interested in bidding on pharmaceutical products. Such companies should notify the Supply Service Center at Perry Point, Md.

Now, of the 102 companies that are on the bid list, there are 53 that are in the small business category and 49 classified as large businesses.

Mr. GORDON. Are you buying these on a formal advertising basis?

Mr. BRANDS. Yes, sir. These are bought on a formal advertising basis by the Supply Service Center at Perry Point for drugs that are supplied by them.

Mr. GORDON. Now, on a dollar basis what percentage of the total purchases are advertised?

Mr. BRANDS. I would have to get that for you, sir. I do not have that now.

(The subsequent information was received and follows:)

PURCHASES BY FORMALLY ADVERTISED BIDS BY HEALTH SERVICES AND MENTAL
HEALTH ADMINISTRATION SUPPLY SERVICE CENTER

Formally advertised bids to purchase drug products accounted for 33.1 percent of the purchases at the Supply Service Center. Below is a breakdown of the drug purchases.

	Value	Percent
Formally advertised bids.....	\$384,503	33.1
Informally advertised bids.....	140,550	12.1
Veterans' Administration.....	8,851	.8
Department of Defense.....	627,260	54.0
Total.....	1,161,164	100.0

Informally advertised bids are for amounts of less than \$2,500 and are sent to about three to five manufacturers for quotations.

Many of the drug products purchased from the Veterans Administration and the Department of Defense were probably purchased after formally advertising for bids.

Dr. STEINFELD. I could add one point. We will look into the Peritrate both as a single compound and in sustained release form and provide a report to you as to why it was not looked at by NAS-NRC, as to what we propose to do.

(The subsequent information was received and follows:)

Peritrate was reviewed by the NAS/NRC. However, the Food and Drug Administration has not yet implemented the recommendation.

Peritrate Tablets were approved for marketing in August, 1951; Peritrate Sustained Action Tablets in October, 1955, and Peritrate Sustained Action with Phenobarbital Tablets in March, 1962.

Dr. STEINFELD. Of course, in addition to Dr. Freis's comments, we would want to review the literature and determine whether indeed it was subject to the law between 1938 and 1962 and all of the other evidence that NAS-NRC considered in making its judgments. We will review that.

I would add as a corollary to Mr. Brands' statements regarding what we have done to make our purchases more rational, that we have certainly tried, as in the recent memorandum of December, to rule out purchases of ineffective and possibly effective drugs.

Senator NELSON. Thank you very much, doctor.

Dr. STEINFELD. Thank you.

Senator NELSON. Our hearings will resume tomorrow in this room at 10 o'clock.

(Whereupon, at 12:20 p.m., the Subcommittee on Monopoly of the Select Committee on Small Business adjourned, to reconvene the following morning at 10 a.m., Tuesday, February 2, 1971.)

(Upon the direction of the Chairman, information pertaining to the hearings follows:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
Rockville, Md., May 12, 1971.

HON. GAYLORD NELSON,
Chairman, Subcommittee on Monopoly, Select Committee on Small Business,
U.S. Senate, Washington, D.C.

DEAR SENATOR NELSON: This is in reply to your February 23, 1971 request for comments on problems raised by letters sent to Commissioner Edwards on February 10 and 19, 1971, by the Pharmaceutical Manufacturers Association, Washington, D.C. We forwarded an interim reply to you on March 10, 1971.

We are enclosing a copy of Commissioner Edwards' March 18, 1971 response to these letters. If we can furnish any additional assistance, please let us know.

Sincerely yours,

M. J. RYAN, Director,
Office of Legislative Services.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
Rockville, Md., March 18, 1971.

C. JOSEPH STETTLER,
President, Pharmaceutical Manufacturers Association,
Washington, D.C.

DEAR MR. STETTLER: Your letters of February 10, 1971, and February 19, 1971, comment on our testimony before the Nelson Subcommittee on January 18, 1971, and my letter of February 5, 1971, to Senator Nelson.

The first letter charges us with a tendency to escalate the role of the agency in drug therapy, beyond the point where Congress has given us authority. You are particularly concerned with our interest in problems of relative efficacy, over-prescribing of drugs, generic equivalency, and class labeling. You also criticize us for removing possibly effective drugs from Federal programs and for our releases explaining the NAS/NRC findings.

We are confident that we are proceeding with the implementation of the 1962 Drug Amendments in the way that Congress intended. We have now substantial judicial support for that belief.

With regard to the question of relative efficacy, it is our interpretation of the intent of Congress that we could not exclude a new drug from the market on the ground that it was relatively less effective than another available drug (except when the benefit-risk ratio requires this), but we can and do require full disclosure labeling and promotion for new drugs which in many instances requires a discussion of precisely where the new drug belongs in relation to other available drugs in safe and effective clinical use. Most advertising of newly-marketed drugs is competitive, requiring us to give consideration to the validity of claims of relative efficacy.

Over-prescribing should be of as much concern to manufacturers as to us. It can only lead to more problems for all of us. Our discussion of this problem was not linked with the social problem of drug abuse, but to promotion, prescribing, and use of drugs of limited or no value and to the consumption of too many drugs, often for no purpose or for the wrong purpose. On drug equivalency, we noted that this problem is being addressed in a number of ways—through good manufacturing practice regulations, intensified drug inspections, and increased surveillance from our National Center for Drug Analysis, for example. And we concluded by saying that on the basis of the evidence available, the quality of marketed drugs in regard to purity and uniformity of composition is not suspect. We think it is a disservice to the public to use a few episodes where drug equivalency was drawn in to question to imply that the whole drug supply is in doubt. We disagree with your conclusion that because a few instances have occurred, this is probably a very frequent phenomena. You raise the question regarding our ability to test all batches of imported antibiotics; this has been going on for several years.

In our opinion class labeling is necessary to provide the profession with reliable and understandable prescribing information. The practice of presenting different

labeling of drugs of essentially the same therapeutic effectiveness and safety is confusing and misleading to physicians and doesn't lead to informed patient care.

We agree with you that your firms have been helpful in developing the rules applicable to current good manufacturing practice. We acknowledge our role in the development for many of the package inserts that are now found to be inadequate and misleading. Under authority of the current law which permits regulation of claims of effectiveness, we hope to correct this problem.

Your letter of February 19 is disappointing to us. All of the points you have made have been argued strenuously before at least two Courts of Appeals and a District Court. There is no need for us to answer them here, as we have in Court. But what is important is to get on with the DESI project. We have been willing to accept NAS/NRC evaluations of claims as "effective," without insisting upon proof by adequate and well-controlled clinical studies. But where the evaluation is less than effective, the product must be withdrawn unless an adequate data base to support the claims can be developed. The sooner your companies turn to this task, the better it will be for all of us.

At Senator Nelson's request, I am forwarding a copy of this letter to him.

Sincerely yours,

CHARLES C. EDWARDS, M.D.,
Commissioner of Food and Drugs.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
Rockville, Md., March 10, 1971.

HON. GAYLORD NELSON,
*Chairman, Subcommittee on Monopoly, Select Committee on Small Business,
United States Senate, Washington, D.C.*

DEAR SENATOR NELSON: This is in reply to your February 23, 1971 request for comments on problems raised by letters sent to Commissioner Edwards on February 10 and 19, 1971, by the Pharmaceutical Manufacturers Association, Washington, D.C.

Answers to these letters are in preparation and we will respond further to your request after these replies have been formulated. If we can furnish any additional information, please let us know.

Sincerely yours,

M. J. RYAN, Director,
Office of Legislative Services.

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., February 23, 1971.

DR. CHARLES C. EDWARDS,
Commissioner, Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C.

DEAR DR. EDWARDS: Enclosed is a letter I received from the President of the Pharmaceutical Manufacturers Association, to which he attached his letters to you of February 10 and 19, 1971.

Since it is planned to place this material into the printed record of the Subcommittee's hearings, as requested, I would appreciate your comments on the problems raised by the PMA's letters. This is to insure a fair and balanced presentation of the subjects under discussion.

Very truly yours,

GAYLORD NELSON,
*Chairman,
Subcommittee on Monopoly.*

PHARMACEUTICAL MANUFACTURERS ASSOCIATION,
Washington, D.C., February 19, 1971.

HON. GAYLORD NELSON,
*Chairman, Monopoly Subcommittee, Senate Select Small Business Committee,
Old Senate Office Building, Washington, D.C.*

DEAR SENATOR NELSON: At the time of the hearings of the Monopoly Subcommittee of the Senate Small Business Committee which were conducted on February 1, 1971, you circulated a statement dealing with correspondence from the

PMA relative to Government agency policy on the procurement of drugs listed as "ineffective" and "possibly effective". Attached to your release was a letter to you from Dr. Charles C. Edwards, Commissioner of Food and Drugs, dated January 29, 1971.

This letter purported to review the actions of the pharmaceutical industry with respect to the submission of proof of effectiveness for drugs approved for marketing between 1938 and 1962. In our opinion, Dr. Edwards' letter does not present a balanced review of the history of the drug industry activities in this regard. We would appreciate it, therefore, if you would insert the enclosed letter to Dr. Edwards in the printed transcript of the hearings for the February 1, 1971 session of the Monopoly Subcommittee.

Sincerely yours,

C. JOSEPH STETLER,
President.

PHARMACEUTICAL MANUFACTURERS ASSOCIATION,
Washington, D.C., February 19, 1971.

CHARLES C. EDWARDS, M.D.,
Commissioner of Food and Drugs, Department of Health, Education, and Welfare, Rockville, Md.

DEAR COMMISSIONER EDWARDS: This is in reference to your letter of January 29 to Senator Gaylord Nelson commenting on a PMA press release and my earlier letter concerning recent efficacy review actions of the FDA and the Public Health Service.

We take issue with your statement that "no real effort to comply" with the efficacy requirements of the 1962 Amendments was made by pharmaceutical manufacturers.

Prior to your appointment as Commissioner of Food and Drugs, the pharmaceutical industry met with officials of the Food and Drug Administration in order to achieve an orderly compliance with the 1962 Amendments. I wrote to FDA Commissioner Larrick on November 29, 1963, requesting that the Agency and the industry work together to formulate a program that would meet the intent of the law in an effective way. Unless such a program is devised, I wrote, "many companies will be spending time and money wastefully in doing unnecessary things, while others may do nothing and have a rude awakening ten months hence when suddenly they are asked to justify the continued marketing of established products."

Commissioner Larrick agreed to a meeting, and representatives of the Agency and the industry met on January 23 and February 6, 1964. The attitude was one of cooperation and the exchange of ideas was helpful to both sides.

A point of prime significance that was discussed at the meetings was the definition of the "substantial evidence" requirement of the law. FDA General Counsel Goodrich made it clear at both meetings that well-documented clinical experience, which would lead experts fairly and reasonably to conclude that the claims are valid, would be considered in answering the efficacy question. Indeed, such evidence was to be controlling in some situations. Accordingly, clinical studies were not commenced by manufacturers on products for which well-documented clinical experience existed.

I might mention that minutes of these two meetings were reviewed by the Office of the Commissioner and no changes or objections were offered. The minutes were, of course, shared with the member firms of this Association of the time of the meetings for their guidance in attempting to fulfill purposes of the law.

Further evidence of the FDA's willingness to recognize well-documented clinical experience was given in a press release issued by the Agency dated February 28, 1964, which presented the FDA position on effectiveness requirements for pre-1962 drugs. It clearly equated "clinical experience" with "substantial evidence of effectiveness" on its first page.

Moreover, the essence of the policy described at the meetings had already been laid down in FDA regulations published January 10, 1964, concerning permissible claims that could be made in advertisements for pre-1962 prescription drug products. They provided in part that "an advertisement may recommend or suggest the drug only for those uses contained in the labeling thereof . . . for which there exists substantial clinical experience, adequately documented in medical literature or by other data (to be supplied to the FDA, if requested),

on the basis of which it can fairly and responsibly be concluded by qualified experts that the drug is safe and effective for such uses". Amended regulations covering the same subject contain substantially the same provision.

Relying on the record so established, the companies proceeded to submit such material as they had reasonable grounds to believe were required.

Virtual silence on this subject followed, until the FDA announced its desire in 1966 to turn the massive task of reviewing the evidence over to the NAS/NRC. The industry commended FDA for this decision, incidentally, and gave its full cooperation to the planning and implementation of the arrangement, contrary to the implication of your letter. The NAS/NRC Report specifically acknowledges "the unrestrained but unobtrusive cooperation of the FDA and of the pharmaceutical industry. Both have responded quickly and sensitively to all requests for information but have never been importunate".

The efficacy review consumed two years, and one of the most interesting general conclusions arrived at lends additional credence to the view that certainty as to the meaning of the law is lacking. Let me quote from the portion of the NAS/NRC Drug Efficacy Study, discussing the definition of "substantial evidence":

"The Legal Definition of Substantial Evidence of Effectiveness.—The definition in the law is an exacting one. Had the panels adhered rigidly to it, a great many claims would have been rejected on the grounds that they were not supported by substantial evidence based on 'well-controlled investigations . . . by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved.'

"In a number of areas of drug action (e.g., psychotherapeutic effects), there is no agreement on what constitutes a well-controlled investigation. More generally, the many imponderables of clinical investigation influence the validity of studies that may appear to be well-controlled methodologically and statistically. If one reviews the hearings on the Bill that led to the Amendments, it becomes evident that it was the intent of Congress to be permissive in the application of the wording of the law. Specifically, Congress did not intend that the word 'substantial' should be read to mean 'predominant'. It is clear from the debates that claims for effectiveness should be accepted if a substantial amount of well-documented favorable evidence is presented, even though there may also exist a weighty body of inconclusive or negative evidence. In the words of Alanson W. Willcox*, General Counsel, Department of Health, Education, and Welfare:

This provision states that there must be a bona fide, responsible and adequately based medical judgment in support of efficacy before a drug may be put on the market, but if this condition is met, a minority opinion may prevail.

It should be emphasized that the law relates primarily to new drugs that have been submitted for approval on the basis of only limited premarketing clinical trials. The drugs that have been reviewed in the Study, on the other hand, have been on the market for 5 to 30 years. In many cases, no reports on well-controlled studies of their efficacy for the claims cited for their use could be found in the presentations of the manufacturers or in the medical literature, and yet many of them have received wide acceptance in medical practice. This situation presented the panels with a very difficult problem. How much weight should they give to the opinion of the marketplace? The final arbiter of the value of a drug is the consensus of the experience of critical physicians in its use in the practice of medicine over a period of years. Approval of a new drug for release to the market is only a license to seek this experience. When the panels were faced with this situation, they have sought to grant liberty but to restrain license by assigning a rating of 'Probably effective' or 'Possibly effective' on the basis of their own clinical experience with the drug and their evaluation of the opinions of their peers."

Does not this suggest that the firms might reasonably have concluded that the efficacy evidence in hand, together with the clinical record, though certainly not of 1971's sophistication, might constitute "well documented" evidence, as the NAS/NRC Report put it, or "bona fide, responsible and adequately based" evi-

*Charles Wesley Dunn lecture, Law School of Harvard University, Cambridge, Massachusetts. 15 March 1963.

dence in HEW General Counsel Willcox's words? Surely individual drug firms are not expected to be more perceptive than the sum of the opinions of the panels of consultants to the National Academy of Sciences.

The virtually complete change in the FDA's posture on the effectiveness question was not evident during the years between 1962 and 1968. On September 19, 1969, FDA proposed new regulations. District Judge Latchum, in his January 16, 1970, opinion called them "new standards of evidence necessary to demonstrate the effectiveness of drug products . . . applied retroactively so as to place in jeopardy the continued marketing of thousands of drug products introduced before 1962 with FDA approval and the effectiveness of which FDA has not yet challenged".

The fact that FDA had changed the rules was recognized by Judge Latchum, who noted that, among other things, FDA had not uniformly insisted on evidence of the kind laid down in the September 19 regulations in the past, that its 1966 calls for information supporting claims was very broad and that they "did not indicate that consideration . . . was to be limited to evidence derived solely from closely controlled clinical investigations. . . ." He also observed that the NAS/NRC panels plainly relied on opinion and impressions in some evaluations, so that if the regulations were to have been enforced uniformly and literally, FDA might well challenge drugs which the NAS/NRC panels had rated as totally effective.

Finally, with the May 8, 1970 publication of regulations on this issue, FDA made final its intention to selectively reject well-documented clinical experience as a test of effectiveness. Companies were then clearly on notice that unless a special exemption from the new criteria were successfully sought, they could be required by FDA to provide 1970-quality evidence for any pre-1962 drug, the clinical record of the product being of no significant moment in deciding the fate of that medication.

I submit that this record shows that the industry has made reasonable attempts to work with the Agency to meet the intent of the law, contrary to your letter's assertions, and that the ground rules have been changed substantially by FDA so as to make the industry's efforts to comply over the last several years appear inconsequential.

One final point. We note that the Food and Drug Administration never fails to cite the Food and Drug Act in justification of its actions. May we remind you that it is this same statute which provides industry with the right to hearings and court review. Yet when we exercise this right, we are criticized by you and other representatives of FDA.

In view of the need for the Record to reflect some balance on this issue, I am asking Senator Nelson to insert a copy of this letter in the transcript of the February 1, 1971 hearings of the Monopoly Subcommittee of the Senate Small Business Committee.

Sincerely yours,

C. JOSEPH STETLER,
President.

PHARMACEUTICAL MANUFACTURERS ASSOCIATION,
Washington, D.C., February 10, 1971.

CHARLES C. EDWARDS, M.D.,
Commissioner of Food and Drugs, Department of Health, Education, and Welfare, Rockville, Md.

DEAR DOCTOR EDWARDS: We have read with considerable interest your testimony of January 18, before the Subcommittee on Monopoly of the Senate Small Business Committee. While we found several points with which we are in agreement, we also noted a number of comments that are quite disturbing.

I am referring not only to portions of your prepared statement, but to the overall tenor of your remarks, as well as those of Dr. Simmons and Mr. Goodrich. They revealed, or so it seemed to us, a thrust that goes beyond the statutory authority given the Food and Drug Administration by the Congress. This includes a tendency to unduly escalate the role of the agency in drug therapy. I trust you will agree with me that there are high risk factors—to medicine and to patients—if the FDA attempts to expand its mandate into arbitrary, wide-ranging dictates in such matters as relative efficacy, certification of all drugs, class labeling, drug equivalency, and even marketing. Given the subtleties of

drug therapy and the imprecision of the art of medicine, we believe the FDA should limit its mission to what Congress specified and intended.

The FDA may not be consciously building a case for the doctrinaire control of all aspects of drug therapy, but it would be difficult to draw any other conclusion from the testimony of January 18.

For example, on the issue of relative efficacy, FDA's assertion of authority would enable it to become the decision maker as to how many drugs should be on the market and from what source as well as what medical practitioners may prescribe in any given case. Such action would contravene the clear intent of the 1962 Amendments to the Food, Drug, and Cosmetic Act. Even a cursory review of the legislative history shows that Congress decided unequivocally not to give the FDA such authority.

We also object to the causal linking of such a grave social problem as drug abuse to the alleged "over-prescribing" of legitimate medicines. Given the current mores, attitudes and conditions of society, we would have the drug abuse problem of the same dimensions regardless of the status of prescription drugs. Consequently, this linkage permits conclusions and implications which are unfair and which I hope were not intended.

Early in your testimony you estimated that prescriptions will increase from two billion to three billion per year in five years—as if this were inherently bad. I would assess such growth as a consequence of expanding health care, in private and governmental programs, to growing populations, to rising family incomes, and to the overall effectiveness of drug therapy in prevention and treatment disease.

The studies you cite on adverse reactions, hospital-acquired infections, and number of drugs received by hospital patients cannot be applied to the total patient population. As you know, these are isolated studies of limited magnitude which hardly meet standards of "substantial evidence".

While a few examples of agency-industry cooperation are noted, the overall tenor of the statement and the responses to questioning suggest a derelict industry which must be held in line by a vigilant agency, whose wisdom and rectitude surpass that of the companies. It would have been appropriate to mention, for example, the extensive cooperative effort that went into the preparation of the recently published regulations on Good Manufacturing Practices. Nowhere is the scientific and technical proficiency of the industry acknowledged as integral to the regulatory area. Yet, as you know, our companies are constantly improving the quality and diversity of our drug supply and with a dedication that is surely the equal of the effort exemplified by the FDA. Moreover, regulations in general are based on the experiences and practices of competent manufacturers. The in-depth inspection program to which you refer is possible because of the cooperation of our member firms as training sites for FDA personnel.

We find the discussion of brands, generics, and equivalency especially contradictory. Much of the testimony discloses the practical problems of assuring the safety and equivalent effectiveness of all drugs, and it also discloses how far we are from achieving such a goal. The extent of recalls, inspections leading to the closing of plants and numerous instances of equivalency failures, indicate that there are fundamental differences among manufacturers. Hence, there must be fundamental differences in the quality of drugs. Skills, experience and competence do count. Even your recital of the situation with Digoxin simply reemphasizes the subtle problems of producing quality medicines. Drugs that go through the NDA process are not always equal, much as FDA wishes that they were. Many studies show otherwise, and we will document this matter shortly in a new PMA publication.

As you know, Food and Drug Administration experts recounted one important study in the January 11 issue of *JAMA*. Surely this example of oxytetracycline unequivalence signalled the potential extent of the problem, just as earlier studies did on Chloromycetin and its "copy" products.

If studies undertaken so far illustrate significant differences in biological response, what would happen if all drugs had to undergo such rigorous testing? A projection of the results so far compiled points to the probability of a *very frequent phenomenon*, not an infrequent one, as suggested. I find it disturbing that you did not emphasize the fact that the agency cannot possibly assure biological equivalency, even for NDA'd products, in the foreseeable future.

On page 9056 of your testimony, in response to a question from Senator Nelson, you stated that batch-testing applied to all "imported anti-infectives" as well as domestic batches. This contradicts past testimony which indicated that FDA has

not been able to test all batches of imported antibiotics. Has FDA capability reached a level where this is now the case?

It would be of interest to have FDA state specifically how many different drugs have been tested and just how many of them were found to be equivalent.

It is also highly questionable what can be accomplished by class labeling in assuring drug equivalency. To suggest that such labeling is an umbrella, under which all prescribers can safely huddle, ignores reality. This type of labeling can hardly be equated with quality and equality assurances across the board.

I have publicly commented on the actions which have been taken to remove drugs in the "possibly effective" category from Federal programs. This is clearly violative of due process and convicts drugs prior to final decisions on the issue of their place in therapy.

We also question seriously FDA's recent handling of NAS-NRC panel results. The raw figures, and the words used in designating categories, have been extremely confusing not only to the general public, but to the health professions and the press itself. Press accounts have been notoriously inaccurate or misleading, at least in part, because the FDA has failed to put these figures into sufficient perspective. I enclose the notices we have released on this subject in case they have not come to your attention.

I note that your statement dealt at some length with the defects of labeling, without any reference to the role of FDA in its preparation and approval. It would certainly have been appropriate for you to stress that labeling represents honest effort made in good faith by both industry and the FDA at the time of preparation, and that of necessity, it is in a state of flux as new information comes to the fore. Surely industry is just as anxious as FDA to have complete and up-to-date labeling on its products. If labeling is obsolete, the responsibility of updating should be shared by the FDA and industry.

Your testimony raised additional questions with respect to combination products, marketing and other areas. However, the above indicates some of the major reasons for our concern.

Sincerely yours,

C. JOSEPH STETTLER,
President.

2. The second part of the document focuses on the implementation of the proposed changes. It details the steps involved in the transition process, from the initial planning phase to the final execution. This section also addresses the potential challenges that may arise during the implementation and provides strategies to overcome them.

3. The third part of the document discusses the long-term impact of the changes. It highlights the expected benefits, such as improved efficiency and cost savings, and provides a timeline for when these benefits are expected to be realized. This section also includes a discussion on the ongoing monitoring and evaluation of the changes to ensure they are meeting the intended goals.

4. The fourth part of the document provides a summary of the key findings and conclusions. It reiterates the importance of the changes and the need for continued support and collaboration from all stakeholders. This section also includes a list of recommendations for future actions and a final statement of intent.

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

TUESDAY, FEBRUARY 2, 1971

U.S. SENATE,
SUBCOMMITTEE ON MONOPOLY OF THE
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C.

The subcommittee met, pursuant to recess, at 10:25 a.m., in room 1318, New Senate Office Building; Senator Gaylord Nelson (chairman of the subcommittee) presiding.

Present: Senator Nelson.

Also present: Benjamin Gordon, staff economist; Elaine C. Dye, clerical assistant; and Keith A. Jones, minority counsel.

Senator NELSON. Our witness today is Dr. Benjamin Wells, Deputy Chief Medical Director of the Veterans' Administration.

Dr. Wells, your statement will be printed in full in the record. You may present it however you desire. I apologize for being late. I had to attend the opening of the meeting of the finance committee which was scheduled subsequent to the scheduling of this meeting. So I apologize for being 25 minutes late.

Go ahead, Doctor. You may present your statement however you desire.

STATEMENT OF DR. BENJAMIN B. WELLS, DEPUTY CHIEF MEDICAL DIRECTOR, VETERANS' ADMINISTRATION; ACCOMPANIED BY DR. PAUL A. L. HABER, DEPUTY ACMD FOR PROFESSIONAL SERVICES; DR. JOHN D. CHASE, ACMD, PROFESSIONAL SERVICES; ROBERT A. STATLER, DIRECTOR, PHARMACY SERVICE; ROBERT G. LOUDON, CHIEF, RESEARCH IN PULMONARY DISEASE; DONALD P. WHITWORTH, DIRECTOR, SUPPLY SERVICE; CLYDE C. COOK, DEPUTY DIRECTOR, SUPPLY SERVICE; PHILIP WARMAN, ASSISTANT GENERAL COUNSEL; ROLAND F. HARDING, ASSISTANT DIRECTOR, PHARMACY SERVICE; ROBERT G. ROSE, MANAGER, VA MARKETING CENTER; DR. EUGENE M. CAFFEY, JR., CHIEF, PSYCHIATRY DIVISION; AND DR. J. N. COHN, CHIEF, HYPERTENSION AND CLINICAL HEMODYNAMICS

Dr. WELLS. Thank you, Mr. Chairman. We certainly understand the need for the delay.

I would invite you to interrupt at any point in this document, so we can use the reading as a point of departure for discussion.

Mr. Chairman, we welcome the opportunity to appear again before this subcommittee to discuss further the policies and practices of the Veterans' Administration in the selection and acquisition of drugs and medicines used in providing medical benefits to the Nation's eligible veterans. At the outset, I would like to state that this subcommittee's efforts have been salutary in stimulating a searching review by Federal agencies into their practices in the selection and use of drugs. In our own case, this review included examination into our current methods of collecting, evaluating, and disseminating information on the effects and efficacy of drugs, examination of the results in terms of which drugs were most commonly used in the Veterans' Administration, and a reexamination of our policies to see if they were sound and if we could improve upon their interpretation and execution.

This subcommittee's expressed interest is in the drug purchasing practices of the Federal Government. The determination as to which drugs will be prescribed for patient therapy is a professional one and procurement practices are designed to obtain quality drugs requested by physicians, as economically as possible. The development of hospital formularies is monitored by the Therapeutic Agents and Pharmacy Reviews Committee with the inclusion or exclusion of a drug being determined by knowledgeable peer action.

Senator NELSON. Doctor, when you testified before, we raised the question of hospital formularies—the development of the formulary and therapeutics committee and the drugs that are placed on the formulary. As I recall, the explanation for a number of drugs of the formulary which were expensive or ineffective was that you didn't feel you could argue with the doctors who make the requests.

Now, this statement here could be interpreted to be saying that the selection of drugs is a professional one which would mean professional in the sense that you use the best professional knowledge available and that the inclusion or exclusion of a drug is determined by knowledgeable peer action.

If that is the case, how do you explain the substantial purchases of Darvon, Peritrate, Terramycin, for all of which there is an equivalent drug that is cheaper or, as in the case of Peritrate, the testimony of your own VA Hospital medical investigator is that they couldn't find any use for Peritrate?

Dr. WELLS. Well, Mr. Chairman, as you know, there are many areas of disagreement about the specific drugs as to their effectiveness or efficacy, and that would certainly be true of Peritrate, less so of Darvon.

Now, as to our committees: the committee that I refer to here is a committee at each hospital which monitors the drug program. In addition we have a central office committee that monitors the programs from Washington for the hospitals in the field.

Now, the person here who has had most action in this and who heads the group in our Washington office is Dr. John Chase. Perhaps he could give you a little background on how this committee has functioned in the past and at present.

We will go into this a little further in the statement.

Dr. Chase, would you care to address yourself to that?

Dr. CHASE. Senator, this is set up in a sequential fashion. By that I mean administratively that each hospital has a requirement to organize a therapeutics committee which is normally chaired by the chief of staff of the hospital, and the membership of the committee is composed of the chiefs of the major clinical services with the pharmacist being the recording secretary for the committee.

The actions of this committee are accomplished by the physicians of that hospital staff. If they wish to have a drug entered into the formulary they must complete an application with supporting documentation which goes to the committee—

Senator NELSON. Supporting documentation?

Dr. CHASE. Supporting documentation on the drug. In other words, a search of the bibliography, some indication that this drug has merit and that they wish to use this particular drug with their patient groups and they want to have that drug entered into the formal structure of the hospital formulary.

The committee reviews this. It may have sufficient expertise within its own body to render a judgment or it may call upon outside people to assist them in their actions.

They may take several forms of action. They may actually deny the inclusion of the drug in the formulary. They may include it, or they may restrict the use of the drug to a specific patient, or group of patients.

Most of our hospitals are urged to review their entire formulary on a recurring basis. I can't honestly say how frequently or how well this is done but we are constantly generating from central office information which goes to the field, some documentation of which you have in your packet here, directing them to review their drug practices both in terms of therapeutic effectiveness as well as the cost-benefit relationship.

Senator NELSON. Well, I hear what you are saying but frankly it doesn't impress me. What you are really saying, I think, is that you may or may not have a good formulary based upon how it is run at the local level; that you are approving the purchase of drugs which the Medical Letter recommends and are not purchasing drugs for which the Medical Letter or other authoritative sources say there are equivalent drugs which are much cheaper. You say the doctor has to submit justification. Well, would you submit to the committee what justification any doctor in any one of your hospitals supplied in the form of scientifically controlled studies showing that Peritrate was an effective drug, and that Darvon was better as an ordinary analgesic than aspirin, or that any of the tetracyclines are better than tetracycline hydrochloride.

We can't find any such studies. So I am wondering what your doctors submitted to the formulary committee to convince them to put it on the formulary.¹

Dr. CHASE. Senator, I believe that, to repeat Dr. Wells' statement previously made, in this particular area of therapeutic effectiveness,

¹ See appendix V, letter to Mr. Benjamin Gordon, Majority Counsel, Monopoly Subcommittee, from Lyndon E. Lee, Jr., M.D., Assistant Chief Medical Director for Professional Services, Veterans' Administration, pp. 8466-8485.

in certain categories of drugs there has been controversy. We readily recognize this. I also readily admit to you that it is possible in submitting documentation to a therapeutics committee that selected portions of a bibliography are being submitted.

However, we must rely upon the sincerity and the professional judgments of the superior people in our hospitals settings to use good judgment for the protection of the patient and to insure the fact that the patient gets the maximum therapeutic benefit at the most reasonable cost.

Senator NELSON. Well, let's be more precise. Dr. Edward Freis, senior medical investigator at your own Washington, D.C., hospital, a member of the National Academy of Science—NRC panel on cardiovascular drugs stated as to Peritrate—that "The few controlled trials that have been done have failed to demonstrate that they are effective," referring to Peritrate and one other drug.

Then I asked him: "Do the controlled studies indicate that they are not effective?" "Dr. Freis: They are not effective compared to a placebo."

Now, here you say you are relying upon your senior people, and yet you have the testimony of Dr. Freis, senior medical investigator, who says that Peritrate is comparable to a placebo.

Dr. WELLS. Mr. Chairman, I know that Dr. Freis made that statement, because I read his testimony, also, but there are frank differences of opinion at high levels on this.

We have with us here Dr. J. N. Cohn, who is an expert in the field of cardiovascular disease treatment and I would like to have him speak to this. He is also an associate of Dr. Freis.

Dr. COHN. Senator Nelson, you will notice in Dr. Freis' statement that he said the few controlled studies that were performed, and while I would feel as strongly as you that we should be able to reach a rational decision whether a drug such as Peritrate is or is not effective, in a strong statement such as that there is still controversy. There are rational, knowledgeable people who feel that this drug is effective and have published papers on demonstrated effectiveness in uncontrolled studies.

Now, these are not acceptable as total scientific proof.

Unfortunately it is much easier to prove effectiveness of a drug than it is to prove ineffectiveness and in small controlled studies—

Senator NELSON. I didn't understand what you said.

Dr. COHN. It is easier to prove effectiveness of an agent than to prove categorically its ineffectiveness and the response of some knowledgeable people in the field to controlled studies showing no response would be, yes, the drug is not effective in all people and is not necessarily potent in a larger series, but in certain individuals the drug does work and therefore the physician wants to use it.

I personally do not use the drug but I cannot marshal any strong evidence to prove to another physician who quotes the literature and who states from the literature that this drug is effective and quotes textbooks which describes this as the most potent and effective long term treatment or prophylaxis for angina pectoris. I can't marshal strong evidence at the moment to tell him he is wrong and

I think it is a clear example of a situation where we need further research before we can make a definite decision whether this drug should be removed from our formulary.

Senator NELSON. You can't come up with carefully controlled studies that demonstrate that it is effective, is that correct?

Dr. COHN. I think that the controlled studies that have been done so far are unfortunately on too small a group of subjects to take a categorical position about its effectiveness.

Senator NELSON. Would the controlled studies that have been done qualify it under the effectiveness provision of the Kefauver 1962 statute—substantial evidence of effectiveness?

Dr. COHN. I think that at the moment—there is no demonstrated substantial evidence of effectiveness, but there is no clear-cut proof of ineffectiveness. There have also been controlled studies of nitroglycerine which is a drug which almost all physicians accept as effective in treatment of angina. There have been in the past controlled studies of nitroglycerine which have shown this drug to be no better than a placebo. There have been other controlled studies which have shown it to be effective and physicians today use this drug with a rather firm feeling that the drug is effective. And we have not really—this drug has not come into conflict because it is generally used.

Peritrate is in the status of a drug which some controlled studies have shown to be ineffective but not enough studies have been done in a large enough series that all physicians are willing to accept the data from these controlled studies.

Senator NELSON. Well, what do you say about Darvon?

Dr. COHN. I think I should turn that over to someone else.

Senator NELSON. The testimony of medical experts, which remains uncontradicted—though there may be somebody in the country who can contradict it—is that the drug of choice for a mild analgesic is aspirin. Of course, there may be special cases where if somebody was allergic or something, you may use Darvon, and they recited a couple of special cases. The witnesses could not explain the substantial, very large purchases of Darvon by DOD and VA. I think DOD bought more than four and a half million dollars' worth and nobody could explain why they would buy that much, when you could have bought the same amount of aspirin for \$180,000. You could have saved about four and a half million dollars.

Well, what is going on in the Department of Defense purchasing and VA purchasing to get all this Darvon?

Dr. WELLS. Mr. Chairman, may I ask Mr. Statler, our Chief of Pharmacy, to take up this point.

Mr. STATLER. Yes, Senator. On Darvon, VA's purchases in the past year admittedly have been around 51 million doses of Darvon and we are not trying to defend the large use of this drug.

In the same period of time, however, we did buy around 110 million doses of other analgesics, notably aspirin. In the drug efficacy study reports which the NAS-NRC sends to FDA are these extracts in addition to the comments which we frequently heard about 32 milligram dosage not being as effective as a placebo.

I would like to read a couple of brief statements. One is that "Darvon is an effective analgesic and can be used for recurrent and chronic pain." They also state that Darvon compound, a combination with aspirin or aspirin compound, "There is reason to believe, on the basis of either actual clinical studies and theoretical considerations, that the combination of Darvon with an antipyretic-analgesic of the aspirin type results in analgesic superior to that achieved by either drug administered alone."

Now, this is what, of course, our physicians are faced with. They have a patient in pain. They usually prescribe aspirin. If they feel they need something a little stronger they will probably prescribe a Darvon compound or use Darvon 65 along with aspirin rather than resort to codeine, because there are frankly some adverse effects from the codeine.

In the same study they mentioned in comparing Darvon with codeine that the relative potency of the two drugs indicated that Darvon is approximately one-half to two-thirds as potent as codeine and this is usually the way it is prescribed. We generally use a 65 milligram dosage of Darvon which is equivalent to about 32 milligram dosage of codeine. This is the recognized dosage. The controversy rages as the therapeutics committee tries to decide whether to standardize. You have clinicians who have used this drug effectively on patients, patients seem to feel better and they are faced with the decision do they want to discontinue Darvon and use only aspirin when there is proof of some effectiveness.

Senator NELSON. I believe the testimony has been in agreement that 32 milligram dosage was no better than a placebo. So there is hardly any point in purchasing that.

Mr. STATLER. We purchase very little of that dosage and generally—most of the dosage prescribed is 65. If they use the 32 it is two capsules at a time primarily for an elderly patient having difficulty swallowing. It provides additional flexibility in dosage. If they feel they need a larger amount rather than 65, they can prescribe a 32 milligram capsule in addition to the 65.

Senator NELSON. I think in the appropriate dosage form it is an effective analgesic. That is not the question. The question raised is whether it is justifiable for the Defense Department, for example, to buy \$4½ million worth, when they are simply substituting a more expensive analgesic for a less expensive dosage form of aspirin. Further, they are not selecting Darvon because of some specific use. It is not the drug of choice as a mild analgesic.

That is the question that I am raising here.

I don't know how you prove all that but—

Dr. WELLS. This is the point. Of course we have made every effort to educate our physicians through our committee here in Washington and through our publications to them. We speak of this a bit later. We point out that we do not recommend Darvon as an expensive substitute for aspirin but simply as an analgesic that may be used in addition to or with aspirin.

Senator NELSON. The Medical Letter of January 23, 1970, says:

No evidence has appeared since this review that establishes the superiority of 65 milligram doses of propoxyphene to two tablets of either aspirin or APC.

And the Lilly Co. itself says:

As for the view that Darvon should not be prescribed routinely in preference to other analgesics, we agree.

But it is obvious from the level it is being purchased that it has been prescribed routinely, anyway, it would seem to me to be so.

Dr. WELLS. We don't think so. We think the routine prescription is being discouraged about as actively as we can. So we don't feel that that will be a continuing problem.

Mr. STATLER. Medical Letter incidentally, is one of the sources of information that all of our therapeutic agency committees have at their disposal. Most of our hospitals have between 80 and 100 of the leading journals as reference sources in addition to the peer reviews of clinicians actually using the drug, so information in Medical Letter is considered. We have seen comments, for example, in the minutes of the therapeutic committees indicating that a specific drug was evaluated in the Medical Letter and they have discussed this and either agreed or did not agree or are looking into it further.

Senator NELSON. The Medical Letter also states that the oral tetracycline of choice is tetracycline hydrochloride capsules. They are as reliably absorbed and as clinically effective as any other oral tetracycline.

Dr. WELLS. We are quite aware of this as a problem and I would like to ask Dr. Robert Loudon, who is an expert in the field of antibiotics, to speak to the point. Dr. Loudon.

Senator NELSON. In other words, my question is, then, why should we be purchasing the other forms that are much more expensive if not more effective?

Dr. LOUDON. Senator Nelson, I think in the testimony before this committee Dr. Heinz Eichenwald who appeared earlier confirmed this belief that the tetracyclines as a group have similar indications and that they have varying costs, varying prices.

The question here, the specific question, about the reasons for these appearing on the formularies of Veterans' Administration hospitals, I think is of a similar order to the answers which have been made about the other instances of analgesics or Peritrate appearing on the formulary.

The tetracyclines which appear on the formulary offer a degree of flexibility to the individual physician who is prescribing these drugs for his patients. The relative usage of the different preparations is something which we will expect to change as a result of the testimony which has been produced here, the efforts which you have made in this direction, and the efforts which the VA is making to implement the findings.

Dr. WELLS. Mr. Chairman, may I add that I think it is important to note that during 1970 the Veterans' Administration bought just

a little over 13 million doses of all the tetracyclines and of this 12½ million were tetracycline hydrochloride.

Senator NELSON. I hadn't remembered that figure. I know AID testified yesterday that there are a number of tetracyclines they were not going to buy any more because of the expense. Chlortetracycline, doxycycline, methacycline HCL, and three or four others.

Well, I don't want to be misunderstood about this. I don't think this committee or any congressional group should in any way attempt to dictate the practice of medicine. All I am attempting to do is insist that good medicine be practiced and that the profession itself insist on the highest standards because, at least so far as the Congress is concerned, these are taxpayers' moneys.

Dr. Edwards in testimony before the committee a couple of weeks ago made the statement with which I agree, and I think you would, too, that—

Government as a major purchaser of drugs should and must insist upon the least expensive of equivalent drugs and upon rational choices among different drugs which satisfy the same medical needs.

That is all I am talking about here, not that we should attempt in any way to tell the medical profession how to practice but that we are entitled to say to Government agencies who are using taxpayers' money that they, at least, follow the best scientific knowledge within the medical profession themselves.

Dr. WELLS. I think we would wholly concur, and we certainly subscribe to the statement of the Commissioner. It is very much in line with our own policies.

Senator NELSON. Well, then, do you scrutinize the formularies of the various Veterans' Administration hospitals as to what goes in the formulary and what drugs are used in the hospitals? Do you have a careful scientific review of that at the national level?

Dr. WELLS. Indeed we do. The Hospital Committee itself has a regular monthly meeting with minutes of all the transactions which are transmitted to the central office. Then the committee that Dr. Chase chairs reviews these in depth and uses consultants for special points, so that this is an extremely well-monitored, carefully scrutinized formulary.

Senator NELSON. What do you do if you find something on the formulary that ought not to be there or that substantial amounts are being used when you know, within the profession, that there is an equivalent therapeutic agent that is much cheaper?

Dr. WELLS. Dr. Chase.

Dr. CHASE. We go back to the hospital, make contact with the chief of staff of the hospital, draw this to his attention and ask him to review this with the station committee.

Senator NELSON. How often have you done that in the past few months?

Dr. CHASE. Not often, principally because it is our impression that the competencies of these groups are good and that since we have been stimulating them to review this in terms of the cost

relationship, that they have done a creditable job in this relationship.

I think this is pointed out actually, Senator, by the figures which Dr. Wells just gave you on tetracycline.

Senator NELSON. All right. Please continue.

Mr. JONES. Excuse me, Doctor. Before you continue your testimony, I would like to ask a couple of questions about Darvon. To clarify the earlier testimony, does the VA purchase 110 million units of aspirin and 51 million units of Darvon?

Mr. STATLER. Right; 110 units of aspirin type analgesics, that is chiefly aspirin, and 51 million doses of Darvon products.

Senator NELSON. Was that part of the—

Mr. STATLER. We purchased 110 total analgesics other than Darvon. That would be primarily aspirin and Tylenol, acetaminophen, as compared to 51 million doses of all the Darvon products.

Mr. JONES. So that roughly speaking, for every two aspirin you dispense, you dispense one Darvon.

Mr. STATLER. That is a fair assumption.

Mr. JONES. I think that has been described as the routine prescription of Darvon and you have also stated you are going to discourage that in the future. What precise steps will you take to discourage that routine prescription?

Dr. CHASE. This has been a continuing effort. This is by personal contact with the field and by written communication. The whole question of Darvon has been a difficult one because of what appears to be therapeutic efficacy to the individual practitioner in dealing with his patient; and as I am sure you are well aware, pain being the kind of symptom it is, the physician is motivated to relieve pain as quickly and as effectively as he can, and after the preliminary trial of aspirin, comparable disease states and comparable type patients, the physician is motivated not uncommonly to go to the top analgesic which he can find which is non-addicting, which is safe for the patient.

This is also related to the high incidence of complicating diseases which we have in the VA, the relatively high frequency of ulcers and the aged patients. The physicians attempt to give the safest analgesic which they can. We are all aware and we have actually been preaching on the other side of the coin, be alert that aspirin produces gastric irritation and this can be a reason many times for not so small gastric bleeding. So a fine line has to be walked in how we wish to stimulate our physicians in the practice of medicine.

Dr. WELLS. We have taken some steps in the last few months which we would like to outline. First, we directed our hospitals to remove from their local formularies all those drugs listed by the Food and Drug Administration in a publication dated November 1, 1970, as lacking substantial evidence of effectiveness or as having an unfavorable benefit to risk ratio. I would like to submit for inclusion in the record our directive on this, Department of Medicine and Surgery Circular 10-70-237, December 4, 1970.

(The information above-referred to, follows:)

8134 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

Veterans Administration
Department of Medicine and Surgery
Washington, D. C. 20420

CIRCULAR 10-70-237

December 4, 1970

SUBJ: Implementation of NAS/NRC Drug Efficacy Studies Information

TO : Directors of Hospitals, Domiciliary, Outpatient Clinics
and Regional Offices with Outpatient Clinics

1. The Executive Committee on Therapeutic Agents, VACO, has reviewed VA's policies regarding the use of drug products whose efficacy was questioned by various panels of the National Academy of Sciences (NAS), National Research Council (NRC).

2. A copy of the drug efficacy study of the NAS/NRC submitted to the Commissioner of Food and Drugs was sent to each VA Therapeutic Agents and Pharmacy Reviews Committee in 1969, and includes the names of the reviewing members. Their professional qualifications for this task are recognized as outstanding.

3. Since that time, and with increasing frequency in recent months, the FDA has been taking action to publicize and remove from the market drug products which they concluded lack substantial evidence of effectiveness, as defined in the Federal Food, Drug and Cosmetic Act, or have an unfavorable benefit to risk ratio. Enclosed is a list of such drug products compiled by the FDA. Subsequent lists will be distributed as they become available with an appropriate covering letter to assure that your pharmacist obtains all lists. It should be borne in mind that additional clinical evidence submitted by the manufacturer may result in a reclassification of some of these products. If this occurs, you will be promptly notified.

4. The Executive Committee on Therapeutic Agents recommends the following procedures for immediate implementation at each VA facility:

a. Drug products on the attached FDA list will be reviewed by the hospital Therapeutic Agents and Pharmacy Reviews Committee and if present, will be removed from the hospital formulary and therefore will be unavailable for prescribing by VA staff physicians or dispensing by VA pharmacies. Wherever reference is made to physicians, it will be interpreted to include dentists, podiatrists or others authorized by law to prescribe for patients. Any drug products from the list which the hospital committee desires to retain in the formulary will be submitted with justification for retention to the Executive Committee on Therapeutic Agents, VACO, for purposes of further review and action.

b. Unless retained in the station formulary, when prescriptions for drug products on the attached FDA list are received from fee physicians treating service-connected patients or private physicians treating A&A patients, the physician concerned will be contacted by a VA physician or pharmacist. VA policy against dispensing these products will be

CIRCULAR EXPIRES DECEMBER 3, 1971

ATTACHMENT A

explained to him and he will be given a choice of alternative available medication. In those infrequent instances where physicians will not agree to an alternative medication, the drug product, if available, will have to be obtained by the patient from a private pharmacy.

5. It is not the intention of Central Office to practice medicine or dictate from Washington the prescribing of drugs for individual patients. We are, however, deeply concerned about the continued use of drug products which, after a review by eminent medical specialists composing the Review Panels of NAS/NRC, have been determined by the FDA to lack substantial evidence of effectiveness or have an unfavorable benefit to risk ratio. Pharmacists will keep Supply Service closely apprised of any action taken by local committees that would affect drug demands.



BENJAMIN B. WELLS, M.D.
Deputy Chief Medical Director

Enclosure

Distribution: COB: (10) only plus (119) 75
SS (10C5A) FSB: HA, DO, OC, OCRO

Food and Drug Administration
Bureau of Drugs
5600 Fishers Lane
Rockville, Maryland 20852

November 1, 1970

This list represents those drug products which the Food and Drug Administration has decided, after evaluations by the National Academy of Sciences-National Research Council Drug Efficacy Study Group, lack substantial evidence of effectiveness*, or that an unfavorable benefit to risk ratio exists. Accordingly, on the dates shown, FDA published in the Federal Register announcements of intention to initiate proceedings to withdraw approval of the new drug applications or to repeal the anti-biotic regulations. These announcements are intended to apply also to similar drug products marketed by the same or other firms.

Some of the products have been removed from the market; others are the subjects of actions contesting our findings. In other cases the applicants are submitting data in an attempt to establish efficacy, or making changes to render the product acceptable.

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Achrocidin Compound Syrup	Lederle Laboratories	9/12/69
Achrocidin Compound Tablets	Lederle Laboratories	9/12/69
Achromycin Pharyngets	Lederle Laboratories	9/19/70
Achromycin SV Capsules	Lederle Laboratories	4/2/69
Achromycin Troches	Lederle Laboratories	9/19/70
Achromycin with Phenylephrine HCl and HC	Lederle Laboratories	12/24/68
Achrostatin V Capsules	Lederle Laboratories	4/2/69
Achrostatin V for Oral Suspension	Lederle Laboratories	4/2/69
Aclor Capsules	Cole Pharmacal Co., Inc.	9/12/69
Acticort	Wilson Laboratories	9/25/70
Actilamide Nose Drops	Broemmel Pharmaceuticals	11/6/68
Actilamide Oral Gargle	Broemmel Pharmaceuticals	11/6/68
Actilamide Throat Spray	Broemmel Pharmaceuticals	11/6/68
Actol Solution	The S.E. Massengill Co.	5/16/70

*As defined in the Federal Food, Drug and Cosmetic Act

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Adrestat	Organon, Inc.	7/10/68
Aerodrin Nasal Solution & Spray	Burroughs Wellcome & Co.	8/21/70
Albamycin G.U. Tablets	The Upjohn Company	12/24/68
Albamycin-T Capsules	The Upjohn Company	12/24/68
Albamycin-T Flavored Granules for Suspension	The Upjohn Company	12/24/68
Alertonic	The Wm. S. Merrell Co.	9/12/69
Alevaire (Tyloxapol 0.125 percent)	Winthrop Products, Inc.	7/17/68
Allergosil (Ethylene Disulphonate) Solution for Injection	Spicer-Gerhart Co.	9/12/69
Amm-I-Dent Toothpaste	Block Drug Co.	7/21/70
Amm-I-Dent Tooth Powder	Block Drug Co.	7/21/70
Ammozyll	High Chemical Co.	11/22/68
Am Plus Improved Capsules	J. B. Roerig & Co.	9/12/69
Amril Tablets	Amfre-Grant Inc.	9/27/69
Analexin 400 Capsules	Mallinckrodt Chemical Works	11/21/69
Analexin Syrup	Mallinckrodt Chemical Works	11/21/69
Analexin Tablets	Mallinckrodt Chemical Works	11/21/69
Analexin-HF Tablets	Mallinckrodt Chemical Works	11/21/69
Anergex (Poison Oak Extract for Injection)	Lemmon Pharmacal Co.	9/5/68
Antivert Tablets	Chas. Pfizer & Co., Inc.	3/27/70
Antizyme Toothpaste	Lambert Pharmacal Co.	7/21/70
Artamide-HC Capsules	Wampole Laboratories	3/28/70
Aristogesic Steriod - Analgesic Compound Cap.	Lederle Laboratories	3/28/70

8138 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Aristomin Capsules	Lederle Laboratories	8/29/70
Atropine and Phenobarbital Tablets	Cole Pharmacal Co., Inc.	3/27/70
Aureomycin Pharyngeals	Lederle Laboratories	9/19/70
Aureomycin Triple Sulfas Tablets	Lederle Laboratories	4/2/69
Aureomycin Troches	Lederle Laboratories	9/19/70
Azotrex Capsules	Bristol Laboratories	4/2/69
Azotrex Syrup	Bristol Laboratories	4/2/69
Bacimycin Tabs.	Walker Laboratories	7/2/70
Betadine Mouthwash/Gargle	The Purdue Frederick Co.	8/4/70
Bicillinimycin All Purpose Injection	Wyeth Laboratories, Inc.	4/2/69
Bicillin-Sulfa Susp.	Wyeth Laboratories, Inc.	4/2/69
Bicillin-Sulfas Tablets (oral)	Wyeth Laboratories, Inc.	4/2/69
Bilcain Tablets	Cole Pharmacal Co.	9/12/69
Biomydrin Antibiotic Nasal Spray, Solution, Drops	Warner-Chilcott Laboratories	8/21/70
Biomydrin-F Nasal Spray	Warner-Chilcott Laboratories	8/21/70
Biosulfa 125M Tablets	The Upjohn Company	4/2/69
Biosulfa 250M Tablets	The Upjohn Company	4/2/69
Bistrimate Tabs.	Smith, Miller, & Patch, Inc.	8/25/70
Blutene (Tolonium Chloride)	Abbott Laboratories	7/11/68
Bradosol Lozenges	Ciba Pharmaceutical Co.	3/28/70
Brisk Activated Toothpaste	Colgate-Palmolive Co.	7/21/70
Pabirin AC Buffered Tablets	Dorsey Laboratories	3/28/70

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Cepacol Mouthwash/Gargle	Wm. S. Merrell Co.	8/4/70
Cepacol Throat Lozenges	Wm. S. Merrell Company	9/12/69
Cer-O-Strep-One	The Upjohn Company	4/2/69
Cer-O-Strep-One-Half	The Upjohn Company	4/2/69
Chlortetracycline Hydrochloride Dental Cones	Lederle Laboratories	9/16/69
Chlortetracycline Hydrochloride Dental Paste	Lederle Laboratories	9/16/69
Chymar Aqueous Injection	Armour Pharmaceutical Co.	6/25/70
Chymar Injection in Oil	Armour Pharmaceutical Co.	6/25/70
Chymar-L Powder	Armour Pharmaceutical Co.	6/25/70
Chymotrypsin Injection	Chicago Pharmacal Div.	6/25/70
Chymotrypsin Injection	Wilson Laboratories	6/25/70
Coco-Sulfonamides Triplex Suspension	Eli Lilly & Company	9/11/69
Colgate Chlorophyll Toothpaste w/Gardol	Colgate-Palmolive Co.	7/21/70
Colgate Dental Cream w/Gardol	Colgate-Palmolive Co.	7/21/70
Compocillin VK w/Sulfas Filmtab Tablets	Abbott Laboratories	4/2/69
Compocillin VK w/Sulfas Granules for Oral Suspension	Abbott Laboratories	4/2/69
Comycin Capsules	The Upjohn Company	4/2/69
Comycin Half-Strength Capsules	The Upjohn Company	4/2/6
Curad Medicated Adhesive Bandage	The Kendall Company	11/6/68
C.V.P. w/Vitamin K.	USV Pharmaceutical Corp.	7/10/68

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Cyclex Tablets	Merck Sharp & Dohme	2/6/70
Cytran Tablets	Upjohn Company	10/15/70
Dactil-OB	Lakeside Laboratories	7/10/68 7/11/68
Decadron Phosphate w/Xylocaine Injection	Merck, Sharp & Dohme	9/23/70
Decadron Phosphate w/Xylocaine Injection, Dilute	Merck, Sharp & Dohme	9/23/70
Declostatin Capsules	Lederle Laboratories	4/2/69
Declostatin for Oral Suspension	Lederle Laboratories	4/2/69
Declostatin 300 Tablets	Lederle Laboratories	4/2/69
Delfeta-sed Plus T. Stedytabs (S.R. Tablets)	Eastern Research Laboratories, Inc.	9/17/68
Dexa-Pyramine Injection	Vitamix Pharmaceutical Inc.	10/15/70
Di-Ademil-K Tablets	E. R. Squibb & Sons	9/5/69
Diapec Oral Suspension	Charles Pfizer & Co. (International)	4/2/60
Dihydrostreptomycin-chlortetracycline-chloramphenicol-bacitracin Dental Cement	Oskar Schaefer, Inc.	6/25/70
Dihydrostreptomycin with streptomycin Sulfate Powder	Merck & Co., Inc.	2/6/70
Dihydrostreptomycin Sulfate Powder (1 gm/vial)	Chas. Pfizer & Co., Inc.	2/6/70
Dihydrostreptomycin Sulfate Powder (1 gm. & 5 gm/vial)	Pure Laboratories, Inc.	2/6/70
Dihydrostreptomycin Sulfate Powder (5 gm/vial)	E. R. Squibb & Sons, Inc.	2/6/70
Dihydrostreptomycin Sulfate Powder (1 gm/vial)	E. R. Squibb & Sons, Inc.	2/6/70

<u>NAME OF PRODUCT</u>	<u>COMPANY</u>	<u>DATE</u>
Dihydrostreptomycin with Streptomycin Sulfate Powder	E. R. Squibb & Sons, Inc.	2/6/70
Dihydrostreptomycin Sulfate Powder & Solution	Merck & Co., Inc.	2/6/70
Dihydrostreptomycin Sulfate Powder & Solution (500 mg./cc.)	Philadelphia Labs., Inc.	2/6/70
Dihydrostreptomycin Sulfate Solution (0.5 gm/cc)	Pure Laboratories, Inc.	2/6/70
Donnagel w/Neomycin Liquid	A. H. Robins Co.	7/2/70
Drilitol Solution & Drilitol Spraypak	Smith, Kline & French Labs.	8/21/70
Duo C.V.P. w/Vitamin K	U.S. Vitamin Corp.	7/10/68
Duografin Injection	E. R. Squibb & Sons, Inc.	2/6/70
Durycin A.S. (Aqueous Suspension)	Eli Lilly & Co.	4/2/69
Durycin F.A. for Aqueous Injection	Eli Lilly & Co.	4/2/69
Emivan Tablets	U.S. Vitamin Pharmaceuticals	4/10/70
Equalysen Tablets	Wyeth Laboratories	10/15/70
Erythrocin Sterate Sulfas Film Tabs	Abbott Laboratories	9/27/69
Erythrocin Ethyl Succinate Sulfas Chewable Tablets	Abbott Laboratories	9/27/69
Erythrocin Ethyl Succinate Sulfas Granules	Abbott Laboratories	9/27/69
Erythromycin Sulfate-polymyxin B Sulfate-pramoxine-Hydrochloride Otic Solution	Abbott Laboratories	9/26/69
Erythrosulfa Tablets	The Upjohn Company	4/2/69
Eskay's Theranates	Smith, Kline & French	9/25/70

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<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Esidrix-K Tablets	Ciba Pharmaceutical Co.	9/5/69
Estrosed Tablets	Conal Pharmaceuticals, Inc.	2/6/70
Flanithin Capsules (glutamic acid hydrochloride)	Table Rock Labs., Inc.	9/12/69
Flavocillin-CS Powder	Philadelphia Laboratories	4/2/69
Flavoserp Tablets	The Blue Line Chemical Co.	7/10/68
Frenquel I.V. Injection	The Wm. S. Merrell Co.	4/2/69
Frenquel Tablets 20 mg.	The Wm. S. Merrell Co.	4/2/69
Frenquel Tablets 100 mg.	The Wm. S. Merrell Co.	4/2/69
Gantriccillin Tablets, 100, 200, 300	Hoffman-La Roche, Inc.	4/2/69
Gantrisin Nasal Solution	Roche Laboratories	9/9/69
Germicidal Detergent, Liquid	Parke, Davis & Company	9/12/69
Geroniazol Injection	Philips Roxane Laboratories	8/26/69
Gluco-Pedrin w/Sulfathiazole Suspension (Nasal)	Parke, Davis & Company	9/9/69
Guanidine Hydrochloride Tablets	Rose-Hoyt Pharmaceutical	3/27/70
Hormatone "T" Tablets	G.W. Carnrick Co.	8/29/70
Hydrodiuril-Ka Tablets	Merck Sharp & Dohme	9/5/69
Hydropres-Ka Tablets	Merck Sharp & Dohme	9/5/69
Ilosone Sulfa for Oral Suspension	Eli Lilly & Company	4/2/69
Ilosone Sulfa Tablets	Eli Lilly & Company	4/2/69
Ilotycin Gluceotate Dental Cones	Eli Lilly & Company	2/21/69
Ilotycin Ethyl Carbonate-Sulfa Pediatric for Oral Suspension	Eli Lilly & Company	4/2/69
Ilotycin Gluceptate Otic w/Polymyxin B & Benzocaine	Eli Lilly & Company	12/18/68

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Ilotycin Sulfa (79) Tablets	Eli Lilly & Company	4/2/69
Intromycin Powder	Pitman-Moore	5/16/70
Isodine Gargle & Mouthwash	Isodine Pharmcal	8/4/70
Kaomycin Suspension	The Upjohn Company	7/2/70
Kasdenol Mouthwash & Gargle	Kasdenol Corp.	8/4/70
K-Cillin Sulfa Powder for Syrup	Biocraft Laboratories, Inc.	4/2/69
Kectil Suspension	Bristol Laboratories	7/2/70
Koagamin Parenteral Hemostat	Chatham Pharmaceuticals, Inc.	3/29/69
Kolynos Fluoride Toothpaste	Whitehall Laboratories, Inc.	7/21/70
Ledercillin Troches	Lederle Laboratories	9/19/70
Lutrexin Tablets (lututrin 3,000 units)	Hynson, Westcott & Dunning, Incorporated	5/24/68
Mannitrau Tablets	Richlyn Laboratories, Inc.	7/3/70
Maxitate w/Rauwolfia Compound Tablets	Strasensburgh Laboratories	7/10/68
Medrol w/Orthoxine Tabs.	The Upjohn Company	8/29/70
Menacyl Tablets	Lakeside Laboratories, Inc.	2/11/70
Mephosal w/Hydrocortisone Tablets	Crookes-Barnes Laboratories, Incorporated	3/28/70
Mesulfin Tablets	Ayerst Laboratories, Inc.	9/27/69
Metreton Tabs.	Schering Corporation	8/29/70
Micrin Oral Antiseptic	Johnson & Johnson	8/4/70
Milprem-200 and Milprem-400	Wallace Laboratories	8/26/70
Mulsopaque Injection	Lafayette Pharmcal, Inc.	2/11/70
Mycifradin N. Tab.	The Upjohn Company	7/2/70

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Mycillin Suspension	Maurry Biological Co., Inc.	4/2/69
Myospaz Tablets	North American Pharmacal, Inc.	9/27/69
Mysteclin F Capsules	E. R. Squibb & Sons, Inc.	12/24/68
Mysteclin F 125 Capsules	E. R. Squibb & Sons, Inc.	12/24/68
Mysteclin F Pediatric Drops	E. R. Squibb & Sons, Inc.	12/24/68
Mysteclin F Syrup	E. R. Squibb & Sons, Inc.	12/24/68
Mysteclin V Capsules	E. R. Squibb & Sons, Inc.	4/2/69
Nasal Spray Neo-Hydeltrasol	Merck Sharp & Dohme	8/21/70
Nasal Suspension Hydrospray	Merck Sharp & Dohme	8/21/70
Naturetin c/K Tablets	E. R. Squibb & Sons, Inc.	9/5/69
Neo-Cortef 1.5% Nasal Spray	The Upjohn Company	8/21/70
Neo-Cortef 0.5% Nasal Spray	The Upjohn Company	8/21/70
Neo-Cortef Sterile Inj. Susp.	The Upjohn Company	8/28/70
Neocyclone Tablets	The Central Pharmacal Co.	3/28/70
Neo-Delta Cortef 0.1% Nasal Spray	The Upjohn Company	8/21/70
Neomycin Sulfate-Kaolin-Pectin Oral Suspension	E. W. Heun Company	7/2/70
Neomycin Sulfate, Kaolin Pectin Suspension	Vitamin Pharmaceuticals Inc.	7/2/70
Neoparbel Tablets	Central Pharmacal Co.	10/24/70
Neopenzine Suspension	Eli Lilly & Company	4/2/69
Neopenzine (150) Tablets	Eli Lilly & Company	4/2/69
Neopenzine (300) Tablets	Eli Lilly & Company	4/2/69
Neo-Semhyten Capsules	The S.E. Massengill Co.	7/10/68
Neo-Synephrine-Sulfathiazolate Nose Drops	Winthrop Laboratories	7/9/68

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Neuro-Centrine Tab	Bristol Laboratories	9/27/69
Nicozol w/Reserpine Tablets	Nysco Laboratories	8/26/69
Nisulfazone Suspension	Breon Laboratories, Inc.	8/28/70
Novahistine w/Penicillin Capsules	Pitman-Moore	9/12/69
Onixol Solution (topical)	Scholl Manufacturing Co. Inc.	6/7/69
Orabiotic Chewing Gum Troches	White Laboratories, Inc.	9/19/70
Pabalate-HC Tablets	A. H. Robins Co., Inc.	3/28/70
Pabicortol Tablets	Nysco Laboratories	3/28/70
Pabirin AC Tablets	Dorsey Laboratories	3/28/70
Pacatal Injection 25 mg/cc	Warner-Chilcott Labs.	5/28/70
Pacatal 25, 50, 100 mg. Tabs.	Warner-Chilcott Labs.	11/29/69
Panalba Capsules	The Upjohn Company	12/24/68
Panalba Half-Strength Capsules	The Upjohn Company	12/24/68
Panalba KM Drops	The Upjohn Company	12/24/68
Panalba KM Granules	The Upjohn Company	12/24/68
Paredrine-Sulfathiazole Susp.	Smith, Kline & French Labs.	9/9/69
Parenzyme Aqueous for Injection	National Drug Company	6/25/70
Parenzyme Ointment	National Drug Company	6/25/70
Piptal w/Phenobarbital Pediatric Drops	Lakeside Laboratories	9/27/69
Pell-Biotic 250 Tablets	Richlyn Laboratories	4/2/69
Penicillin-dihydrostreptomycin- bacitracin Dental Paste	Biotic Drug Co., Inc.	6/25/70
Penicillin-dihydrostreptomycin Dental Cones	Strong Cobb Arner, Inc.	6/25/70

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<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Penicillin G Potassium w/Three Sulfas Buffered Powder for Syrup	Nysco Laboratories	4/2/69
Penicillin G w/Triple Sulfonamides, Flavored	Vitamix Pharmaceuticals, Inc.	4/2/69
Penicillin Streptomycin Readimixed Sterile Aqueous Suspension	Upjohn Co.	4/2/69
Penicillin-Streptomycin Bacitracin Dental Paste	Procol-Sol Chemical Co.	6/25/70
Penicillin w/Sulfonamides Powder for Solution	Biocraft Laboratories, Inc.	4/2/69
Penicillin Three Sulfonamide Tablets "100"	Nysco Laboratories, Inc.	4/2/69
Penicillin Three Sulfonamide Tablets "300"	Nysco Laboratorienc.	4/2/69
Penicillin w/Triple Sulfas Tabs.	Biocraft Laboratories, Inc.	4/2/69
Penicillin w/Triple Sulfas No. 1, No. 2 and No. 3 Tablets	Richlyn Laboratories, Inc.	4/2/69
Penicillin w/Triple Sulfas Tabs.	Supreme Pharmaceutical Co.	4/2/69
Penicillin G w/Triple Sulfas Tabs.	Vitamix Pharmaceuticals, Inc.	4/2/69
Penicillin w/Triple Sulfonamides (100,000 units) Tablets	Zenith Laboratories, Inc.	4/2/69
Penicillin w/Triple Sulfonamides (200,000 units) Tablets	Zenith Laboratories, Inc.	4/2/69
Penicillin w/Triple Sulfonamides (250,000 units) Tablets	Zenith Laboratories, Inc.	4/2/69
Penicillin w/Triple Sulfonamides (300,000 units) Tablets	Zenith Laboratories, Inc.	4/2/69
Pen Strep Powder for Injection (4:1; 4:1/2)	Merck & Company, Inc.	4/2/69
Penid Sulfas for Syrup	E. R. Squibb & Sons	4/2/69

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Pentid Sulfas "400" for Syrup	E. R. Squibb & Sons	4/2/69
Pentids-Sulfas Tablets	E. R. Squibb & Sons	4/2/69
Pentocin	Pure Laboratories, Inc.	4/2/69
Pen-Vee Cidin Capsules	Wyeth Laboratories, Inc.	9/12/69
Pen-Vee Sulfas Suspension	Wyeth Laboratories, Inc.	4/2/69
Pen-Vee Sulfas Tablets	Wyeth Laboratories, Inc.	4/2/69
Pepsodent Antiseptic Mouthwash	Lever Brothers	8/4/70
Perithiazide SA Tablets	Warner-Chilcott Laboratories	8/29/70
Pharycidin Concentrate	Purdue Frederick	10/7/70
Phemerol Solution (benzethonium chlorldie) 1:750	Parke, Davis & Company	9/12/69
Phemerol Tincture (benzethonium chloride) 1:500	Parke, Davis & Company	9/12/69
Phemerol Topical	Parke, Davis & Company	9/12/69
Plimasin Tablets	Ciab Pharmaceutical	10/15/70
PMB-200 & PMB-400 Tabs	Ayerst Laboratories	8/26/70
Polanil Tabs	Schering Corporation	8/29/70
Polycycline Suspension w/Triple Sulfonamides	Bristol Laboratories, Inc.	4/2/69
Polymagma Oral Suspension	Wyeth Laboratories, Inc.	7/2/70
Polymagma Tablets	Wyeth Laboratories, Inc.	7/2/70
Potassium Penicillin G. w/Triple Sulfonamides Tablets	Philadelphia Laboratories, Incorporated	4/2/69
Powdalator ES	Abbott Laboratories	12/9/69
Prednaman Tabs	Dome Laboratories	8/29/70
Presniscord Tablets	Nysco Laboratories, Inc.	3/28/70

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Free MT Tablets	Wallace Pharmaceuticals	2/6/70
Procaine Penicillin in Streptomycin Sulfate Solution	Roehr Products Co., Inc.	4/2/69
Protamide Injection	Sherman Laboratories	7/17/70
Quercetin Tablets	Abbott Laboratories	7/10/68
Quintess-N Suspension	Eli Lilly & Co	7/2/70
Raumannite-50 Tablets	Nysco Laboratories, Inc.	7/10/68
Rautrax Improved Tablets	E. R. Squibb & Sons, Inc.	9/5/69
Rautrax N Modified Tablets	E. R. Squibb & Sons, Inc.	9/5/69
Rautrax N Tablets	E. R. Squibb & Sons, Inc.	9/5/69
Rautrax Tablets	E. R. Squibb & Sons, Inc.	9/5/69
Rauwiloid and Hexamethonium Tablets	Riker Laboratories	10/15/70
Rauwolfia Serpentina-Mannitol Hexanitrate-Rutin Tablets	Best Pharmaceuticals	7/10/68
Rauwolfia Serpentina-Mannitol Hexanitrate-Rutin-Veratrum Viride Tablets	Robin Pharmacal Co.	7/10/68
Remanden-250	Merck Sharp & Dohme	7/1/70
Reserthonium Tablets	Nysco Laboratories	10/15/70
Retrogratin Solution	E. R. Squibb & Sons, Inc.	1/14/70
Retropaque Solution	Winthrop Laboratories	1/14/70
Rhinazine (nasal solution)	Lederle Laboratories	9/9/69
Ritonic Capsules	Ciba Pharmaceutical Co.	9/12/69
Robaxisal	A. H. Robins Co., Inc.	2/11/70
Robaxisal-PH Tablets	A. H. Robins Co., Inc.	2/11/70
Roniacol w/Aminophylline Tablets	Roche Laboratories	9/17/70

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Ruhexatal w/Reserpine	Lemmon Pharmacal Co.	7/10/68
Rusyntal	Central Pharmacal Co.	10/7/70
Rutin Tablets	Abbott Laboratories	7/10/68
Rutin Tablets	The Maltine Company	7/10/68
Rutin Tablets	Parke, Davis & Co.	1/23/68
Rutorbin Tablets	E. R. Squibb & Sons, Inc.	1/23/68
Salcort-Delta Tablets	The S. E. Massengill Co.	3/28/70
Sergynol Tablets	B. F. Ascher & Co., Inc.	2/6/70
Seromycin w/Isoniazid	Eli Lilly & Co.	9/18/69
Signemycin Capsules "250"	J. B. Roerig & Co.	4/2/69
Signamycin Capsules "250"	Chas. Pfizer & Co.	4/2/69
Signemycin Capsules "375"	J. B. Roerig & Co.	4/2/69
Signamycin Capsules "375"	Chas. Pfizer & Co.	4/2/69
Signemycin Pediatric Drops	J. B. Roerig & Co.	4/2/69
Signemycin Pediatric Drops	Chas. Pfizer & Co.	4/2/69
Signemycin Syrup	J. B. Roerig & Co.	4/2/69
Signemycin Syrup	Chas. Pfizer & Co.	4/2/69
Siltrobarb Tablet	Cole Pharmacal Co., Inc.	3/27/70
Sinaxar Tablets	Armour Pharmaceutical Co.	9/27/69
Skelaxin Tablets	A. H. Robins Co., Inc.	2/6/70
Somacort	Wallace Pharm.	5/7/70
Sorboquel w/Neomycin Tabs.	White Laboratories, Inc.	7/2/70
Spectrocin Nasal Spray	E. R. Squibb & Sons, Inc.	8/21/70

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Spectrocin-T Troches	E. R. Squibb & Sons, Inc.	9/19/70
Stenediol Sublingual Tabs.	Organon, Inc.	2/11/70
Sterisol	Warner-Lambert Pharm. Co.	8/4/70
Strep-Combiotic Aqueous Suspension (multidose)	Chas. Pfizer & Co. Inc.	4/2/69
Strep-Combiotic for Aqueous Suspension (single dose)	Chas. Pfizer & Co. Inc.	4/2/69
Strep-Combiotic Isoject Aqueous Suspension	Chas. Pfizer & Co., Inc.	4/2/69
Strep-Dicrysticin	E. R. Squibb & Sons, Inc.	4/2/69
Strep-Dicrysticin-800	E. R. Squibb & Sons, Inc.	4/2/69
Strep-Dicrysticin Fortis	E. R. Squibb & Sons, Inc.	4/2/69
Strep-Dicrysticin Fortis-800	E. R. Squibb & Sons, Inc.	4/2/69
Strep-Districillin-A.S. Sterile Suspension	E. R. Squibb & Sons, Inc.	4/2/69
Streptomagma Liquid	Wyeth Laboratories, Inc.	7/2/70
Streptomagma Tab.	Wyeth Laboratories, Inc.	7/2/70
Streptomycin-Bipenicillin Injection	Pure Laboratories, Inc.	4/2/69
Strexate Tablets	Armour Pharmaceutical Co.	9/27/69
Strycin Syrup	E. R. Squibb & Sons, Inc.	7/2/70
Sulfaguanidine Tablets (0.5 gram)	Lederle Laboratories	6/7/69
Sulfa-Sugracillin 125M Granules	The Upjohn Company	4/2/69
Sulfa-Sugracillin 250M Fortified Granules	The Upjohn Company	4/2/69
Sulfathiazole Gum Tablet	White Laboratories, Inc.	11/6/68
Sulfathiazole Tablet (0.5 gram)	Bowman, Mall & Co.	9/11/69

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Sulfathiazole Tablet (0.5 gram)	Vale Chemical Co. Inc.	9/11/69
Sulfathiazole Tablet (0.5 gram)	Eli Lilly & Co.	9/11/69
Sulfathiazole w/Tuamine Sulfate Suspension	Eli Lilly & Co.	9/9/69
Sulfedex Nasal Solution	Abbott Laboratories	9/9/69
Sulfel Tablet	The Vale Chemical Co., Inc.	11/6/68
Sulfonamets w/Topicalaine Lozenges	National Drug Co.	9/6/68
Super Amm-I-Dent	Block Drug Co., Inc.	7/21/70
Super Anapac Cough Syrup	Rexall Drug & Chemical Co.	7/10/68
Syndecon for Oral Solution	Bristol Laboratories	9/12/69
Syndecon Tablets	Bristol Laboratories	9/12/69
Tace with Ergonovine Capsules	William S. Merrell Co.	10/24/70
Tain Oral Suspension	Dorsey Laboratories	9/12/69
Tain Tablets	Dorsey Laboratories	9/12/69
Tao-AC Capsules	J. B. Roerig & Co.	9/12/69
Taomid Oral Suspension	J. B. Roerig & Co.	9/5/69
Taomid Tablets	J. B. Roerig & Co.	9/5/69
Tenserine Tablets	Abbott Laboratories	7/10/68
Tergemist (Inhalant)	Abbott Laboratories	7/17/68
Terramycin Dental Cones	Chas. Pfizer & Co., Inc.	2/21/69
Terramycin Dental Paste	Chas. Pfizer & Co., Inc.	2/21/69
Terramycin S.F. Capsules	Chas. Pfizer & Co., Inc.	4/2/69
Terrastatin Capsules	Chas. Pfizer & Co., Inc.	4/2/69
Terrastatin for Oral Suspension	Chas. Pfizer & Co., Inc.	4/2/69

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
Tetracydin Capsules	J. B. Roerig & Co.	9/12/69
Tetrastatin Capsules	Chas. Pfizer & Co., Inc.	4/2/69
Tetrastatin for Oral Suspension	Chas. Pfizer & Co., Inc.	4/2/69
Tetrex-AP Syrup	Bristol Laboratories, Inc.	9/12/69
Tetrex APC w/Bristamin Capsules	Bristol Laboratories, Inc.	9/12/69
Tetrex Syrup w/Triple Sulfonamides	Bristol Laboratories, Inc.	4/2/69
Theoglycinate w/Rutin & Phenobarbital Tablets	Brayton Pharmaceutical Co.	7/10/68
Thizodrin Solution (nasal)	Eli Lilly & Co.	9/9/69
Toldex Tabs.	Pitman-Moore	8/29/70
Trexinest Tablets	Hynsen, Westcott & Dunning	5/24/68
Triaminic HC Tabs	Dorsey Laboratories	8/29/70
Triple Hormone Suspension	Taylor Pharmaceutical Co.	8/29/70
Trisem-Pen Powder	The S. E. Massengill Co.	4/2/69
Trisem-Pen Tablets	The S. E. Massengill Co.	4/2/69
Trisocort Spraypak	Smith, Kline & French Labs.	8/21/70
Trypsin Injection	Wilson Laboratories	6/25/70
Tyrolaris Mouthwash	Merck & Co.	8/4/70
Urethane Tablets	Eli Lilly & Co.	8/21/70
Urobiotic Capsules, 100, 250	Pfizer & Co.	6/30/70
V-Cillin K Sulfa Pediatric for Oral Suspension	Eli Lilly & Company	4/2/69
V-Cillin K Sulfa Tablets	Eli Lilly & Company	4/2/69
V-Cillin Sulfa Pediatric for Oral Suspension	Eli Lilly & Company	4/2/69

<u>NAME OF DRUG</u>	<u>COMPANY</u>	<u>DATE</u>
V-Cillin Sulfa Tablets	Eli Lilly & Company	4/2/69
V-Kor	Eli Lilly & Company	9/12/69
Visciodol	E. Fougera	2/11/70
Wybiotic	Wyeth Laboratories, Inc.	9/19/70
Wycillin SM Injection 400	Wyeth Laboratories, Inc.	4/2/69
Wycillin SM Injection 600	Wyeth Laboratories, Inc.	4/2/69

Senator NELSON. Well, are you referring to the list of drugs that the NAS-NRC evaluated for the FDA?

Dr. WELLS. Yes.

Senator NELSON. And what exactly does your regulation do? Are you saying that you are ordering that no drugs found to be ineffective by NAS-NRC be included in any formulary?

Dr. WELLS. Yes, sir. May I read from the circular specifying that each therapeutic committee will review the formulary drugs in use at that activity:

If any drugs classified by FDA as ineffective are present they will be removed from the hospital formulary and therefore will be unavailable for prescribing by VA staff physicians and dispensing by VA pharmacists.

Senator NELSON. What about the "possibly effective" drugs?

Mr. STATLER. Senator, we are aware of the list of 159 possibly effective drugs that was put out by HEW, that Dr. Steinfeld mentioned yesterday. We have screened this listing, which is unofficial, since it was not put out by the FDA. We have been in contact with FDA asking for such a list. In fact, on November 2d, 1970, our Chief Medical Director wrote to Dr. Edwards asking for a listing of not only the ineffective but the possibly, the probably, and the effective drugs and said we would make such information available to our hospitals. To date there has not been an official release of other than the ineffective. We understand they have been published in the Federal Register and we are aware of the listing by HEW—we have obtained that and furnished it to our Marketing Center on Drugs to be sure that no drugs on the list are procured on Central Procurement.

As of now the list has not gone out to our therapeutic committees and hospitals because we are advised that FDA is preparing an official listing which is expected to come out within a 2-week period.

Senator NELSON. What do you expect?

Mr. STATLER. That the list will be sent to our committees for prescribing guidance and appropriate action.

Senator NELSON. What does that mean?

Mr. STATLER. Whatever action they deem necessary. If, for example, a drug is on the possibly effective list and there is a drug on the effective list that can be used, certainly they would change over. If there is a drug on the possibly effective list of which there is no substitute for good therapeutic management of the patient, they will be faced with the decision whether to continue to use it because it is not officially off the market yet and is needed.

Senator NELSON. I don't know whether that list would show the drugs I am familiar with as I read the list. For all of them that I can recall there was an alternative, effective drug, at least for all the fixed combination anti-infectives. Is that correct?

Mr. STATLER. Generally that is right.

Senator NELSON. Now, of course, they have all been labeled ineffective anyway, so you don't allow any of them to be used.

Mr. STATLER. Ineffective we are not using, right.

Senator NELSON. But what do you say to the therapeutic committee? Do you say this is listed as "possibly effective" and there is an effective drug that is available for the same purpose, therefore, we will not pay for any possibly effective drugs?

Mr. STATLER. No. Of course, they will have that information or arrive at a decision which one they will use. However, it should be clearly understood, and I am sure you understand that, FDA in this listing is going to have some difficulty because not all drugs are in black and white or in a gray area. Some of them have a classification of effective for this but not for that, possibly effective for this condition and not for that, and in some instances ineffective for certain conditions, so that total information is going to have to be provided to all physicians and, of course, to our therapeutic committees so they will take necessary action.

An example would be a drug might be on the possibly effective list for a certain condition but ineffective for something else, so they will hope the physicians would prescribe it only for the effective use.

Senator NELSON. Well, I would, too.

Mr. STATLER. I would, too.

Senator NELSON. If a drug is listed and published by the NAS-NRC and the FDA as "possibly effective" for a specific purpose, and there is an alternative drug that the NAS-NRC says is effective, will you direct that VA physicians use the effective one and that you won't pay for the possibly effective one? That is my question.

Mr. STATLER. I would think that this peer review will certainly settle that question. They will be looking at all angles, at all information available, and will be making decisions based on this.

Senator NELSON. Peer review within the hospital?

Mr. STATLER. By these knowledgeable individuals composing the therapeutic committees.

Senator NELSON. When you were here in August you said that you had great difficulty influencing the therapeutic committee at the local level because these doctors just came in for 2 or 3 years and didn't like to be dictated to. So what you are really saying is—even though this is an effective drug, as demonstrated by well-controlled clinical trials, and there is one that is listed "possibly effective" for which there haven't been well-controlled clinical trials, that you will permit them to put the possibly effective on the formulary even though there is an effective one for exactly the same purpose, and that you will pay for it? Or rather that you will let the local group decide that question?

Mr. STATLER. No. There will be a monitoring, there is a continual monitoring of what is going on in our committees from our central office staff. Any drug that is going to be approved for formulary inclusion is monitored. Obviously anything on the possibly effective list or certainly on the ineffective list, if by chance or error they decided they were going to approve it, we would contact them about something else being available.

Senator NELSON. A few moments ago I understood you to say that this question of using a possibly effective and effective drug would be decided by the local formulary group at the hospital.

My question is: Will you refuse to permit them to use a possibly effective drug when there is, in fact, an effective one that is available? Did I understand you to say that would be decided at the local level?

Or did you say that it would be decided at the national level?

Dr. WELLS. We are certainly going to have something to say about this at the national level. Although I think that we may as well say at this point that our problem is an educational one as much as anything else and one of gradual evolution in this course.

I would like to go on with the rest of this paragraph which I believe really answers a large part of your question, Senator.

Senator NELSON. All right. I am not satisfied with what I have heard, but go ahead.

Dr. WELLS. All right; now, as additional assurance that procurement of these drugs as referred to would be discontinued, we also issued Department of Medicine and Surgery Circular 10-70-286 which I would also like to submit for the record.

(The information above-referred to, follows:)