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# SHORTAGES OF PRESCRIPTION DRUGS, 1974

GOVERNMENT

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## JOINT HEARING BEFORE THE SUBCOMMITTEE ON HEALTH OF THE COMMITTEE ON LABOR AND PUBLIC WELFARE AND THE

## SUBCOMMITTEE ON ADMINISTRATIVE PRACTICE AND PROCEDURE OF THE

## COMMITTEE ON THE JUDICIARY UNITED STATES SENATE

NINETY-THIRD CONGRESS

SECOND SESSION

ON

EXAMINATION OF SHORTAGES—CURRENT AND IMPENDING—OF PRESCRIPTION DRUGS IN THE UNITED STATES

DECEMBER 5, 1974



Printed for the use of the Committee on Labor and Public Welfare  
and the Committee on the Judiciary

U.S. GOVERNMENT PRINTING OFFICE

WASHINGTON : 1975

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## SHORTAGES OF PRESCRIPTION DRUGS, 1974

THURSDAY, DECEMBER 5, 1974

U.S. SENATE, SUBCOMMITTEE ON HEALTH OF THE  
COMMITTEE ON LABOR AND PUBLIC WELFARE,  
SUBCOMMITTEE ON ADMINISTRATIVE PRACTICE AND  
PROCEDURE OF THE COMMITTEE ON THE JUDICIARY,  
*Washington, D.C.*

The subcommittees met, pursuant to notice, at 10:01 a.m., in room 4232, Dirksen Senate Office Building, Hon. Edward M. Kennedy, chairman of the subcommittees, presiding.

Present: Senator Kennedy.

Senator KENNEDY. The subcommittee will come to order.

During the past year, shortage has become an essential word in the American vocabulary. We have seen how fragile our economy is and how dependent we are on our neighbors around the world.

In a year of unpredictable events, the only certainty has been a steep rise in the price of almost everything.

The health care system is as vulnerable to the changing ground rules of American life as any other part of our economy.

Today, we will examine shortages—current and impending—of prescription drugs in the United States.

The Nation is already experiencing shortages in two important drugs—heparin and injectable sodium ampicillin. It will soon face the prospect of an extremely serious shortage of opium products—morphine and codeine. It is currently paying double the price for quinine—an important heart drug—that it paid just several months ago.

The reasons for these shortages differ. Some are due to natural resource limitation; some to market manipulation; some to a drastic but temporary reduction in production capability.

The consequences, and potential consequences, are grave. What is lacking is an early warning system that would enable prediction of shortages early enough to allow preventative measures to be taken.

It is my hope that today's hearing will spur the development of such a system and a solution to these problems. The alternative is to react only after shortages occur, and the consequences of that may be measured in terms of lives.

Our first witness representing the Food and Drug Administration is Dr. John Jennings, Associate Commissioner for Medical Affairs of FDA, a position he has held since April 1970. Prior to that, he was Acting Director of the Bureau of Drugs.

He came to the FDA as a medical officer in the Drug Surveillance Branch in October 1964.

He is accompanied by Robert Wetherell, FDA's Office of Legislative Services, and J. Joseph Belson, Special Assistant to the Director of the Bureau of Drugs.

We welcome you to the committee.

**STATEMENT OF JOHN JENNINGS, M.D., ASSOCIATE COMMISSIONER FOR MEDICAL AFFAIRS, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE; ACCOMPANIED BY ROBERT C. WETHERELL, JR., DIRECTOR, FDA'S OFFICE OF LEGISLATIVE SERVICES; AND J. JOSEPH BELSON, SPECIAL ASSISTANT TO THE DIRECTOR, BUREAU OF DRUGS**

Dr. JENNINGS. Thank you, Mr. Chairman.

We welcome this opportunity to discuss with your subcommittee the role of the agency with respect to the shortages of drug supplies.

I have submitted for the record a 14-page double-spaced statement, which I will read or attempt to summarize, as you choose.

Senator KENNEDY. We will include it in its entirety in the record at the conclusion of your testimony. You can summarize it and highlight it any way you'd like.

Dr. JENNINGS. I might start by saying that I agree completely with your very concise summary of the situation and with your conclusion that what is needed is an early warning system to attempt to prevent such shortages from occurring.

Although the Food and Drug Administration has no statutory authority in this area, we are consulted—

Senator KENNEDY. Do you know if any governmental agency has any authority that you know about to perform that function?

Dr. JENNINGS. No, sir, not to my personal knowledge.

In the defense area there is sufficient authority to take steps to prevent any shortage of raw material from affecting the national security. But, an admittedly rather superficial inquiry on our part disclosed no civilian counterpart.

Senator KENNEDY. Do you think there should be statutory authority?

Dr. JENNINGS. I think it deserves serious consideration.

In certain circumstances, there would exist critical shortages of basic raw materials, which would make necessary an allocation to essential civilian needs.

Senator KENNEDY. If you agree that an early warning system is desirable, and you recognize the limitation in statutory authority, do you agree it would be useful and helpful to have such a mandate for the FDA?

Dr. JENNINGS. I am not sure that the FDA is the place for it.

I think perhaps our best contribution to the solution of this problem would be to become a focal point for information relating to shortages of drugs and other medical products.

As you are undoubtedly aware, and as we will discuss and others will discuss in greater detail, these shortages arise from diverse etiologies.

Senator KENNEDY. We certainly want to get into the reasons for the shortages. But just you are able to collect the information. Who is going to have the power to act? You have indicated no one does at the present time.

Dr. JENNINGS. In many cases it would undoubtedly be unnecessary to make specific allocations.

Once the problem was recognized, steps could be taken under current conditions to alleviate or to prevent shortages.

The question of allocation, I think, would be transcendental to any particular agency. It would have to be lodged in a relatively high place in the Government, because of the concern with these materials that would be vital not only to the health and safety areas of our life, but perhaps to the national security.

One example I can offer in this regard is the fairly recent shortage of a product called hydrazine hydrate which is used in the production of a drug for the treatment of gout, and which is also used in the production of rocket fuel. This material came into short supply partially as a result of the oil embargo. It would be rather difficult for the Food and Drug Administration to assume responsibility of allocation of material that, let us say, was deemed vital to national security.

Senator KENNEDY. That is certainly so. But, should there not be some agency of Government that is performing the early warning system function?

You can determine now when shortages occur, but you have not got access either to production figures or to information that would permit you more lead time to estimate what drugs are going to be in short supply, and the importance of such a supply. Why are you reluctant to comment that such a system would be worthwhile?

Dr. JENNINGS. I am afraid I misunderstood you.

I certainly agree with you completely that we should have all of the authority we need to implement an early warning system regarding a possible drug shortage.

Senator KENNEDY. Do you or do you not have that authority?

Dr. JENNINGS. We do not have complete authority in that regard.

I might point out two things. One, Mr. Wetherell brought to my attention, and our statement includes reference to a National Commission on Supplies and Shortages which was established in the latter part of this year and which is scheduled to report in March 1975 on the various factors relating to essential materials and their possible shortages.

The second thing is that we have long been concerned with our lack of overall authority in the area covering complete data on drug production and distribution. We do have this authority in certain other areas, such as for new drugs and for certifiable antibiotics.

In such instances, we are fairly well informed as to the amount of material, the actual drug products that are produced and distributed. But, in those drugs that are not covered by new drug applications or by insulin and antibiotic certification, our authority is somewhat less and we do not have actual access to the data.

When the Drug Listing Act was passed a year or so ago, this was one of the provisions that was removed prior to the passage of the act, and I don't believe it is any secret that the Food and Drug Administration was and would still be in favor of including that provision in the act.

Senator KENNEDY. I am not familiar in detail with what the Commission on Resource Allotment will come up with in February or March. I am roughly familiar with the rather detailed study that was done by Brookings recently at their Tokyo meeting. It has been published in the last several months. It goes into a wide variety of raw materials, and does attempt to dampen some of the speculation about critical resource shortages.

But tying the area of drug shortages completely up with these sorts of studies and conclusions does not seem to me to be really the answer.

It seems that FDA does not want additional responsibility for coming up with conclusions on this. But, I think you have identified that the development of an early warning system is clearly in the interest of health policy of this country.

If you do not have the statutory authority to get the material needed to make projections on these shortages, which we hear are in very critical short supply, I don't see how you can cope with this serious problem. You do not, quite frankly, have nearly the sense of urgency which later witnesses are going to show in terms of some of these drugs and the lack of availability of them.

But it seems to me that if we agree that some kind of early warning system is useful and important, that it is not asking too much, both of you and the agency, to make some recommendations as to what you think is necessary to gain such information.

It seems to me that the Food and Drug Administration is the prime candidate for such responsibility.

Let us move on in your testimony, but I hope you will bring this up into your policy body of the FDA, and come back to us stating either you do think it is necessary and desirable, you think it should not be yours for various reasons, or you think it should be, and let us see where we can go from there.

Dr. JENNINGS. I hope nothing I have said, or nothing in my statement, gives the idea that we do not consider it a responsibility. We certainly do, and we are actively pursuing the implementation of an early warning system.

We are relatively new to this phenomenon. It has not attracted a lot of attention until fairly recently, although sporadic shortages have been reported to us over the past several years.

We are taking active steps to define the scope and depth of this problem, and I can assure you that we will be back to you with recommendations regarding any additional authority that we feel we should have.

We do have a sense of urgency about shortages. I want to dispel any notion that this does not exist. However, we have to put it in the proper perspective. There are possibilities for harm if we upset users of drugs about shortages that can be treated with measures short of a public alarm.

So far to my knowledge, we have had no instances where anybody has been seriously injured, or treatment hampered, by any of these shortages. They have referred mostly to inventories, rather than to the actual availability of the drugs.

Senator KENNEDY. That is certainly a prime consideration, although I think it is important to understand where the curve is moving on some of these drugs.

I would think that you would be very much alarmed at the way these curves are moving in terms of shortages.

Dr. JENNINGS. Yes, sir.

Senator KENNEDY. A doctor, Dr. George Wysof, from Long Island, Hillside Medical Center wrote to me stating, in part:

I would like you to be aware of the lack of heparin in the United States. It has produced a difficult situation for lack of medical care for patients. In our hospital there is no heparin available for anticoagulant treatment of patients following heart surgery.

I understand that signs have been posted in some of our outstanding medical schools that warn of the shortages and the need to conserve these drugs. So we cannot say that nobody has suffered. That does not get into the other side of the question, which is the enormous increase in the cost of many of these items to consumers, although that is obviously a secondary consideration to the factor of health.

Let us move ahead.

Dr. JENNINGS. Yes. Heparin is one of the drugs that we have discussed, and is to be dealt with in detail by some of the manufacturers. This is a prime example of one particular type of shortage.

The demand for heparin has increased markedly over the past several years due to its use in heart surgery and in kidney dialysis, and now more and more in routine treatment of pre- and post-operative patients.

Heparin also demonstrates one particular type of shortage, that of a drug for which there is no substitute. Because of its *in vitro* activity, heparin is indispensable in bypass procedures and renal dialysis for kidney failure.

Senator KENNEDY. There is no substitute? It is not a shortage of one drug that can be substituted for which a substitute can be found.

Dr. JENNINGS. Exactly. That is what I am saying. In some of the other shortages, a substitute drug or treatment could be employed. In the case of heparin, this is not so. That is why we consider it a very serious matter.

The problem again, as I say, stems from rapidly increasing demands, with a supply that is more or less fixed, because of the situation regarding the basic raw material. Heparin is produced from either bovine lungs or the intestinal mucosa of swine, and the mucosa accounts for approximately 90 percent of production, which until recently was a byproduct of the sausage casing industry. The sausage casing industry is on the decline to some extent, because of the use of synthetic substitutes for hog intestines and the problem now is basically one of making the saving of hog intestinal mucosa for medical progress economically attractive to the meatpackers.

In a recent meeting with the producers of heparin, and representatives of the meat industry, several facts came out which are of importance in this particular shortage. One is that the pharmaceutical industry has adequate facilities to produce enough heparin to meet current and future demands, provided they get sufficient raw material. Many companies have already begun to seek additional sources of raw material and have increased their production.

The supply of raw material is basically adequate, providing the saving of the mucosa can be made economically attractive to the meat packers. There has already been significant relief of this particular shortage, and we expect that by early next year the supply will be sufficient to meet all demands, including those that are perhaps less than absolutely essential.

The other kinds of problems that have confronted us, other than the basically economic one as demonstrated by the heparin shortage, are such things as adverse weather conditions affecting the production of basic raw commodities, exemplified by poppy production in India; the shortage of basic raw materials such as hydrazine hydrate which is also used as rocket fuel; and shortages which may be totally artificial, such as the quinidine shortage due to manipulation of supply.

With your permission, I will talk about each of these very briefly.

To take up quinidine first, we have been unable to verify that there is an actual shortage of this material. I think the reason that the shortage was perceived was that the price had increased some fourfold in the past year. Quinidine is derived from quinine, which comes from a tree bark found mainly in Indonesia and Africa.

Although we can only speculate on this, we believe that the rapid price increase was due to manipulation of the supply by a cartel, which in effect has cornered the market.

Senator KENNEDY. Is that still going on now?

Dr. JENNINGS. To the best of my knowledge, that situation still obtains.

The Dutch apparently control practically the entire basic raw material supply. Of course, this is outside of the purview of the Food and Drug Administration, and I am really giving you second hand reports on this, but I can tell you that the General Services Administration's emergency stockpile at the present time is 1.8 million ounces of quinidine.

Senator KENNEDY. When you find this out, what do you do as far as the State Department is concerned? Chancellor Schmidt is here today with the President. He has got all of his advisers here. Is this something that is added to his roster of agenda items to discuss with the Germans?

Are we raising this thing at the ambassadorial level with the Dutch Government? What kind of cooperation are we getting? You know about this. Are you brought into this kind of discussion?

It seems to me we are working with our allies on a common energy problem, and they appear to be involved in exercising their leverages in terms of matters which have a very important effect on the health of the people in this country, and I am just wondering what are we doing about it?

Dr. JENNINGS. Well, sir, I would hesitate to get into that. As I say, it is beyond our purview and we are at a very early stage in our investigation of this particular problem.

Senator KENNEDY. Was this not up before Senator Hart's committee?

Dr. JENNINGS. Yes. There were very detailed Senate hearings in 1966, and Senator Hart, I believe, chaired the subcommittee of the Judiciary.

Senator KENNEDY. Antitrust Committee. I happen to be on that committee.

Dr. JENNINGS. There was considerable information brought out at that time.

What we are seeing today is a parallel situation.

Senator KENNEDY. What do we have to do about it? Do you have to crank up the Antitrust Committee again in order to try to get a handle on some of these costs?

Dr. JENNINGS. It probably would be well to get both the antitrust machinery, and perhaps the diplomatic process, involved in this. It is parallel, perhaps, to the oil situation.

Senator KENNEDY. How do you see the responsibility of your agency in this?

Dr. JENNINGS. What we hope to do eventually is to be able to develop sound hard information on these problems and then translate that information to the proper area.

For example, in another shortage that will be discussed today, the opium shortage, we were able to work with the State Department and the Drug Enforcement Agency to develop hard information on needs and supplies and to suggest steps that might be taken to alleviate the situation.

I would think that we can do this in the case of any shortage. As I say, we are in the very early stages of developing a system to do this, and on November 15, 1974, the Commissioner designated my office as the focal point for any information relating to drug shortages. We are now in the process of acquiring knowledge and in identifying all of the agencies and individuals involved.

This will be our role, that of providing prompt and reliable information relating to current or potential shortages.

Senator KENNEDY. A clear illustration of how Quinidine has gone up is a letter I have from an irate consumer, and what is even more interesting, an irate pharmacist, who encouraged Mr. Graham to write me. I quote from the letter:

Since my pharmacist is unable to explain why the price of Quinidine Sulfate has doubled in one month's time, I am hoping you might be able to find a reasonable explanation. Enclosed is a copy of the last four prescriptions I have purchased in Ithaca, New York. Any help in the matter would be greatly appreciated.

Now, this says on July 31, 1974, \$6.99 for 200 milligrams of Quinidine.

Then, September 9, the same amount for \$13.98. Virtually doubled for the exact same amount in a 2-month period.

The pharmacist sent me his costs, which show that he started paying \$49.50 for a thousand tablets, and then after the two companies

dropped it from their catalogs, he is paying \$101.18, so his cost has gone up from \$49.50 to \$101.18 for the thousand capsules. And the increase goes to the consumer.

I do not know how much clearer evidence you need to raise this with the State Department.

Now, what can you do about that? What do I say when those people write me? What should I do?

Dr. JENNINGS. I am not sure I can answer, Mr. Chairman.

We have no authority at all in the area of drug prices. However, HEW is beginning to move into this area through its recently published regulations relating to the maximum allowable costs of drugs that are reimbursed by the Federal Medical Services. The example you are using now is obviously not representative of a true shortage, but simply of somebody taking advantage of a monopoly. We would have to defer a problem of this sort to those Federal agencies which are in a position to take steps.

Senator KENNEDY. When did you do that?

Dr. JENNINGS. As I say, we have become aware of this particular problem only very recently and have not done anything under our current authority to attempt to control or regulate or to affect the price of the product.

Senator KENNEDY. This is part of our problem.

These costs went up in the 1-month period from the end of July to the first day of September, and now we are in December.

Why does action have to wait on this type of crisis situation until we happen to hear from a pharmacist and his customer, when in fact FDA should have the responsibility and manpower to investigate these enormous cost increases before they reach the consumer level.

Dr. JENNINGS. As I have said, and will repeat, we have no authority in this area. I would not deny that we share some responsibility in it.

Senator KENNEDY. How is the antitrust division going to hear about it?

Dr. JENNINGS. I assume they have as much opportunity to hear about it as we have. I certainly can assure you that we will make sure that they learn about it if they do not already know.

There is, of course, within the Office of the Secretary a position of emergency coordinator to serve as a focal point for gathering information relating to emergency situations, including drug shortages; but I must again repeat that what we are dealing with is a relatively new problem, and we are in the early stages of developing a system to deal with it.

I do not know that we will ever, as an agency, be in a position to deal effectively with questions of drug costs. This as you know better than most, is a very complex problem, and I think our major contribution should be to develop a system for obtaining information and to take whatever actions we can to alleviate shortages, as well as to bring the problems to the attention of others within the Government who might have the authority and the ability to affect the price.

For instance, I am not even sure that the antitrust mechanism could handle a situation where we are dependent on foreign supplies of raw materials. Certainly, I do not know that the antitrust measures would

be effective against the coalition of Emirs, Sultans, and Shahs who are controlling the oil supply, but I defer to the Justice Department in this regard.

Senator KENNEDY. They did act on this drug in 1966.

Dr. JENNINGS. Well, I think, again, I am out of my depth, but there may be diplomatic or other channels that might affect it.

Senator KENNEDY. I want to move on, but this is information that you people ought to have. It should not take a Senate committee to come up with it. It really should not.

When it does come up, I would like to see it referred to the appropriate agency of the Government, whether it's the antitrust division, or you. We want to know what additional authority you need to get the job done.

Dr. JENNINGS. I can assure you, Mr. Chairman, that we will come back to you with an analysis of any needs that we perceive for additional authority.

I can also assure you that we will discuss this with the other agencies, within HEW, where concern with this problem has already been expressed.

Senator KENNEDY. Then let us know what conclusions you reach.

Dr. JENNINGS. Yes, sir.

[Information subsequently supplied for the record follows:]

#### FDA'S PROPOSAL ON ADDITIONAL AUTHORITY CONCERNING DRUG SHORTAGES

A review of current authority and proposals pending in the Ninety-third Congress did not reveal any existing or proposed authority which allows the Department of Health, Education, and Welfare to require drug manufacturers to submit information on drug shortages. Section 301 of the Public Health Service Act provides broad authority authorizing the Department to promote the coordination of investigations "relating to the causes, treatment, control, and prevention of physical and mental diseases and impairments of man," 42 U.S.C. 241, which clearly could include requests for submission of information concerning drug shortages. This section authorizes the Department to request the submission of data on drug shortages, but does not authorize the Department to require that information be submitted; no penalty attaches to refusals to provide the requested information. It is arguable that section 361 of the Public Health Service Act, which authorizes the Secretary to issue regulations "to prevent the introduction, transmission, or spread of communicable diseases into the States or possession, or from one State or possession into any other State or possession," may allow promulgation of regulations to obtain information on drugs used to treat "communicable diseases," but this authority would not help to deal with shortages of most drugs. (Except with respect to law enforcement functions of the FDA—which would not include drug shortages—this authority has been delegated to the Center for Disease Control.)

The Bureau of Narcotics and Dangerous Drugs possesses authority to obtain information relating to medical needs for Schedule II controlled substances and to establish production quotas for these substances.

The Department had pending in the Ninety-third Congress a bill, the Food, Drug, and Cosmetic Amendments of 1974 (S. 3012) which would enable the Department, through the FDA, to require the submission of "such information as the Secretary may, by regulation, reasonably require for the purposes of implementing this Act, or to determine compliance with rules or orders prescribed under this Act." S. 3012 would also give the Department authority to utilize the reports and subpoena authority of the Federal Trade Commission for purposes of administering and enforcing the Federal Food, Drug, and Cosmetic Act. This proposal would provide FDA with broad authority which the Department considers essential in assuring that drugs are safe, effective, not adulterated, and not misbranded. However, this proposal cannot reasonably be construed to in-

clude authority to order submission of data relating to drug shortages for general public health objectives rather than for the specific purposes of the Federal Food, Drug, and Cosmetic Act—simply because the scope of existing purposes of the present Act would not encompass public health problems caused by drug shortages. As indicated by Dr. Jennings at the hearing in 1971 and 1972 when Congress was considering the Drug Listing Act of 1972, the Department favored broad authority to obtain “any production data the Secretary may require,” concerning all drugs (H.R. 4749, 92d Congress). Such authority, which was included in early versions of the bill but omitted from the final bill, would aid the Department in developing an early warning system concerning drug shortages.

Since the hearing, the Food and Drug Administration initiated a review of the question of need for new authority for the Department to identify developing drug shortages in context of the Agency’s legislative planning process. Problems caused by shortages of other materials regulated by FDA will be considered as well. The experience of the Department in its current informal role tracking drug shortage situations and the report of the National Commission on Supplies and Shortages will be helpful to the Department in deciding the type of authority which may be needed.

Senator KENNEDY. Thank you.

Can you go on to opium.

Dr. JENNINGS. There is a worldwide problem relating to the shortage of opium. There are a number of factors, both manmade and natural, which have led to a decreased supply of crude opium for the legitimate market.

One of the most significant factors is the sharp increase in worldwide demand for opium, which is up from 800 tons to over 1,200 tons in less than a decade.

Senator KENNEDY. Why is that?

Dr. JENNINGS. There seems to be a number of reasons. For one thing, there are more people in the world. More people now have access to medical care than ever before. Wherever we look, we find there is an increase in the actual prescribing and use of practically all types of medication.

The principal drug derived from opium is codeine. In this country it accounts for about 90 percent of the drugs derived from opium. This is an extremely useful drug. It is an excellent mild analgesic, intermediate between the aspirin level and the morphine-demerol level.

It is also an extremely useful antitussive medication, and since it is so effective, it is widely used by physicians. With the everincreasing access to medical care, there is an inevitable increase in the use of codeine.

Senator KENNEDY. Do you think there is irrational prescribing of these opium derivatives in the United States.

Dr. JENNINGS. That is a little difficult. I would say that the only area in which I personally might look to curtail in any way the use of natural opium would be in the area of antitussive medication for the relatively mild conditions, that is, cough medicines.

As far as its use as a major analgesic is concerned, there seems to be no substitute for morphine for severe pain, such as that due to coronary occlusion, or severe trauma.

I would not consider that any effort to curtail the use of the opium derivatives in legitimate practice would be extremely productive. As a matter of fact, we have some data relating to a survey, admittedly conducted by the pharmaceutical industry but, nonetheless, appar-

ently in keeping with experience, which shows that 70 percent of 700 physicians, representing a variety of specialty groups, reported a real need for opium-based analgesics or antitussives. And 88 percent of them indicated that they considered these products essential to their practice.

But as I have already discussed, for some of its indications, there is no substantial evidence that the available synthetics would be adequate substitutes for morphine.

The role of our Government in curtailing the production of Turkish opium is so well-known that I do not think we need to discuss that in any depth. Turkey is now about to go back into production, and that undoubtedly will have an effect on the supply and, hopefully, will alleviate some of the shortage.

There are indications that the demand might be increasing in areas that were unsuspected heretofore.

Senator KENNEDY. As I understand it, the processing of the Turkish poppy is quite a bit different. We are going to hear testimony later this morning to the effect that just increased production of poppies in Turkey is not necessarily going to have a salutary effect upon the needs that we are facing in this country.

Dr. JENNINGS. I will ask Mr. Belson to discuss that.

Senator KENNEDY. Just briefly, if you would.

Mr. BELSON. We have been told that the Turks will not be incising the poppy which gives an increased flow of latex. What they are going to do is use the Kaon process, using the entire pod and stem, after removing the poppy seed, and there will be opium produced this way, but considerably less than if they deliberately stimulated the flow of the natural latex.

But the people I spoke to did not have any specific quantitative data to give. They just said it would be less.

Senator KENNEDY. We are going to hear some other testimony on this.

So, let us keep moving on.

Dr. JENNINGS. Ampicillin represents still another kind of shortage, and a different cause. Ampicillin, as you will hear in some detail later, I am sure, is a broad spectrum antibiotic that is extremely useful, although its spectrum of use is covered in almost every case by some other drug.

The major producer of sodium ampicillin, which is the injectable form, shut down its production facility in September 1973, because of problems of manufacturing.

Senator KENNEDY. What sort of problems?

Dr. JENNINGS. This involved good manufacturing practices, and in particular, the contamination of the facility producing the injectable form and its packaging.

This was an extremely difficult problem for them to solve, and the plant was not back in production until July 1974. Full production was not reached until October 1974.

This shutdown led to a depletion of the pipeline, and to a spotty shortage of this antibiotic which, as I said, is extremely popular and very useful, but which in almost every instance could be covered by an adequate substitute.

We think that this particular problem is on its way to solution, and it illustrates one kind of shortage where the action of the agency contributed to the shortage.

What is of interest to us, and what we will have to think about as we develop our system for dealing with shortages, is why production in facilities of competitors, or even other facilities of the same company, was not increased to take up the slack during the shortage caused by the shutting down of this one facility.

The problem of having a single company or facility being a major or sole supplier of a useful drug, is something we have encountered in the past, and is an area where we might very well consider taking some sort of action that would prevent problems of this sort.

We will have to discuss this with the industry at large.

Senator KENNEDY. How could a situation like that take place in a competitive system like the pharmaceutical industry?

Dr. JENNINGS. I am afraid I cannot give you any definitive answers. Again, we have heard a lot of second-hand information. The basic material from which ampicillin is made is also used for other antibiotics which perhaps represent more attractive products for some of the manufacturers. That is one possibility.

It may be that the market price of ampicillin at the time the shortage began was not sufficiently attractive for competitors to gear up to meet the demand.

I really do not have any definitive answers, because, as I say, this kind of information is not that which ordinarily comes within our purview.

Senator KENNEDY. Did they close down voluntarily? Did you discover it?

Dr. JENNINGS. It was a voluntary shutdown. I will let Mr. Belson give you the details on that.

Mr. BELSON. The actual shutdown was a decision of the company itself. We did not ask them to close down. It was, I think, following inspections by FDA, and when the information turned up during the inspections, it reached management, and they made that decision.

Senator KENNEDY. What was the difference in the cost of the price prior to their closing down, and after their closing down?

Mr. BELSON. My information is based on querying hospital pharmacists, so it is secondhand. In the Greater Washington area, I have been told, that a half gram vial ran about 23 cents on open-end contract. Today, I think it is probably twice that. During the shortage, I had heard the prices were in the 70-cent, 80-cent, and 90-cent range.

Senator KENNEDY. I did not hear the last part.

Mr. BELSON. I was saying that before the shortage, on the opening contract, I was told that prices ran 23 cents per half gram vial. During the shortage, I heard hospitals were paying 70, 80, or 90 cents. And I understand that at this time, it is somewhere in the neighborhood of 50 cents.

Senator KENNEDY. More than doubled, then?

Mr. BELSON. Yes, sir.

Senator KENNEDY. You do not know the reasons for that, whether it was increased cost of raw materials, or what? I am just trying to think out in my own mind whether this is the sort of situation where

the company has made a mistake and the consumer is paying for it, or whether during that period of time the cost of the various materials used have gone up, or what the various factors were that would have produced the kind of dramatic increase that we have seen in the other drugs.

Mr. BELSON. I do not know, sir.

Dr. JENNINGS. Mr. Chairman, I will close by saying that we are relatively new to this problem. As I indicated earlier, my office has been designated by the Commissioner to serve as the focal point for information relating to shortages of drugs.

The Secretary has designated the emergency coordinator for problems relating to such situations, including drugs and drug materials, and we are attempting now to develop just such an early warning system as you alluded to in your opening statement.

To this end, we have entered into an agreement with the American Society of Hospital Pharmacists to set up an early warning system by using a network of the hospital pharmacies to alert us to possible drug shortages so we can follow up on them.

And as Mr. Wetherell has reminded me, there is the National Commission on Supplies and Shortages, which has a very long mandate which is included in my prepared statement and which I will leave for the record, rather than attempt to read through it now.

In other words, we have become acutely and intensely aware of this problem, and I can assure you that we are going to do everything we can to develop our capability in dealing with it.

We will let you know through the usual legislative services process of any authority that we feel we need over and above that which now exists.

I also can assure you that the Assistant Secretary of Health and Commissioner Schmidt are both aware of this problem and interested in its solution, and that the other agencies of HEW which are not already aware of it, will be involved. We will do everything we can to contribute to the development of information and to the solution of these problems as they arise.

I will be pleased to answer any further questions.

Senator KENNEDY. I want to thank you for your statement and the responses and your willingness to follow up on some of these matters.

At the bottom of page 12, you indicated that in terms of being able to make some accurate projections and predictions of shortages: "At the same time, if we are able to obtain appropriate data from industry together with their projections of future capacity, we should be able to gage the true extent of the shortage and what the future holds."

As I understand it, you cannot get that at the present time; is that correct?

Dr. JENNINGS. We do not have absolute authority to obtain that information in all instances. We do have it, as I indicated, for new drugs and for certifiable antibiotics and insulin. I might also say that, in most situations of this sort, we have found the industry generally to be cooperative in supplying us with information although, in some cases, they consider some of this material to be a vital trade secret and are extremely reluctant to release it, because we cannot always guarantee confidentiality of such information.

Senator KENNEDY. As I gather, you feel it is needed, though, in order to perform your function in guiding the FDA and the Congress on these shortage areas?

Dr. JENNINGS. That would be my personal opinion. That was the opinion taken by the agency during the hearings and legislative process leading to the passage of the Drug Listing Act.

Senator KENNEDY. I hope you get that language up here, and we will try and help you get what you need.

Dr. JENNINGS. Thank you, Senator.

We will be glad to develop some language.

Senator KENNEDY. Thank you very much. We have got some followup, then, with each other.

Dr. JENNINGS. Yes.

Senator KENNEDY. Thank you.

[The prepared statement of Dr. Jennings follows:]

STATEMENT BY JOHN JENNINGS, M.D. ASSOCIATE COMMISSIONER FOR MEDICAL AFFAIRS, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Mr. Chairman, we welcome this opportunity to discuss with your Subcommittee the role of the Food and Drug Administration (FDA) with respect to shortages of drug supplies.

#### BACKGROUND

As you know, Mr. Chairman, the FDA is responsible for the enforcement of the Federal Food, Drug, and Cosmetic Act as well as several sections of the Public Health Service Act. These laws provide us with authority to insure that all marketed drugs are safe, effective, and properly labeled. Neither of these laws, however, provides us specific authority to act in any way to alleviate shortages of drug supplies if they occur. Nor are we required to determine the reasons behind any shortages, be they real or not. However, as the Federal Agency charged with regulation of the Nation's drug supply, we are consulted by consumers, physicians, pharmacists, and the pharmaceutical industry for solutions to problems they may experience in obtaining drugs and materials for the manufacture of drugs assuming that we do have the authority to do something. Soon after any shortage of a drug is perceived, we receive inquiries about it. We feel a responsibility, albeit not legislated, to help insure that an adequate supply of drugs is available to the public and to do what we can. In discussing drug shortages, I believe it important that the number be put in its proper perspective. We know of no situation where a patient has been harmed because of the unavailability of a necessary or essential drug. Also, all situations of drug scarcity or shortage of which we are aware have primarily affected inventories rather than the availability of the drug to the patient. From our limited knowledge of this rather recent phenomenon of drug and drug material shortages, it appears that by far the majority of them are resolved by the natural forces of the free enterprise system.

#### CAUSES OF SHORTAGES

Our knowledge of the reasons for shortages suggest they are very diverse and may include:

- Economic (cost of hog intestines for heparin)
- Adverse weather conditions which reduce the production of the basic raw commodity (poppies in India)
- Shortages of raw materials (hydrazine hydrate used in rocket fuel)
- Manipulation of supply (quinidine)

Drug shortages experienced at the consumer level, and shortages of raw materials at the manufacturing level, are rarely the result of an FDA action, either directly or indirectly. However, in our regulatory role, we are required from time to time to take action to remove certain batches of drugs from the market and our actions may also cause temporary shutdown of drug manufac-

turing facilities. Such actions are only usually taken after a careful evaluation of their total impact on patient health, and a careful appraisal of the benefit-to-risk balance of the ultimate action. In all such situations, the effect to the patient is the primary consideration. An example of such consideration is the temporary suspension of production of large volume parenterals at several of the major producers in recent years. Because of the large share of the market each of these producers had, any precipitous action to halt production could have had serious adverse consequences to patients. Therefore, interim measures were taken to protect patients using drugs produced by these plants. Until there were replacement stocks from alternate sources adequate to assure continuing patient care, controlled release of batches of the questionable material was monitored by the FDA.

The drugs you have asked us to discuss (heparin, ampicillin, opium derivatives, quinidine) are products which illustrate some of these factors.

#### HEPARIN

Heparin differs from other anticoagulants in that it can be injected directly into the blood stream and becomes effective immediately. Other anticoagulants, such as dicumarol and sodium warfarin, are administered orally and it takes many hours for them to take effect. There is presently no substitute for heparin. Also, heparin is effective *in vitro* which makes it indispensable in cardiovascular surgery and dialysis for treatment of kidney failure where the rapidly increasing demand for the drug has outstripped production.

Heparin is derived from either bovine lungs or the intestinal mucosa of swine, with the latter accounting for approximately 90 percent of the drug produced. The swine mucosa used for heparin manufacture has been a by-product of sausage casing production. While this supply of raw material was formerly sufficient to meet the demands for heparin manufacture, this is no longer the case. At present, approximately 50 percent ( 55,000,000 lbs.) of the available swine mucosa is being saved and used for heparin production. The remainder of this material is currently diverted to rendering plants as tankage. Those meat packers who are not presently saving the mucosa have not considered it profitable, at its present market price, to process and to preserve the mucosa solely for heparin manufacture.

In October of this year, the FDA received our first reports from physicians and hospitals that they were experiencing difficulties in obtaining heparin.

On November 13, we held a meeting with representatives from heparin manufacturers, meat packers associations, pharmacy, and medical associations and the USDA to explore the intent, reasons, and possible resolution of the heparin shortage. At this meeting, it was brought out that:

The pharmaceutical industry has adequate facilities to produce enough heparin to meet current and future demands for the drug;

The supply of raw material (swine mucosa) is basically adequate for present and future demands of heparin;

The pharmaceutical industry has been able to secure raw materials from new sources (meat packers who had not previously saved mucosa);

There has already been significant relief of the heparin shortage;

Efforts at synthesizing have not been successful;

At this time, increased production of bovine lung heparin is not a practical solution to the shortage because of greater manufacturing difficulty and expense in production.

We have no information indicating that any patient has been harmed because of inability to secure heparin. The pharmaceutical industry has indicated that its supplies have been adequate to meet all emergency demands and that what has lagged has been routine shipments. The industries' best estimates are that the shortage will end in about three months, the period needed to secure the additional new sources of raw materials and to fill the distribution pipeline.

#### QUINIDINE

Your staff has indicated that your Committee has received reports that there may be a developing shortage of this drug. In contacts with both users (hospitals) and producers, we are unable to confirm that there is a shortage of this drug.

Quinidine, and its optical isomer quinine, are derivatives of cinchona bark, which is found primarily in Indonesia and Africa. The information we have obtained indicates that the price of quinidine has increased some fourfold in the past year. While we can only speculate, we believe that this rapid price increase may account for the present reports of shortages because it parallels the situation that was experienced in the mid-60's.

In 1966, hearings before the Subcommittee on Antitrust and Monopoly of the Senate Committee on the Judiciary established that the shortages of quinidine at that time, and the subsequent fivefold increase in price of the drug, was a result of the activities of a Dutch cartel which controlled virtually 100 percent of the raw material for production of the drug. This cartel was able to create an artificial shortage of the drug and to set the price at an artificially high level. Supplies of this raw material are apparently still within the control of the same group.

General Service Administration's emergency stockpile at the present time is 1.8 million ounces of quinidine, and over 3 million ounces of quinine (which can be converted to quinidine). There are bills in both Houses of Congress to declare a considerable amount of this stockpile surplus. If the bills pass, 2.4 million ounces of quinine and 1 million ounces of quinidine will be released to the market.

#### OPTIUM

We are facing an impending problem arising from a domestic and worldwide shortage of opium. This problem can be traced to a number of factors including manmade and natural causes which have led to decreased international supplies of crude opium for the legitimate market. Current projections indicate that shortages of opium-based products will occur in 1976 or 1977.

One of the most significant factors is a sharp increase in worldwide demand for opium (up from 800 tons to over 1200 tons in less than a decade). India has reacted to the increased demand by increasing its crop size each year for the past few years but actual production for export is highly variable. The world demand for opium has exceeded the supply in recent years. United States importers have been unable to import sufficient opium to maintain adequate inventories. Imports are currently about 230 tons per year and this is being supplemented through the release of strategic stockpile opium by the GSA.

A second significant factor was the agreement between the United States and Turkey to halt production of crude opium because large quantities of Turkish opium had been diverted to the illicit market where it was converted to heroin. There are six countries, (Russia, Yugoslavia, Greece, Bulgaria, Iran, and India) authorized by international agreement to produce opium for export other than Turkey. India has, however, for the past several years produced the bulk of the licit worldwide opium. Turkey produced the remainder until the 1971 agreement. Turkey's recent decision to resume production will alter the situation but we cannot yet assess the potential impact.

Short term factors adding to the problem include adverse growing conditions (India exported only approximately 900 tons in 1972 because of losses due to adverse weather) and unusual or emergency situations which effect demand (catastrophies, epidemics, etc.). One such situation recently occurred when Russia purchased a large amount of Indian opium ostensibly in response to an epidemic (Russia is normally capable of meeting its own needs).

In a recent survey sponsored by the pharmaceutical industry, over 70 percent of 700 physicians representing seven specialty groups reported that their practices would be significantly impaired if opium-based analgesics or antitussives were removed from the market. Eighty-eight percent of these physicians indicated that opium-based products are essential in the practice of medicine. In the United States, approximately 90 percent of the opium is used to manufacture codeine.

Physicians questioned in this survey also objected strongly to the idea of a U.S. ban on legitimate opium derivatives. In their view, such a ban would interfere substantially with medical practice. This survey disclosed that physicians think almost exclusively of morphine (an opium derivative) and meperidine for use in severe pain (terminal cancer, bone fracture, coronary attack, obstructions). These physicians further indicate that adequate replacements for opium-based products are not available to them. More effective analgesic properties are generally attributed to morphine than to meperidine (a synthetic product).

## AMPICILLIN

Ampicillin is a semi-synthetic penicillin for injection and oral use. It has the same general spectrum of activity as penicillin. Therefore in the case of ampicillin, alternative antibiotic therapies are available for almost every need.

One plant of a major producer of sodium ampicillin injection was voluntarily shut down in September 1973 following an FDA inspection which uncovered good manufacturing practices problems. The renovations took longer than originally anticipated and the plant remained closed until July 1974 when ampicillin production was resumed. Full production was reportedly reached in October. The shut-down of a plant responsible for a significant portion of the U.S. production was significant. A shortage of this antibiotic was first reported to FDA in July and August 1974. Presumably, it took this long to drain the pipeline of sodium ampicillin injection stocks and to decrease hospital reserve to near a marginal level. By the time the reports began to come in, the plant was back in production. Other manufacturers did not adequately increase production for the available market or to take up the slack in supply. Other factors which, combined with the plant shutdown, produced the shortage were:

The popularity of the antibiotic and its wide use by the medical profession.

Competition between ampicillin and other antibiotics (specifically the cephalosporins) for raw materials.

With the plant back in full production, we anticipate that the shortage should end. Problems in obtaining desired quantities are expected to diminish as the pipeline is refilled.

## OTHER DRUG AND DRUG MATERIAL SHORTAGES

Reports of drug and drug material shortages which have been brought to our attention cover a broad spectrum of situations from chemicals essential to the manufacturer of glass for pharmaceutical containers to shortages of the finished drug product itself. In every instance of shortage which has come to our attention to date, the circumstances which caused the shortage were different. In addition to specific situations concerning possible shortages of heparin, injectable ampicillin, quinidine, and opium and its derivatives, other shortages which we have known about include:

In 1973 a glass manufacturer reported a serious problem in obtaining barium carbonate and soda ash, essential ingredients in the manufacture of glass for injectables. The scarcity of these materials was apparently a worldwide phenomenon.

A pharmaceutical manufacturer reported problems in obtaining supplies of hydrazine hydrate, an intermediate in the production of a drug used in the treatment of gout. The situation occurred because of the increased demand for the chemical in rocket fuel production and other industrial uses. The chemical was already in scarce supply because of the oil embargo.

In summary, although there have been drug and medical product shortages in the past, we have recently become increasingly aware of and involved with these problems. They seem to occur more frequently and with greater rapidity in today's world.

In our recent experience, we have found that each shortage carries its own set of underlying circumstances which have been unique to each problem. If a pattern is emerging, it is one of cost in a competitive market. The necessary materials, e.g., swine mucosa, can be obtained but the price will be affected by competition and similar factors.

One of the most difficult problems faced by the FDA is that of securing early, accurate information regarding impending shortages. We must also distinguish between true shortages (finite limitations on critical components) and apparent shortages (fluctuating availability of critical components because of price competition) and non-shortage shortages (distribution problems). We must also distinguish between shortages of a critical nature (a lifesaving product for which there is no substitute) and noncritical nature (a popular or convenient drug or product, but for which there is one or more suitable substitutes or alternatives readily available). Our ability to obtain such information with adequate lead time will allow us to assist in the development of plans which will avoid or minimize disruptions in the delivery of drugs or products which are critical to

the Nation's health. We can also avoid or minimize patient concern about the continuing availability of crucial drugs.

In an action designed to provide necessary means to obtain accurate information and to assure the speedy flow of such information, Commissioner Schmidt recently designated my office as the focal point within FDA to receive and to coordinate information regarding such drug or medical material shortage. In carrying out this responsibility, we will explore and devise mechanisms to identify pending shortages, to identify their causes, and to initiate steps to alleviate the situation, insofar as we can.

In cooperation with the American Society of Hospital Pharmacists, we are initiating the development of a new surveillance system. We plan to arrange for a sampling of hospital pharmacies throughout the country to report any problems they encounter in obtaining necessary drugs for their hospitals. We will monitor their reports very closely and if there is any indication that the problem is more than a shortage at a local distribution point, we shall then survey a larger sampling of hospitals to determine the extent of ordinary usage, supplies on hand, and anticipated use. From this survey, we should be able to project the extent of market demand. At the same time, if we are able to obtain appropriate data from industry together with their projections of future capacity, we should be able to gauge the true extent of the shortage and what the future holds.

Additionally, the Assistant Secretary for Health has established the position of Emergency Coordinator in his office to serve as a focal point for gathering information on emergency situations including shortages of drugs and drug materials.

In addition, we have looked into the matter of whether there is any existing authority for making allotments of scarce drug materials to meet critical civilian health needs.

We are aware of some Federal programs designed to keep abreast of shortages that may affect the Nation. In September of this year, the Defense Production Act was amended to establish a National Commission on Supplies and Shortages (P.L. 93-426). This Act establishes a commission as an independent instrumentality of the Federal Government to report not later than March 1, 1975, to the President and the Congress on the existence or possibility of any long or short-term shortages; employment, price or business practices; or market adversities affecting the supply of any natural resources, raw agricultural commodities, materials, manufactured products (including any possible impairment of productive capacity which may result from shortages in materials, resources, commodities, manufactured products, plant or equipment, or capital investment, and the causes of such shortages, practices, or adversities). We will follow with interest the activities of this commission as they relate to problems such as we have discussed here today.

At the time of the energy crisis last year, FDA met with representatives of the drug industry to evaluate the impact of the anticipated shortages of petrochemicals on the drug supply. The pharmaceutical industry was advised that we would cooperate in authorizing necessary changes in New Drug Applications, insofar as manufacturing processes, raw materials, or packaging were concerned, to assure the continuing availability of the drug supply. It developed that no major problems to the pharmaceutical industry were brought about by petrochemical shortages. Those difficulties which some firms encountered were handled expeditiously on an individual basis. Most shortages in drugs which have occurred to date were not energy related.

It is our view that many of these drug shortages will be resolved through the functioning of the marketplace. This has occurred with the resolution of the heparin supply problem. In selected instances, however, the necessary raw materials for drug production may be in short supply. In these cases, allocation of such materials may be required to assure the continuing availability of critical drugs or medical supplies.

In closing, Mr. Chairman, let me say that I think you and your Committee are to be commended for your interest in this potentially critical national health problem. We will certainly do all we can to assist you in determining the facts and arriving at an appropriate solution.

We will be pleased to try to answer any questions you or members of your committee may have.

Senator KENNEDY. Our next witnesses this morning are a panel of representatives from the various industries who are affected by the problematic issues.

Cornelius Pettinga, Ph. D., assumed the office of executive vice president of Eli Lilly Co. in 1972, and has been a member of the Eli Lilly board of directors since 1966.

Charles Adams, vice president and general manager of Riker Laboratories, a subsidiary of 3-M Co.

Michael Bongiovanni, president of the U.S. Pharmaceutical Co., Squibb & Sons.

John Kolbas, vice president, Bristol Laboratories.

Richard Lyng, president of the American Meat Institute and also director of the National Livestock and Meat Board.

Jane Lang McGrew, Washington attorney from the law firm of Steptoe & Johnson. She served as legal consultant to the National Commission on Marihuana and Drug Abuse, and is here this morning representing Mallinckrodt, Inc., Merck & Co., and S. B. Penick & Co. Ms. McGrew, maybe you would start us off.

**STATEMENT OF JANE LANG MCGREW, ESQ., ATTORNEY, STEPTOE & JOHNSON, FORMER LEGAL CONSULTANT, NATIONAL COMMISSION ON MARIHUANA AND DRUG ABUSE, REPRESENTING MALLINCKRODT, INC., MERCK & CO., INC., AND S. B. PENICK & CO., A DIVISION OF CPC INTERNATIONAL OF NEW YORK, N.Y.; ACCOMPANIED BY CORNELIUS W. PETTINGA, PH. D., EXECUTIVE VICE PRESIDENT, ELI LILLY & CO.; CHARLES R. ADAMS, VICE PRESIDENT AND GENERAL MANAGER, RIKER LABORATORIES, SUBSIDIARY OF 3M CO.; MICHAEL BONGIOVANNI, PRESIDENT, U.S. PHARMACEUTICAL CO., E. R. SQUIBB & SONS, INC.; JOHN M. KOLBAS, VICE PRESIDENT, MANUFACTURING BRISTOL LABORATORIES, DIVISION OF BRISTOL-MYERS CO.; RICHARD LYNG, PRESIDENT, AMERICAN MEAT INSTITUTE, AND DIRECTOR, NATIONAL LIVESTOCK AND MEAT BOARD; A PANEL**

Ms. MCGREW. I am Jane Lang McGrew. I am an attorney with the Washington law firm of Steptoe & Johnson.

I am here today on behalf of three companies—Mallinckrodt, Inc., of St. Louis, Mo.; Merck & Co., Inc., of Rahway, N.J.; and S. B. Penick & Co., a division of CPC International of New York, N.Y.—to discuss with you the current shortage of licit opium which threatens our domestic supply of medicinal opium derivatives.

Mallinckrodt, Merck, and Penick have imported crude opium into the United States since before the turn of the century without a single instance of diversion of the substance into illicit channels.

Senator KENNEDY. That is a very impressive record.

Ms. MCGREW. I might add, Senator, that this was acknowledged by DEA officials during testimony on the Controlled Substances Act in 1970.

Senator KENNEDY. I think it is to be commended. It shows that with safeguards they can meet the responsibility in terms of public health issues, and also be sensitive to the dangers of diversion. And I am sure that is done at no small expense to the companies.

I think it is to be commended.

Ms. McGREW. Thank you very much. We are very proud of that.

These companies produce and sell derivatives of opium, 95 percent of which is codeine, primarily to pharmaceutical companies, to be used in manufacturing analgesics for the relief of pain and antitussives for the relief of cough.

Other medicinal derivatives of opium include morphine and oxycodone, both strong analgesics, and naloxone and nalorphine, antagonists used to counteract the effects of narcotic overdoses.

Approximately 80 percent of the codeine currently consumed in the United States is prescribed for pain relief. In prescribing an analgesic, physicians consider its potency, speed of onset and duration of action, its side effects and abuse potential, and any allergies or idiosyncrasies of the patient.

Codeine is unique in this context. According to the National Academy of Sciences/National Research Council, it is twice as effective as its most popular synthetic alternative, propoxyphene, has no greater side effects, and provides a wider dosage range.

Physicians also continue to prefer codeine and other opium derivatives for the relief of severe cough. As an antitussive, codeine was acknowledged by the American Medical Association, in a resolution adopted in June 1973, to have "unequaled \* \* \* efficacy."

Other cough suppressants, both synthetic and opium-based, are effective in suppressing experimentally induced coughs, but many such synthetics have proven ineffective in suppressing cough of pathological origin.

An adequate supply of crude opium is essential, as well, to meet the medical demand for morphine, a strong analgesic. In some cases, synthetic substitutes may be superior to morphine because of a more rapid onset and shorter duration of action.

These same characteristics operate as disadvantages, however, where the patient requires treatment for persistent, long-term pain. Moreover, substitution is unsatisfactory in patients who require unusually high doses for relief of severe pain.

While knowledge about the effects of high doses of morphine is quite extensive, little information is available about the effects of large doses of synthetics. Similarly, the lack of experience with synthetic morphine substitutes often limits their use in certain patient populations, such as children, women in early pregnancy, or patients concurrently receiving other medications.

I have also mentioned the narcotic antagonists, nalorphine and naloxone, both of which are derived from opium.

An antagonist, such as naloxone, is capable of reversing the life-threatening effect of acute narcotic overdose. For these patients, it may be the only alternative to death. In addition, the use of narcotic antagonists in the treatment of narcotic dependence is currently a field of extensive research which may lead to an understanding of the nature of drug dependence.

Naloxone, as the most potent of the only three available antagonists, is a prime subject in this area.

In short, while some success has been achieved in developing acceptable synthetic substitutes, opium derivatives remain essential to

adequate medical care. As SAODAP's Dr. Robert Dupont stated before the House Armed Services Committee last year:

Synthetics which would replace substantial portions of the market \* \* \* have not yet been found. Indeed, while some synthetics may be fully appropriate in a certain prescribing situation, in other situations there is not yet known any adequate substitute.

His views were emphatically confirmed by representatives of the three Surgeon Generals of the Armed Services during those hearings, and are shared by other eminent physicians and pharmacologists.

Just last month, GAO investigators, reporting to Congressman Charles Rangel on the licit opium supply situation, reaffirmed this judgment, which is further supported by the rapid growth in medical demand for these drugs in recent years.

The projections which I will turn to now suggest that this trend in demand is continuing.

Because codeine constitutes about 95 percent of the demand for opium derivatives in the United States, sales of this substance provide a good yardstick to measure the growth in domestic medical needs for opium.

As documented by the first GAO report to Congressman Rangel this past summer, bulk codeine sales to formulators have risen substantially over recent years showing an aggregate increase of 73 percent from 1967 to 1973. While medical demand has been growing, however, the supply of opium has been dwindling.

As of December 31, 1973, consolidated inventories of the three processors, including crude opium, work in process and finished goods, had fallen to a 4½ months' supply. This represented a 50-percent decline in the processors' stocks from 1972 levels.

During the first 10 months of 1974, sales of codeine again exceeded imports of crude opium, this time by more than 100 percent. Had Indian imports plus inventories constituted the sole available supply this year, today the operations of all three processors would probably be closed down.

This has not happened yet for one reason only. In December 1973, Congress authorized the release of 238 tons of opium from the strategic materials stockpile. The contracts for sale of this material to the processors contemplated delivery over a 5-year period, during which a processor could purchase stockpiled opium only if his combined inventory of crude opium, work in process and finished goods fell below a 6-month supply relative to his yearly production quota.

Senator KENNEDY. Now, wait a minute.

Therefore, it was Congress that actually released the sufficient stockpiling so that we had the balance last year?

Ms. McGREW. That is correct.

Senator KENNEDY. What would have happened if we had not?

Ms. McGREW. If we had not, right now we would be experiencing the situation which we now project for a year from now. That is, patients would not be able to fill the prescriptions which they receive from their physicians in hospitals and pharmacies.

Senator KENNEDY. Why cannot Congress continue to release strategic reserves?

Ms. McGREW. We have discussed this matter extensively with Congressman Bennett, who is chairman of the subcommittee involved on the House side, and with Senators Cannon and Symington on the Senate side. They believe that the remaining stock of opium, which is only about 150 tons in the stockpile now, is essential to our national defense, and we are certainly in no position to argue with them on that assessment.

Senator KENNEDY. Now, what have you found to be the projected production in India and in these other source supplies?

Ms. McGREW. Well, we have no great hope for any increase in the Indian production. We were advised by Ambassador Moynihan that India does not plan to increase its plantings in 1975 or any time thereafter. India has said that we can expect a 12-percent yield increase this coming year because farmers will have more experience—they had apparently licensed some new farmers—and they hope that weather conditions will be more favorable.

This is a very unreliable projection to base any hope on.

But, our projections on supply take into account this 12 percent increase. If that is realized, we would get about 220 tons from India next year. That would permit the production of about 60 percent of our projected demand for next year.

Senator KENNEDY. That is the most hopeful sign, is that correct?

Ms. McGREW. That is correct, Senator.

There is a small amount of opium remaining in the stockpile that was authorized for release. When we add that together with the Indian imports, and assume that just the minimum inventories are maintained to permit the process to continue, we would expect to be able to satisfy a maximum of 80 percent of the demand next year.

Senator KENNEDY. Then, what happens? Then you run out?

Ms. McGREW. That is correct, Senator, unless remedial action is taken, and we do believe there are some other alternatives to consider.

Senator KENNEDY. You are going to elaborate on the other alternatives, is that correct?

Ms. McGREW. I will go to that right now.

Senator KENNEDY. Just before you do, what percentage do we get again from India now?

Ms. McGREW. This year's allocations, so far this year, we have only received adequate opium to produce about 50 percent of the amount of the bulk codeine which was actually sold.

If we receive our total allocation from India this year, and, as I have indicated, the shipments have been very slow in coming, we might be able to get as much as 60 percent.

Senator KENNEDY. Has anybody considered the possibility that countries with millions of starving people might hold critical medical supplies hostage to receipt of food shipments from wealthy countries?

I am not trying to suggest that a responsible Indian Government would get into that kind of a situation, and certainly I would not suggest that the current Government would ever behave in this manner.

India remains as one of the great democracies of the world and certainly one of the most complex. We think of all kinds of turmoil that boil up in these countries which have these exaggerated problems of poverty and misery and are being so completely handicapped by the

extraordinary cost of new energy supplies and facing, as I understand from the figures of the food conference in Rome recently, the potential danger of 12 to 15 million Indians starving.

I would suppose in the land of desperate people that that would not be an unthinkable thought.

Ms. MCGREW. Senator, you have outlined a very frightening possibility. I think this was in the minds of many of the representatives of the Department of Defense last year when they testified about their need to retain opium stocks in the stockpile.

I think this is also—I know this has also been a very real, though unspoken, worry of the companies, relying upon a single source at great distance with unreliable weather conditions. That is a small part of it, when you outline the very vast and dangerous possibility of an actual cutoff of supply.

Senator KENNEDY. Let's hear a little bit about some of the things we ought to be trying to do to avoid such a possibility.

Ms. MCGREW. We have considered a number of alternatives for relieving this situation.

In the past, the purchase of confiscated opium, opium seized from illicit markets by foreign governments, has provided a minor supplement to our supplies in the United States. However, we do not regard this as a substantial possibility for improving the future supply picture.

The difficulty of obtaining this material which has sporadically provided a minor supplement to Indian imports, plus its generally poor quality, make this source very unreliable. In addition, the State Department has suggested recently that U.S. treaty obligations may preclude further imports of this material despite the fact that such trade is authorized by the 1961 Single Convention on Narcotic Drugs.

I would add, Senator, that we believe that these legal problems can be worked out, and we look forward to doing that with the State Department.

Additionally, although Turkey has resumed the planting of opium poppies this fall, which you alluded to earlier, it agreed for control purposes not to lance the poppy capsule to collect the crude gum opium. Rather, for the first time next summer, Turkish farmers will harvest only the poppy straw. Thereafter, the straw will be shipped to European alkaloid factories for processing.

Legal and practical barriers stand in the way of utilizing the Turkish straw or the processed materials in the United States, however. First, under present circumstances, U.S. law prohibits the importation of poppy straw or any of its extracts or derivatives. Although the law permits the Attorney General to authorize the importation of such a substance, the United States has no domestic facilities for processing straw. Only extracts suitable for further manufacturing in the United States would be of any use to the processors.

Senator KENNEDY. Has the Attorney General, to your knowledge, been made aware of this? Has he given any reaction or response to it?

Ms. MCGREW. There is a task force on the opium shortage which has recently been reconstituted in the Office of Management and Budget. I have reason to believe that they have considered this possibility, as well as the others that I have outlined for you. What action they plan to take on this, I cannot say.

Senator KENNEDY. I think it would be useful for us to inquire from that task force?

Ms. MCGREW. I think it would be very useful, Senator. Unfortunately, the law is only one problem in this.

At this time, it is unclear whether the European factories have the capacity to process the Turkish crop to obtain these extracts. In future years, some of these problems may be resolved.

The production of poppy straw in Turkey may then relieve the pressure upon India, and ultimately increase the supply of crude opium for the United States. However, we do not foresee such relief in 1975 or 1976.

Senator KENNEDY. What is that going to mean in terms of health implications?

Ms. MCGREW. In terms of the effect it has on the Indian crop, it means we are saddled with the projections that I outlined earlier. We cannot rely upon India to produce or to allocate adequate opium to the United States sufficient to meet more than 60 percent of next year's demand.

Now, in terms of future demand, assuming that India continues to resist any increase in planting, and certainly we do not suggest that they should unless they feel that they can control it, it is clear that India as a source must be supplemented.

It may be that in the shortrun, 1975-76, the importation of poppy straw extract, which could be utilized by the processors in the United States may be the solution. That, as I said, depends not only upon the law being altered, but also upon the practical facts which may affect the availability of that supply next year.

Senator KENNEDY. What about Mexico? Does that not offer an opportunity?

Ms. MCGREW. Mexico is not, to my knowledge, a country designated under the 1961 Convention on Narcotic Drugs a producing country for export. There are very few countries in the world which are permitted under the International Convention to export opium. Mexico is not among them.

As a result, the only thing we can obtain from them might be the illicit opium seized by that government. There has been none available. I do not know whether that is because the Government has not taken steps to confiscate it, or whether we simply have not had information available on that score.

Senator KENNEDY. How difficult is it to amend that act? That international act?

Ms. MCGREW. The Convention?

Senator KENNEDY. Yes.

Ms. MCGREW. That would be very, very difficult, Senator. It would require the agreement of the various parties to that Convention.

What steps a country could take to become authorized under the provisions of the convention I am not fully aware of. I would certainly be glad to find that out for you.

I think the discussion so far illustrates the proportions of the impending shortage.

In summary, it suggests that at best with the remaining amount of stockpile released and Indian imports we can count on supply of no more than 80 percent of the demand next year.

In the long run, and we believe that the long run must be addressed now, there is a realistic hope of developing a domestic source of codeine—

Senator KENNEDY. Just before we skip over to that, you missed the rest of that paragraph, which I think is very important.

Ms. MCGREW. I am sorry. The balance of medical needs could be satisfied only by reducing the processors' inventories to a level which would require periodic suspension of production thereafter.

In order to avoid such an eventuality a year from now, a formal program of rationing bulk codeine will be inevitable in 1975—in the beginning of 1975, I might add.

Senator KENNEDY. That is about 15 or 18 days.

Ms. MCGREW. I think you are right, Senator.

Senator KENNEDY. Are you suggesting that we should begin that now, the rationing?

Ms. MCGREW. I am suggesting that as a commercial matter it is going to be inevitable unless the companies are prepared to close down shop or unless they see a sure supplement coming, and right now we do not.

Senator KENNEDY. What is this going to mean in terms of cost?

Ms. MCGREW. I really do not know that, Senator. The only cost factor I am aware of is the cost of Indian opium. That is the price has gone up, raw material has doubled in recent years.

As far as I know, that increase has been absorbed or passed on as appropriate, but I am simply not aware of the commercial aspects of this.

Senator KENNEDY. We are only dependent on the Middle East for 6 percent of our oil and look at what that cost us in terms of the U.S. production when they raise their prices, you are now suggesting we are going to have a 20-percent short fall in this area, it seems to me that as a practical marketing effect it will be an extremely sizable increase.

It certainly would appear that way. I know you do not come here as an economist, but you come as someone who has given a great deal of thought to this area of supply and demand, and I would think you could agree with me that that shortage is going to be reflected in sizable increases. I would think that we could agree on that without going out on a limb too far.

Ms. MCGREW. I would suspect that any shortage situation in any industry would have an impact upon production costs. I have no idea what the numbers are, or what effect this will have upon the cost of the goods sold.

I would also point out at this point that my clients represent the top of the pipeline. We manufacture the bulk codeine which is sold to the formulators. I suggest that your questions in terms of the patient-pharmacy level would have to be directed to them.

Senator KENNEDY. If I understand you correctly, this is really going to be a first in this area of critical drugs. You have outlined, and I think very carefully and accurately, the critical nature of this particular drug and its derivatives in terms of the whole health system of this country and the importance of it.

I think you have been very understated in your representations, very fair, and extremely accurate, about the importance of this problem in terms of the whole health care industry.

Then you have outlined, as a very important authority the very real situation where we are going to have a critical shortage of this material, and I think you have been very fair in estimating where there could be potential relief. Your conclusion is that we are going to have critical shortages of this product that would only be resolved by a system of rationing.

As I understand it, that will be the first time in the history of this country where we have had the rationing of a critical drug, in the absence of war, and I do not know what we did in those circumstances. This is an extremely ominous and distressing situation which you spelled out for this committee, and I think it is something we must be very much concerned with.

Ms. MCGREW. I certainly agree with your assessment, Senator. I think it should be taken as a warning sign, which in a sense is too late for our industry. I think it is important to realize that we cannot wait in the drug industry generally, and specifically in the narcotics industry, for a signal at the hospital level.

We have to deal with the crisis at the manufacturers', at the bulk processors' level, and for this reason we address ourselves to the long-run solutions which we must proceed to solve now.

Senator KENNEDY. I think you have put your finger on another point. That is that we should not have to wait until we find or hear from our friend, Dr. Wysof, up in Long Island, or Mr. Graham, who wrote me that letter about the increases in the cost, and for the Food and Drug Administration to send up the flares in these areas.

Ms. MCGREW. That is certainly true. One of the most intense frustrations that we found in dealing with this problem, and I have been working on this for 18 months, is the feeling that unless we have to line up at the pharmacy to get something which is in short supply, you cannot get a solution. We need people who are going to recognize, who are going to take a longer perspective on a problem like this, and be prepared to work out a solution before it is a crisis that consumers are frightened of.

Senator KENNEDY. Well, I agree with you 100 percent. That is not only true in this particular issue, but it is true with regard to most of the problems in the country.

OK, let us move on.

Ms. MCGREW. In keeping with those remarks, Senator, I raise the possibility of developing a domestic source of codeine through the cultivation of *papaver bracteatum*, a poppy which does not produce morphine from which heroin is derived. Acceleration of the research already begun by the Department of Agriculture and establishment of a regulatory framework by DEA would contribute substantially to the success of this project.

Industry recognizes its responsibilities in finding a solution to the opium supply problem which threatens the adequacy of medical care in the United States. Direct Government assistance is essential, however, in negotiating with India for increased allocations, in dealing with the legal problems involved in the importation of confiscated opium and other raw materials, and in developing a regulatory scheme for the cultivation of a domestic source of codeine.

We understand and share, of course, the concern felt in Congress and the agencies for the problems of drug abuse in our country and we are certainly proud of the record of the licit narcotics industry in this regard.

At the same time, we hope to see a stronger expression of concern for the other side of the issue—the objective of assuring that the health care needs of Americans for medicinal opium-based drugs will be met in 1975 and thereafter.

Senator KENNEDY. An excellent presentation.

Ms. MCGREW. Thank you, Senator.

Senator KENNEDY. Your clients are well represented.

Ms. MCGREW. Thank you.

[The statement of Ms. McGrew on behalf of Mallinckrodt, Inc., Merck & Co., Inc., and S. B. Penick & Co., follows:]

#### STATEMENT ON THE OPIUM SHORTAGE, BY JANE LANG MCGREW

This statement is submitted to the Committee in behalf of Mallinckrodt, Inc. of St. Louis, Missouri; Merck & Co., Inc. of Rahway, New Jersey; and S. B. Penick & Company, a division of CPC International of New York, New York, the three registered importers of crude opium in the United States. It is intended to amplify the oral statement presented on December 5, 1974 before the Committee concerning the current shortage of licit opium which threatens the adequacy of our domestic supply of opium derivatives.

#### DESCRIPTION OF THE INDUSTRY

A brief description of the legitimate narcotics industry in the United States will help to put the supply problem we face in perspective. The three companies whom I represent—Mallinckrodt, Merck and Penick—import crude opium into the United States and have done so since before the turn of the century without a single instance of diversion of the substance into illicit channels. Today, the sole source of this opium is India though in the past Turkey was a major—and at one time exclusive—supplier. These same three companies process the opium and extract its alkaloids, predominantly morphine and codeine. Virtually all of the morphine is converted to codeine and sold in the form of bulk codeine salts. The operations of the companies are conducted under the tightest security restrictions and their production is subject to quotas set by DEA. All transactions in these substances may be monitored through the reports and order forms filed with the DEA.

Mallinckrodt, Merck and Penick produce and sell opium derivatives, 95% of which is codeine, primarily to pharmaceutical companies, the formulators, to be used in manufacturing analgesics for the relief of pain and antitussives for the relief of cough. Other medicinal derivatives of opium include morphine and oxycodone—both strong analgesics—and naloxone and naltorphine—antagonists used to counteract the effects of narcotic overdoses.

#### MEDICAL NEEDS FOR OPIUM DERIVATIVES

The medical demand for these derivatives establishes our country's need for opium. To understand what a shortage of opium means to health care in the United States, it is, therefore, necessary to understand the uses of these products. Approximately 80% of the codeine currently consumed in the United States is prescribed for pain relief. Although codeine, along with other opium derivatives, continue to be the drugs of choice by physicians for the relief of severe cough, the increase in medical demand for codeine analgesics has far outstripped the increase in demand for antitussives. As a result, the portion of bulk codeine which is utilized in analgesics has been expanding and we expect it to increase over the next few years.

In prescribing an analgesic, physicians consider its potency, speed of onset and duration of action, its side-effects and its abuse potential, and any allergies

or idiosyncracies of the patient. Codeine is unique in this context. According to the National Academy of Sciences/National Research Council, it is twice as effective as its most popular synthetic alternative, propoxyphene, has no greater side effects and provides a wider dosage range. This means that codeine, unlike propoxyphene, is useful for both mild-to-moderate pain and moderate-to-moderately severe pain. At the upper levels of pain, codeine has other alternatives, of course, but they have substantially greater abuse potential whereas the abuse of codeine is rare and its addiction liability is minimal.

As an antitussive, codeine was acknowledged by the American Medical Association in a resolution adopted in June 1973 to have "unequaled . . . efficacy". Synthetic cough suppressants have been effective in suppressing experimentally-induced coughs, but many have proven ineffective in reducing cough of pathological origin. Even where objective measurements demonstrate effective cough suppression, as in the case of dextromethorphan, these synthetic substitutes can't provide the combined antitussive, analgesic and sedative action offered by codeine which is often necessary to relieve cough due to colds and respiratory infections. For these reasons, codeine is regarded by physicians as the most effective antitussive.

An adequate supply of crude opium is essential as well to meet the medical demand for morphine, a strong analgesic. In some cases, synthetic substitutes may be superior to morphine because of a more rapid onset and shorter duration of action. These same characteristics operate as disadvantages, however, where the patient requires treatment for persistent, long-term pain. Moreover, while synthetic analgesics may replace morphine in many cases, substitution is difficult in patients who require unusually high doses for relief of severe pain. While knowledge about the effects of high doses of morphine is quite extensive, little information is available about the effects of large doses of synthetics. Similarly, the lack of experience with synthetic morphine substitutes often limits their use in certain patient populations as children, women in early pregnancy or patients concurrently receiving other medications. Thus, while synthetics may replace morphine under many circumstances, there are other patients and conditions for whom substitution cannot be made without risking serious adverse effects.

I have also mentioned the narcotic antagonists, nalorphine and naloxone, both of which are derived from opium. An antagonist such as naloxone, when administered alone to an individual who has had no narcotics previously, has no effect on that individual. However, it is capable of reversing the life-threatening effect of acute narcotic overdose. As such, this drug has a small patient population. For this population, however, it may be the only alternative to death. In addition, the use of narcotic antagonists in the treatment of narcotic dependence is currently a field extensive research through which an understanding of the nature of drug dependence may some day be achieved. Naloxone, as the most potent of the only three available antagonists, is a prime subject in this area.

In short, while some success has been achieved in developing acceptable substitutes, opium derivatives remain essential to adequate medical care. As SAODAP's Dr. Robert Dupont stated before the House Armed Services Committee last year: "Synthetics which would replace substantial portions of the market . . . have not yet been found. Indeed, while some synthetics may be fully appropriate in a certain prescribing situation, in other situations there is not yet known any adequate substitute."<sup>1</sup>

His views were emphatically confirmed by representatives of the three Surgeons General of the Armed Services during those hearings. Opiates, testified Major General Richard Taylor, Deputy Surgeon General of the Department of the Army, "are required for the delivery of health care. . . . Our experience in Vietnam and similar combat situations have proven that morphine is a most vital commodity and any other drug is a fair to poor second choice in relation to the resuscitation and treatment of combat casualties . . . . The elimination of opiate drugs from the medical and surgical practice is not professionally sound. While synthetic products are becoming more widely accepted in lieu of codeine, we have not had enough experience with these substitutes to eliminate codeine. In addition, most synthetic pharmaceuticals bear warnings contraindicating their use in selected populations or age groups."<sup>2</sup>

<sup>1</sup> Hearings on Stockpile Legislation Before the House Armed Services Committee, 93rd Cong., 1st sess., at 52 (1973).

<sup>2</sup> *Id.* at 28.

These opinions are shared by other eminent physicians and pharmacologists. Just last month, GAO investigators reporting to Congressman Charles Rangel on the licit opium supply situation, reaffirmed this collective medical judgment. It is further confirmed by the rapid growth in medical demand for these drugs in recent years. The projections which I will turn to now suggest that this trend in demand is continuing.

#### OPIMUM SUPPLY AND DEMAND PROJECTIONS

Because codeine constitutes about 95% of the demand for opium derivatives in the United States, sales of this substance provide a good yardstick to measure the growth in domestic medical needs for opium. As documented first by the GAO report to Congressman Rangel this past summer, bulk codeine sales to formulators have risen substantially over recent years showing an aggregate increase of 73% from 1967 to 1973. The largest single increase in one year was 20%, occurring in 1972 followed by an additional 17% increase in 1973. While medical demand has been growing, however, the supply of opium has been dwindling. As of December 31, 1973, consolidated inventories of the three processors, including crude opium, work in process and finished goods, had fallen to a four-and-a-half months' supply. This represented a 50% decline in the processors' stocks from 1972 levels.

During the first ten months of 1974, sales of codeine again exceeded imports of crude opium, this time by more than 100%. Had Indian imports plus inventories constituted the sole available supply this year, today the operations of all three processors would probably be closed down. Once work in process is depleted, it would take at least one month to refill the pipeline before any more codeine would be produced. Under these circumstances, we would currently be feeling the impact of the opium shortage at the hospital and pharmacy levels.

This has not happened yet for one reason only. In December 1973, Congress authorized the release of 238 tons of opium from the strategic materials stockpile. The contracts for sale of this material to the processors contemplated delivery over a five-year period, during which a processor could purchase stockpiled opium only if his combined inventory of crude opium, work in process and finished goods fell below a six-months' supply relative to his production quota for that year. Despite these strict limits, inadequate and slow shipments of Indian opium resulted in the rapid depletion of the processors' inventories in 1974 with the result that over 60% of the stockpile release has already been exhausted. Even assuming a small increase in opium imported from India next year, the processors will be able to meet little more than 80% of projected medical demand in 1975.

Future years look no more promising. While medical demand for codeine is expected to increase at an average of 10% per year through 1978, India has indicated that it will not expand its poppy cultivation any further. It is hoped that the 1975 planting will yield approximately 12% more opium than this year's crop, but even this modest increase would only bring our allocations up to about 220 tons, or only 60% of next year's needs.

These data depict the severity of the impact of the opium shortage which will affect the codeine industry in 1975. The impact will gradually reach the consumer level as it becomes difficult and then virtually impossible to fill codeine prescriptions at the pharmacy and in the hospital. Even this bleak assessment is based upon a conservative estimate of demand and an optimistic estimate of supply.

#### POSSIBLE SOLUTIONS TO THE SUPPLY PROBLEM

It is relatively easy to describe the problem; it is far more difficult to find a solution. Indeed, the alternatives for remedial action have narrowed over the past year. Once the currently authorized stockpile release is completed, we cannot count on any further supplies from that source since we are advised that Congress considers the balance of the opium in the stockpile necessary for the national defense. Moreover, the purchase of confiscated opium from foreign governments does not offer a substantial possibility of improving the supply picture. The difficulty of obtaining this material which has sporadically provided a minor supplement to Indian imports, plus its generally poor quality, make this source very unreliable. In addition, the State Department has recently suggested that United States treaty obligations may preclude further imports of this material despite the fact that such trade is authorized by the 1961 Single Convention on Narcotic Drugs. As a result, we cannot reasonably expect that confiscated opium will supplement United States supplies in 1975.

Finally, although Turkey resumed the planting of opium poppies this fall, it agreed for control purposes not to lance the poppy capsule to collect the crude gum opium. Rather, for the first time next summer, Turkish farmers will harvest the straw consisting of the stem and unlanced capsule. Thereafter, the poppy straw will be shipped to European alkaloid factories for processing. Legal and practical barriers stand in the way of utilizing the Turkish straw or the processed materials in the United States, however. First, under present circumstances, United States law prohibits the importation of poppy straw, its extracts or derivatives. Although the law permits the Attorney General to authorize the importation of such substances, the United States has no domestic facilities for processing straw. Only extracts of the straw suitable for further manufacturing in the United States would be of any use to the processors. At this time, it is unclear whether the European factories have the capacity to process the Turkish crop to obtain these extracts. Some of these problems may be resolved in future years. The production of Turkish straw may then relieve the pressure upon India and ultimately increase the supply of crude opium for the United States. Currently, however, with the demand so great and the Turkish crop a year away, we do not foresee such relief in 1975 or 1976. This conclusion is exemplified by a recent event in Turkey. Because of the resumption of poppy production, the Turkish government proposed to release 30 tons of crude opium which it had stockpiled to relieve the shortage in other countries. In response to the offer to sell 30 tons, Turkey received requests which totalled 250 tons. Rather than antagonize any of the would-be purchasers, Turkey withdrew its offer. This suggests that the current rate of demand upon India for crude opium will continue unabated in the next year or so. As a result, the promise of Turkish production is unlikely to improve the supply picture in the United States at this time.

The proportions of the impending shortage thus are clear. The remaining opium authorized for release from the stockpile combined with projected Indian imports, will meet approximately 80% of next year's projected demand. The balance of medical need could be satisfied only by reducing processors' inventories to a level which would require periodic suspension of production thereafter. In order to avoid such an eventuality a year from now, a formal program of rationing bulk codeine will be inevitable in 1975.

My remarks this morning indicate that the prospects for a short-term solution to this problem are dim. In the long run, however, there is a realistic hope of developing a domestic source of codeine through cultivation of papaver bracteatum, a form of the poppy which does not produce morphine from which heroin is derived. Acceleration of research already begun by the Department of Agriculture at its Beltsville, Maryland station and establishment of a regulatory framework by the Drug Enforcement Administration would contribute substantially to the success of this project.

Industry recognizes its responsibilities in finding a solution to the opium supply problem which threatens the adequacy of medical care in the United States. Direct Government assistance is essential, however, in negotiating with India for increased allocations if the United States is to compete successfully for the needed share of production. In this regard, it is also crucial that the United States send accurate estimates of our opium production requirements to the International Narcotics Control Board in Geneva. Deficiencies in these estimates in recent years have increased the difficulties which the companies face in dealing with India.

The Government also has a substantial role to play in dealing with the legal problems involved in the importation of confiscated opium and other raw materials. With regard to confiscated opium, we look forward to working out a solution with DEA and the State Department in the near future so that even the minor supplement occasionally provided by confiscated opium in the past will be a factor in the future. In addition, we have discussed the possibility of providing for the dissemination of State Department information on illicit opium seizures so that United States importers can compete for the material as it becomes available. With respect to other raw materials, Government action will be crucial in evaluating the circumstances which might provide a legal foundation for emergency importation under tight security.

In considering a long-range solution, the need to develop a regulatory scheme for the cultivation of a domestic source of codeine must be recognized. Government leadership in advancing this project and providing a controlled foundation

for its development is essential. Indeed, we believe that there can be no solution on either a long-term or short-term basis unless the Government's efforts are centralized in one high-level office capable of initiating coordinated action based upon relevant data and policy considerations from all the concerned agencies.

We understand and share, of course, the concern felt in Congress and the agencies for the problems of drug abuse in our country and we are certainly proud of the record of the licit narcotics industry in this regard. At the same time, we hope to see a stronger expression of concern for the other side of the issue—the objective of assuring that the health care needs of Americans for medicinal opium-based drugs will be met in 1975 and thereafter. Only when the problem is acknowledged, and the urgency of the need to solve the problem is recognized, will it become possible to deal with the situation effectively.

Senator KENNEDY. Mr. Kolbas.

Mr. KOLBAS. My name is John M. Kolbas. I am vice president-manufacturing of Bristol Laboratories Division of Bristol-Myers Co. I am a chemical engineer with a BCHE degree from Ohio State. I have been with Bristol-Myers Co. for 27 years.

Bristol-Myers Co. is a diversified health care, pharmaceutical and consumer products company which markets more than 700 products in the United States, Canada, and some 100 countries overseas through 10 major divisions. The company employs more than 26,000 people in this country and overseas.

Our Bristol Laboratories Division, headquartered in Syracuse, N.Y., produces four major classes of antibiotics—semisynthetic penicillins, aminoglycosides, tetracyclines and cephalosporins—and, further, markets a wide range of prescription medicines. Included in this product line is polycillin, a broad spectrum penicillin generically known as ampicillin.

We have been invited to comment on the current shortage of sodium ampicillin in the United States. Before going directly into the shortage, we would like to provide some background.

Senator KENNEDY. I have the background. We would appreciate hearing the principal parts of your statement.

Mr. KOLBAS. Bristol's sterile bulk production facility at Syracuse performed normally through May 1973. However, on May 27, 1973, a microorganism problem was detected in Bristol's own testing of sodium ampicillin produced in the facility. This was completely unexpected, but is always a possibility in any sterile antibiotic production, which is of course the reason for the rigid sterility testing requirements imposed on every batch produced.

Bristol promptly undertook to determine the source of this problem, but without immediate success. None of the sodium ampicillin produced from the time this problem was encountered was ever submitted to FDA testing or released for sale.

By September 1973, the microorganism problem had still not been completely eliminated. It appeared that no satisfactory solution could be obtained without a complete renovation of the sterile bulk antibiotic production facility, the FDA having taken the position on September 14, 1973 that they could accept no more product for certification from the Syracuse bulk sterile manufacturing location. Bristol therefore closed the plant and commenced a complete renovation.

Senator KENNEDY. What percent of the market did you have then?

Mr. KOLBAS. Approximately 60 percent.

Senator KENNEDY. At what cost, or at what price, before and after.  
Mr. KOLBAS. Our list price for a half gram of sodium ampicillin was \$1.02.

Senator KENNEDY. Is this before the shutdown?

Mr. KOLBAS. That was in January 1973.

Senator KENNEDY. And today what is it?

Mr. KOLBAS. Our price today, after the increase of the cost line, is \$1.24.

Senator KENNEDY. That is quite a bit different. You heard the testimony of Dr. Jennings from the FDA?

Mr. KOLBAS. I have.

Senator KENNEDY. Was that inaccurate, the way they described it?

Mr. KOLBAS. Mr. Chairman, that is the list price of sodium ampicillin. In the hospital market much of that business activity is on a bid basis, so that the prices will range from list down to whatever the winning award is or will be.

Senator KENNEDY. We are interested in what the real price is. Has it gone up or down?

Mr. KOLBAS. The real price?

Senator KENNEDY. Yes.

Mr. KOLBAS. The price ranges in bids from as low as 23 cents, to the catalog price. So it was in that range.

Operations in the sterile bulk manufacturing area were discontinued in September 1973 to begin renovation of the facility and installation of new equipment. At that time we anticipated a startup in 6 months. However, delivery of stainless steel equipment and doors was extended because of tight supply of materials and labor problems at some of the suppliers. Plastic components also were late in delivery as were the materials for the air handling equipment. All of this resulted in a delay of production startup in the new facility until August of 1974, almost 12 months after the discontinuance of operations.

At the time of the closing of the sterile bulk manufacturing facility we had close to normal inventories of sodium ampicillin. We were unable to build further inventories because of the force majeure nature of these events. Shortly after the shutdown, we contacted other manufacturers and purchased quantities of sodium ampicillin. These purchases, along with our estimate of 6 months to renovate the sterile bulk manufacturing area, led us to conclude that adequate supplies would be available through the spring of 1974.

It is useful for present purposes to understand how Bristol Laboratories distributes sodium ampicillin to its customers. Bristol Laboratories sells directly to hospitals or through pharmaceutical wholesalers. Most hospitals purchase their requirements directly.

In 1973, 98 percent of Bristol's sodium ampicillin sales were direct to hospitals. Thus, as the shortage of sodium ampicillin developed, wholesalers had only very small quantities on hand, since they receive little demand from hospitals. Because of this, available supplies were limited to inventories carried by the hospitals, our company, and other suppliers.

Many hospitals maintain limited inventories of products because of inadequate storage facilities or financial restrictions that do not permit the purchase of large quantities. For these reasons, the shortage developed rapidly.

In early fall of 1974 when the shortage became apparent, pharmacists and physicians brought to the attention of our representatives situations which were felt to be critical. These were cases where sodium ampicillin was required because it was the treating physician's choice in serious infections. We have made every effort to react to such situations as they occurred.

At all times we maintained an inventory of sodium ampicillin to use for cases brought to our attention by hospitals, pharmacists, or physicians.

Bristol's representatives also played a part in responding to shortages at hospitals within their territories by borrowing from one hospital to supply another with a more critical need. This happened frequently.

We also attempted to make the best use of all available dosage strengths of sodium ampicillin. On occasion we did not have available the size ordered but would recommend an alternative that met with the hospital's approval.

We are now processing sodium ampicillin at a level above the pre-shutdown period and plan to continue to do so until adequate inventory levels are established and demand is stabilized. It is now estimated that ample inventories will be established by the second quarter of 1975. We believe normal inventories will be achieved even more rapidly if hoarding does not take place.

To sum up, the basic cause of the sodium ampicillin shortage was the shutdown of the facility required in the manufacture of sodium ampicillin. There has not been any shortage of the oral forms of ampicillin.

We recognize that a concern of the subcommittee is whether any general lessons can be learned from the injectable sodium ampicillin shortage. It appears to us that this was a unique event, resulting in the closing down of a major production facility. Bristol believes that it successfully met the problems that were presented, and that they are now ended. The reduction in inventory experienced seems unlikely to occur again in the foreseeable future.

Senator KENNEDY. Thank you, very much.

I suppose one of the questions that comes to mind is not only the fact that there is a shortage, but how does the competitive system work in a situation where you have 60 percent of the market, and then you close down your shop for awhile, and when you reopen you have 60 percent again, in effect? What are the competitive forces that play on this that precluded other companies from moving in to fill in the vacuum?

Mr. KOLBAS. I am not sure I understand your question, Mr. Chairman.

Senator KENNEDY. Let me be more precise.

You had 60 percent of the market before you closed down your shop. No one else moved in to take up the slack, even though, as your testimony points out, there were very important shortages. You open your doors again and get 60 percent again.

Mr. KOLBAS. Senator we have just begun to put material back into the pipeline. As of this moment I do not believe Bristol has 60 percent of the market.

Senator KENNEDY. Are you going to full production?

Mr. KOLBAS. We are returning to full production, yes, sir.

Senator KENNEDY. Why are you going to full production? Do you think you will be able to sell your products?

Mr. KOLBAS. To establish the demand we believe exists there.

Senator KENNEDY. When you get to full production, what percentage of the market will you have?

Mr. KOLBAS. At this point we are not sure. We anticipate we will be obtaining a significant portion of the market.

Senator KENNEDY. What percent? You must have some idea.

Mr. KOLBAS. I would like to believe we could regain it all.

Senator KENNEDY. That is what you are planning for; that is what you are producing for?

Mr. KOLBAS. That is correct.

Senator KENNEDY. That was the point I was trying to make. If you are planning to go to 60 percent and believe that you can get to 60 percent, the people committing the financial resources to get you there believe that to be so. I am just inquiring about how that phenomenon works. I do not know many other industries or businesses where you, in a competitive situation, could have that take place.

Mr. KOLBAS. We are optimistic, but it is still not an accomplished fact.

Senator KENNEDY. Mr. Bongiovanni, you make the same drug, do you not?

Mr. BONGIOVANNI. Yes, sir.

Senator KENNEDY. Why did you not increase your percent of the market, or did you?

Mr. BONGIOVANNI. Well, we did increase the percent of the market. We went from 6 percent to 11 percent. Internally, as we looked at the situation, we assessed that it was a medical problem. But we honestly did not feel that it was a medical crisis, I think, for the reasons that have been outlined. We thought about the possibility of building new facilities. But if you just have 6 percent of the market, you are not really going to seriously consider spending some \$20 million when there is no medical crisis and when, in fact, you could not solve the problem because the solution that you are contemplating is some 2 years away. We did increase our actual output for the year by some 60 percent. This was done not completely through greater production. A portion of it was done through greater production, but it was a matter of inventory on hand which we sort of exhausted, plus the holding back of inventory of the other items that were made in that facility.

So that we tried to pick up the lag as much as we could.

I think the dominant thing was the fact that there were other drugs that could be used and that it was not a medical crisis.

Senator KENNEDY. How do you rate in your production of the drug? Besides Bristol, how many larger producers are there?

Mr. BONGIOVANNI. Bristol had 60 percent. Wyeth had 23 percent, Beecham-Massengill had about 4 percent, Ayerst had about 3 percent, and we had about 6 percent.

Senator KENNEDY. How did that come about; how do you have this sort of wide spread? You go 60 to 22 down to, I guess what you had, 6, is that right, approximately?

Mr. BONGIOVANNI. Yes. I think we are sort of discussing a marketing problem which has to do with lots of variables. For example, as I remember it, Bristol was the first company to come out with the drug and establish it. And they, therefore, had a larger share of the market.

Senator KENNEDY. So it was under patent at that time?

Mr. BONGIOVANNI. I would assume so.

Also, as you start to deal with hospitals and as bidding takes place, you have to assume that Bristol, because of its facilities and because of its know-how and because of its expertise, could maybe make it more economically than other companies.

But at any rate, the fact is that as hard as you try to get a larger share of the market, that is sort of the way we end up.

Senator KENNEDY. When did it come off of patent?

Mr. KOLBAS. I am not sure that the patents have officially expired. However, there have been a number of companies licensed to manufacture ampicillin abroad and in the United States.

Senator KENNEDY. You do not know when the patent will expire?

Mr. KOLBAS. Not exactly.

Senator KENNEDY. Approximately, do you know?

Mr. KOLBAS. Perhaps in the next several years.

One does not consider these things when you have as many as 57 companies manufacturing oil ampicillin and at least a half a dozen or more in the injectable area.

The question is, what is the patent?

Senator KENNEDY. Mr. Bongiovanni, are there any other comments which you would like to make?

Mr. BONGIOVANNI. Well, I think most of it has been said. I do want to comment that I agree that there ought to be an early alert system somehow, particularly in the times as we live in them today.

Fortunately, it seems to me that one of the strengths of the pharmaceutical industry is that for the most part there are very few drugs that are unique. One of the strengths is that there are, most times, alternatives.

But certainly, those drugs that are unique ought to be looked at and looked at very carefully. So that I concur with your thinking—

Senator KENNEDY. Sure. One of the questions in making that determination is the accessibility to production material, is it not? What would be your attitude toward making that kind of information available?

Mr. BONGIOVANNI. Are you talking making—I do not quite understand you.

Senator KENNEDY. The FDA indicated that in fulfilling responsibility for early warning, heavy production materials would really be essential to that function. I read the proportion. It is on page 12 of the FDA's testimony.

Having now recognized the importance of such an effort yourself, would you be willing to make available production materials?

Mr. BONGIOVANNI. As a company, I think, on request, we have, where that information has been pertinent and necessary.

Senator KENNEDY. How about the rest of the panel on that particular issue?

Yes, sir?

Mr. PETTINGA. Senator Kennedy, I was taught in the Navy never to volunteer. But I would like to.

My name is Cornelius Pettinga.

Senator KENNEDY. We have the same thing in the Army, too. [Laughter.]

Mr. PETTINGA. At least, we are both now civilians, sir.

My name is Cornelius Pettinga. I am with Eli Lilly & Co., and I was very pleased to hear Dr. Jennings of the FDA suggest additional new ways to think about the problem of drug supply in uncertain times.

I think the responsibility of those companies and agencies who are interested in assuring medicine, medical people, the public, patients, continuous steady supply of codeine and morphine, is a very valid interest.

One of our major problems is the assurance of continued supply. Drugs not available in the hospital do not do anyone any good.

If I may, sir, I would like to read a very short summary of the statement that I furnished to you. Would that be agreeable?

Senator KENNEDY. All right.

Mr. PETTINGA. On drugs, generally, we have developed highly sophisticated techniques to try to anticipate demand, product for product, package size for package size, region by region, state by state.

We have five regional distribution centers in each part of the country to get our product to every doctor and hospital in the country. As a result, I am proud to tell you that we fill over 99 percent of all of our orders immediately.

Nevertheless, we can foresee situations in which shortages—not of our making, but springing from outside conditions—could arise. We would like to offer suggestions for meeting them. The most obvious problem that we are confronted with is a possible cutback on petrochemicals that would arise from limitations on oil consumption imposed on our country, either by ourselves or by foreign nations.

Petrochemicals—and I am not just referring here to fuel oil and gasoline, but to solvents, alcohol, and acetone—are critical to almost every product we make.

During the recent oil embargo, we cut back on the use of petrochemicals where we could. Benzene use, for example, was cut back from 3.7 million liters to 2.2 million liters in less than 1 year. But there is a limit to how much we can cut back without curtailing production and causing shortages of vital drugs.

In this connection, we were very grateful, Senator, for what you did a year ago to urge the pharmaceutical industry to get a No. 1 priority in fuel allocation under the FEO. Unfortunately, petrochemicals were generally not covered. We think they should be. We think the petrochemical feedstocks should also be.

We strongly feel the necessity for continuing FEO petroleum products authority beyond the present expiration date of June 30, 1973. Secondly, we recommend that the system of communication and feedback of information that seems to be working in the case of heparin shortages be expanded into an extent formalized.

We recommend a representative group of participants from the pharmaceutical industry, health professions, and Government be assembled as a task force to examine the broad question of raw material

availability to assure adequate supplies of medically strategic materials, rather than have a hastily conceived program at this time.

And I would point out all antibiotics are certified. The FDA already has complete detail as to production figures of these items, and knows that codeine and morphine are controlled by a number of Government agencies. Because they are controlled drug substances, rather than to have a hastily conceived proposal at this time, we recommend that thoughtful study be given to this complex problem before any firm proposals are made and implemented regarding the overall supply.

Members of the industry and health professional organizations should—and I am confident will—consider it an essential responsibility to voluntarily alert suppliers, health professionals, and the FDA. when situations are observed which have a potential for creating significant shortages in medically strategic materials.

Such situations would include: one, cutoff of our material supply by foreign countries; and two, a breakdown of production facilities in other situations. While our concept is admittedly general at this time, our company would be happy to work with anyone who is willing to cooperate, including your committee, in order to develop a more specific proposal.

Thank you, Senator.

Senator KENNEDY. Well, I appreciate your comments. But I wondered how much more you have to study to realize that you need an early warning system. We obviously need one.

With heparin, it is just not working; at least according to doctors or patients in terms of the availability of that drug or the cost of it.

I don't know how much time we have to spend in studying whether we need an early warning system. If we accept that we do, then certainly basic to that is going to be accessibility to materials of production.

I don't know why that is a disputable factor. I can understand some of the concerns of the companies regarding revelation of trade secrets and its deleterious effect on competition. This is understandable, and perhaps a protective mechanism could be built in. But for the reasons you have outlined, that we have to have more work on the study using the example of an antibiotic which is only one drug. I don't find the case terribly convincing.

Mr. PETTINGA. They are an important category of drugs, Senator. When you think that our own company has over 700 products offered for sale—and there must be thousands in this country—we have heard today of shortages. I don't know how many people have been deprived of heparin or antibiotic drugs. Perhaps we ought to actually look at this in critical detail, you know, there are shortages and there are shortages.

Senator KENNEDY. There are shortages and there are shortages, and there is a sign out in the Stanford Hospital saying to doctors, don't use this unless it is a dire emergency.

Mr. PETTINGA. Do they say, don't use it, or, don't waste it? You see, there is quite a difference. We have checked 300 hospitals within the last 2 weeks. According to our information, over 75 percent of those hospitals have 3 or more weeks of inventory.

Now, we don't know the situation precisely in detail in each hospital. I can't promise you that no patients have ever been deprived.

Senator KENNEDY. Did you check with the Hillside Medical Center on Long Island?

Mr. PETTINGA. No, sir, I did not, but we wrote it down.

Senator KENNEDY. Here is one from George Wisoff, who is a surgeon, a cardiovascular surgeon. He said he would like me to be aware that the lack of heparin in the United States has produced a difficult situation for adequate medical care of patients. In his hospital, there is no heparin available for anticoagulant management of patients following heart surgery.

Mr. PETTINGA. Senator, I am surprised and shocked at that, too.

Senator KENNEDY. We have the other example of publications put out in hospitals about the availability and cautioning against use of this drug. Maybe there are only a few. Maybe there are a lot. It does not seem to me that we know very much. It seems that if we are going to know about it, we ought to be able to devise a system where we will know the exact extent. We don't have that currently. I find it difficult not to feel that there should be a sense of urgency about developing a system which will be able to guide us along in this complex and difficult area.

Mr. PETTINGA. We share your concern, and that is why we are proposing that a careful study be made. It doesn't have to take a long time.

Senator KENNEDY. But you say it must be ongoing.

Mr. PETTINGA. It must be ongoing, because the unrest in Indonesia, the bad weather in India, these things cannot be forecast. It is too late when the hospital pharmacy is low. You have to be able to predict. In my statement, you will see comments made about Vinca Rosea, which is the plant source for two Vinca alkaloids that are useful in the treatment of certain cancers.

We keep a 2-year stock of leaves, we keep 14 months' inventory. It is precisely for these uncertainties that we keep these supplies available so that we can continue to deliver.

Senator KENNEDY. Do you make quinidine?

Mr. PETTINGA. We are not a bulk manufacturer of quinidine.

Senator KENNEDY. Do you sell it?

Mr. PETTINGA. We sell it.

Senator KENNEDY. Is there a shortage of that?

Mr. PETTINGA. We presently are on allocation.

Senator KENNEDY. What does that mean?

Mr. PETTINGA. A wholesaler cannot order unlimited quantities. We ship out what we can acquire.

Senator KENNEDY. Are you having trouble getting it, or not?

Mr. PETTINGA. Yes.

Senator KENNEDY. Why?

Mr. PETTINGA. For a variety of reasons that Dr. Jennings already spoke to. The unrest, the damaging of the plantations. A number of years ago, there were hearings by Senator Hart. We participated in those hearings.

You see, Senator, the situation varies from product to product and from time to time. It has to be ongoing. We discuss with the FDA

problems of antibiotic certification because we are a major supplier. And they do alter the timing of their certification schedule for us, as they do for all of the rest of the industry.

If we say we are short or we anticipate problems, can you assay this lot first. If it is possible, they do it.

Senator KENNEDY. We want to get on with the other witnesses. But are you for an early warning system, or not?

Mr. PETTINGA. If you can develop an appropriate one.

Senator KENNEDY. Have you made suggestions on it?

Mr. PETTINGA. I don't know what it would be. I just know that in the hospital pharmacy, it is too late. You have to look a year to 2 years—

Senator KENNEDY. I know, but this is coming right back to us, you see. Now, you are the ones who know how these things ought to be done. Either you have suggestions about how we are going to do it, or we have to proceed the best way we think we should. So if you have some ideas that are going to address this particular problem, then we welcome them.

Mr. PETTINGA. We will be glad to give them to you in detail on those products where we have significant knowledge.

Senator KENNEDY. Do you feel there is a cartel on quinidine?

Mr. PETTINGA. I have no information about what is happening in Germany or the Netherlands. I really don't know, Senator. I can tell you what has happened to the price.

Senator KENNEDY. You seem to me to be a pretty shrewd businessman. You sell the drug. Do you want to leave your response that way, that you don't know what is happening? You can't get much of it, you know what is happening in price, but don't know what is happening in Germany? I will let it rest at that.

Mr. PETTINGA. I am not a shrewd businessman. I was trained as a scientist and that is why I am a little bit careful about saying I know there is a cartel. I honestly don't know those things.

Senator KENNEDY. Mr. Lyng.

Mr. LYNG. I am president of the American Meat Institute in Washington, D.C. The institute is the national trade association of the meat packing industry. I have a prepared statement, but in the interest of time, I will summarize it.

I do not think I need to go into detail about all the byproducts of animals, and particularly those that are used in drug manufacturing. My testimony indicates that many drugs in addition to heparin, which is the drug that I was asked to talk about, are made from animal sources. It is our understanding that the anticoagulant drug heparin is prepared from a raw material called mucosa. Mucosa is removed from the small intestines of swine as a byproduct in the preparation of natural sausage casings. Beef lungs are another source of the raw material for heparin, but pork intestines are the dominant source. Two factors affect the available supply of mucosa. First is the total supply of hogs. In my testimony I list for the past 5 years the total commercial hog slaughter which has ranged from 76 million head in 1973, to 94 million in 1971. In 1974 we estimate 82 million head as being the commercial hog slaughter. We estimate that in 1975, that figure will be down sharply.

The second major supply factor has been the growth of synthetic casings which have moved into a position of heavy usage in sausage manufacture. As a result of this, there has not been significant growth in the natural casing industry.

A key question is, how much mucosa is being saved?

Unfortunately, we are unable to completely answer this question because statistics are not available to us on either the total production of mucosa or the rate of increased usage of heparin. We can say with a fair degree of certainty that mucosa is not being saved in a large number of swine slaughtering operations. The market value of mucosa alone is too low to justify the labor cost of saving it. The available supply of mucosa, then, depends upon the demand for natural casings.

It is our estimate that mucosa is being saved from approximately one-third of the swine being commercially slaughtered. Theoretically, the total supply of mucosa could be tripled if all swine slaughtering plants were to begin to process for mucosa.

Senator KENNEDY. Is it an economic problem?

Mr. LYNCH. Yes. To the packer, the present value of mucosa is low. Here is an example.

Senator KENNEDY. Before we get to that, if it is not saved, where would it go?

Mr. LYNCH. Generally, the entire intestine goes to a rendering plant.

Senator KENNEDY. What happens to it?

Mr. LYNCH. Then it is converted into the things that they make in rendering plants, which in this case would probably be mostly animal feeds, meat scrap, that kind of thing.

Senator KENNEDY. Pet food?

Mr. LYNCH. Non-human edible materials.

Senator KENNEDY. Among which is pet food, too?

Mr. LYNCH. Yes; I think meat scrap is used in some pet foods. More heavily, I believe, in animal foods.

Just an example of the economics, on November 30, 1974, a typical market-weight hog had a value to the packer of \$89.19. The hams from that hog could be sold for \$25.92. The belly could be sold for \$14.64. The loins could be sold for \$20.16. The average yield of mucosa from that hog would be 1½ pounds, and the average price would be no more than 8 cents per pound. The gross return from mucosa from a single market hog would be 12 cents. The gross return from the sale of small intestines as natural sausage casings would be approximately 45 cents, or four times as much as the mucosa. Both products together—that is, the natural casing and the mucosa—represent approximately one-half of 1 percent of the wholesale value of an average market hog.

The meatpacking industry has long understood that it has a special responsibility in this area. We have, as a trade association, been in contact with the various committees of our organization—the packers. Virtually every swine packer has now become aware of this. We are beginning to see some increasing interest being shown on the part of pharmaceutical companies.

We need, in order to move into this, some assurances about the future demand, new techniques, synthetics, and that sort of thing.

But the industry is willing, as they have been in the past, to do everything possible to supply this, even though it is a very minor item in terms of dollars and cents of the total product we sell.

The meatpacking industry has long understood that it has a special responsibility to the public to take advantage of the best possible use of every part of the meat-producing animal it processes.

Senator KENNEDY. I want to make it exceedingly clear that there is no feeling on my part that industry isn't attempting to meet its responsibilities in this area. It seems to me that the action that was taken by the Congress from what I consider to be the sound social policy of making available the hemodialysis for needy people, brought about a very sizable increase in the need for this product which perhaps was not well understood when the measure was being considered by Congress.

But that is past history. Obviously, your trade association is trying to cooperate in the ways in which they can. But it seems to me that there is some economic consideration, both from your own point of view in a highly competitive situation, and from the pharmaceutical companies' point of view.

Where they supply the drugs, they are going to have to pay a good deal more for obtaining the materials from which the products from which the drugs are derived.

That would mean, of course, a very sizable increase in terms of the consumers and the consumers paying for this. But it seems to me to be an area—there has to be a spirit of cooperation and some kind of real assessment as to what we are talking about.

I think that this is the obvious concern on this particular question and one which you can't solve yourselves, nor can the industry solve in itself. Yet, the result is that there are important health considerations in terms of the decisions which are being made by your members as well as the pharmaceutical companies, and which are going to impact on the public.

There are matters of policy questions which we are very much interested in. So we want to make sure that the manner in which this product is produced is not going to make the cost prohibitive.

We are going to try to find out ways. Mr. Adams, could you make a comment about that?

Mr. ADAMS. Yes, sir, may I read my statement?

Senator KENNEDY. Yes. Maybe you could pick up this point and then go through it. Or maybe you will develop it in your statement.

Mr. ADAMS. Thank you.

I would like to thank you, Mr. Chairman, for allowing us to testify on this particularly important product.

One of our products is sodium heparin. It is an anticoagulant medication. It is critical in the treatment of several life-threatening conditions, and there is no known suitable substitute.

We appreciate this opportunity to bring to your attention the facts, as we know them, concerning the current critical shortage of this important drug product.

We appreciate and understand the concern of this committee and many others, and we want to assure you that we and other manu-

facturers are successfully making every effort to see that no patient in need of the anticoagulant activity of heparin will be denied its use.

Although we have not been able to meet the demand for heparin, and will not be able to do so for some months to come, we do feel we have been able to meet the critical need. To our knowledge, there have been no reports of patients being denied heparin when the use of this anticoagulant was critical.

Mr. Chairman, in order that all may have a more complete understanding of the current situation, my statement will cover four major areas of concern.

First, I wish to speak to some of the more important reasons for the current short supply of heparin.

Second, we will discuss the total approach at Riker we have taken to date to help alleviate this problem.

Third, we will give our best estimate as to what we see for the future, and discuss our forecasts for meeting future needs for heparin. We believe these assessments are fairly representative of the activities of most manufacturers of heparin.

All of this, I can only speak for my own company. We believe these figures are fairly representative. Some of the major factors that have contributed to the heparin shortage are—the most important factor has been the vastly increased medical uses of heparin. Primarily these are:

1. A tremendous increase in the number of kidney patients undergoing hemodialysis treatment.
2. An increase in the number of open heart surgeries.
3. The usage of heparin prophylactically to prevent postsurgical deep-vein thrombosis.

So that the committee might have a better appreciation of the impact these three medical uses have had on the demand, the following information is of importance:

1. It is estimated that the number of kidney patients undergoing hemodialysis has doubled in the past 11 months. The latest estimate is that 14,000 Americans undergo hemodialysis treatments two to three times each week. Each patient requires up to 30,000 units of heparin per treatment. The increased demand resulting from this one medical usage is more than 30 billion units of heparin annually.

2. Open heart surgery figures for 1974 are not currently available, but most who are knowledgeable on this subject state that there has been a dramatic increase in the number of open heart surgeries performed.

We are informed that the minimum heparin requirement for each of these patients is 20 10-milliliter vials containing 10,000 units of heparin per vial, or 200,000 units of heparin per surgery. Through November, we at Riker have experienced a demand of over twice last year's for the same period of time for this particular size and concentration of heparin.

3. The relatively new and less critical usage of heparin prophylactically to prevent postsurgical deep vein thrombosis is just beginning. However, it has had and will have a dramatic impact on heparin needs in the future. Some authorities have recommended that all surgical cases should receive 5,000 units, two times each day, 1 to 2 days prior to surgery and 7 to 12 days after surgery.

Another factor in the current shortage has been the stockpiling by some hospitals which has resulted in a maldistribution of heparin. This problem has continued to increase and is now evidenced by what we see as panic ordering of quantities which are sometimes double actual needs. This has been determined through discussions with hospitals requesting unusually large quantities of heparin as compared to past ordering.

Senator KENNEDY. Tell me, what would happen if you did not have heparin?

Mr. ADAMS. A lot of people would die, especially those in those critical conditions, such as patients who are on hemodialysis and those who have to have open heart surgeries.

Senator KENNEDY. Did you have any estimate, if that did not exist, if we did not have the heparin, of how many people would die a year?

Is there any way of knowing really?

Are you talking about a few hundred? Are you talking about a few thousand?

Mr. ADAMS. No. I am talking about thousands, Senator.

Senator KENNEDY. All right.

Mr. ADAMS. Another major factor, and the one most often discussed by the media, is the problem relative to the collection of sizable additional quantities of raw material.

We believe this latter problem, although critical in meeting future needs, has been overstated and misrepresented. One fact that should be of interest is that Riker is currently producing heparin at twice the rate of just a year ago and we expect to more than double this rate by mid 1975.

In order to eliminate the confusion regarding what constitutes our raw materials, and what factors are involved in our collection of this material, I would like to spend a few minutes discussing this subject.

Our raw material is hog mucosa and comes from the intestinal lining of the small intestines of hogs. This material—mucosa—is a byproduct of the collection of sausage casings. In other words, the amount of raw material available to process into heparin is dependent upon the amount of sausage casings collected, so the limiting factor until now has been the production of sausage casings and not the size of the hog slaughter, since in the United States casings are collected from only a relatively small portion of the total hog slaughter.

Unless used in the production of heparin, this material—mucosa—would be a waste product since, to our knowledge, it has no other use. We do not compete with pet food processors for this material as has been reported.

I have seen mucosa put down the sewer.

Virtually all of the material available as a byproduct of sausage casing collection is currently being used or is contracted for.

Therefore, additional raw materials must come from making mucosa a primary product instead of a waste product, or byproduct, of sausage casing collection. This, of course, means much more raw material is available if it can be made economical for the meat packers to collect it.

There are two obstacles then to the expansion of the available raw material, costs and just the time to bring these new sources into production within the realities of the meat processing industry.

Our efforts to alleviate the critical heparin problem have been many and varied. This problem has been made more complex by two separate needs. We consider our first obligation a moral one in that we must do everything in our power to insure that any patient who needs heparin will not be denied its use.

Second, because we see the expanded use of heparin increasing at a rapid rate, we must secure long-term sources of raw material to meet future needs.

To help meet the immediate needs of hospitals and, more important, the needs of their patients, we initiated a program of manufacturing primarily those vials of heparin required for hemodialysis and open heart surgery.

We also established a system of maintaining a backup supply of heparin to handle emergency needs for those hospitals whose prior sources had failed them temporarily.

Our medical service representatives have worked with hospitals in switching inventories from one hospital to another and advising in the establishment of conservation measures.

An exhaustive search throughout the United States to secure more raw materials was and is being conducted by Riker people expert in this area. Their success in this area is evidenced by the fact that our current production rate is double that of a year ago.

All of these programs have been successful, but they have not been enough to place us ahead of the increasing demand for heparin.

Our programs to prepare us for the increased future needs have been to literally search the world for additional sources of raw material. I have personally made two trips to Europe in the past 4 months to explore the possibility of obtaining additional materials there.

My associates have traveled throughout the world and have held discussions with authorities in such places as Poland, Hungary, Yugoslavia, the Peoples' Republic of China, Taiwan, as well as most of Western Europe.

We have made good progress in this area, but a positive impact from these sources cannot be reasonably expected for at least a year. We have also intensified research efforts in other areas of anticoagulation therapy and into the nature of heparin itself.

We believe that everything that can be done by our company has either been done, or is being done, and good progress is being made.

The trend is that of continued growth in the demand for heparin. We at Riker feel confident that the progress we have made in securing raw materials for immediate needs, as well as future needs, permit us to assure you that the critical heparin needs can and will be met.

Our best estimates are that we will continue to experience a critical shortage for the next several months, necessitating careful handling of orders to meet emergencies.

During the second quarter of 1975, we expect the problem will be greatly alleviated, although we expect heparin to remain in somewhat short supply for at least a year. Past that time, we expect to be able to meet all foreseen requirements.

I would be happy to answer any questions, Senator.

Senator KENNEDY. Let me ask you, what are the other raw materials that you are looking for?

Mr. ADAMS. We are looking for mucosa, primarily.

Senator KENNEDY. Do you mean they might be able to process it from other countries?

Mr. ADAMS. That's right. In this country, we feel there are adequate supplies available. Actually, our figures differ a little from the other view, but we estimate that actually only 20 percent of the hog kill, at the present time, casings are collected from only 20 to 25 percent of the hogs killed.

The mucosa available from that additional kill would make four times as much heparin available as there is now. But the heparin shortage is worldwide. Of course, people die in other countries, too, from these same conditions.

Senator KENNEDY. As you see it, the only limitation is the economic limitation, is it not?

Mr. ADAMS. That and time. From the time we visit a meatpacker and they agree, and they have been most cooperative in most cases, agree to start collecting material for us, there is about a 6- to 8-month lagtime, because it takes time to acquire equipment, to train people, to set up collection procedures, and monitor the quality. Then from the time we receive the material, it takes about 8 weeks to process it before we have the finished material to ship.

So we began increasing our efforts; I guess you might call this sort of our early warning system, we began about 18 months ago. As a result, we are up to double now what we were last year.

Senator KENNEDY. Next year, even if you can double last year's supplies, will you still be short, do you feel, in terms of demand?

Mr. ADAMS. We think there will still be something of a shortage at least through next year and possibly longer because of these rapidly expanding uses. But we certainly feel we would be able to meet any critical need; that is, any life-threatening situation.

We have handled hospitals on an emergency basis. When a hospital has been down to a 2- or 3-day supply, we have shipped by air, hand-delivered, we have done everything possible.

To our knowledge at this point, in no critical situation was a patient denied heparin.

Senator KENNEDY. I think that we have seen just in the cases this morning, ampicillin and heparin, the fact that we have had shortages. It seems now that we are really playing catchup ball with these for the different reasons.

But nonetheless, the instances which have been pointed out are life-supporting drugs. On the other hand, we had the testimony about the very real potential shortage of opium derivatives for next year. It does appear to me that this type of a situation where we are playing catchup ball with two important drugs, and also as we have been warned about the real limitations that we are going to be facing in this other area, that as a matter of sound public policy, we are going to have to derive a better system for warning the policymakers about these situations.

## GUIDE AND MONITOR

I think we need the warning in the Congress, in the administration, and I would think in the industry, as well. It seems to me that the real challenge we are presented with is trying to develop a system which will be able to guide and monitor in this area. This is going to need the full cooperation and participation of the industry, itself, and also the active support of the various regulatory agencies, so that we as a society can make the kind of decisions which are so important to maintain and sustain these vital contributors to sound and good health in our society.

I want to thank the panel very much. Thank you all, gentlemen.  
[The prepared statements of Mr. Kolbas, Mr. Bongiovanni, Mr. Pettinga, Mr. Lyng, and Mr. Adams follow:]

STATEMENT OF DECEMBER 5, 1974  
BY  
JOHN M. KOLBAS  
VICE PRESIDENT-MANUFACTURING  
BRISTOL LABORATORIES  
DIVISION OF BRISTOL-MYERS COMPANY  
TO THE  
SENATE SUBCOMMITTEE ON HEALTH

My name is John M. Kolbas. I am Vice President-Manufacturing of Bristol Laboratories Division of Bristol-Myers Company. I am a chemical engineer with a BCHE degree from Ohio State. I have been with Bristol-Myers Company for 27 years.

Bristol-Myers Company is a diversified health care, pharmaceutical and consumer products company which markets more than 700 products in the United States, Canada and some 100 countries overseas through 10 major divisions. The company employs more than 26,000 people in this country and overseas.

Our Bristol Laboratories Division, headquartered in Syracuse, New York, produces four major classes of antibiotics--semisynthetic penicillins, aminoglycosides, tetracyclines and cephalosporins--and, further, markets a wide range of prescription medicines. Included in this product line is POLYCILLIN, a broad spectrum penicillin generically known as ampicillin.

We have been invited to comment on the current shortage of sodium ampicillin in the United States. Before going directly into the shortage, we would like to provide some background.

Ampicillin is an antibiotic which is used to treat a wide variety of infections. It is in the penicillin class of antibiotics but is effective over a wider spectrum of infections than most other penicillins, viz, upper respiratory tract infections of the ear, nose and throat; lower respiratory tract infections of the lungs and bronchi; infections of the intestinal tract; infections of the genitourinary tract; infections of the skin, generalized severe infections, such as meningitis and blood stream infections.

Because of its wide spectrum of effectiveness and relative safety, ampicillin is one of the most widely prescribed antibiotics. It is particularly useful in Hemophilus influenzae infections such as croup and meningitis. In addition, it is a useful agent in the treatment of acute infections of the kidney, infections of the gallbladder and destructive infections of the heart valves.

There are 6 different formulations of ampicillin---capsules, oral suspension, pediatric drops, chewable tablets, intramuscular suspension, and parenteral solution. Sodium

ampicillin is the parenteral form and is used only as an intramuscular or intravenous injection. In this form it is injected directly into the vein or muscle and, as such, it is used primarily in the hospital with limited usage in the physician's office.

Ampicillin in its various oral forms represents about 90% of the ampicillin used in the United States. Sodium ampicillin, the injectable form, accounts for the remaining 10%. The short supply situation pertains to the sodium ampicillin form only-----the oral forms have been available in normal quantities.

Market research services report that sodium ampicillin is sold in the United States by Bristol, American Home Products (Wyeth and Ayerst), Squibb, Beecham-Massengill, Lederle, Parke-Davis, Pfizer, SKF and Upjohn.

As far as we are aware, sodium ampicillin is made in the United States by Bristol, American Home Products, Beecham-Massengill and Squibb.

Since late summer of this year, there has been a shortage of sodium ampicillin in that inventories have been below traditional levels. A major factor in this shortage has been the closing of the sterile bulk processing area in our Syracuse plant site. To put this factor in perspective, it is necessary to understand something of the production process.

Penicillins are produced by fermentation in large fermenters and recovered as a solid by a series of extractions, concentrations, crystallizations, filtrations and drying operations. The dry penicillin is further processed to split off the 6-aminopenicillanic acid, which is recovered as dry crystalline powder.

The "6-APA" is then further reacted with specific chemicals to produce ampicillin, which is recovered in a dry crystalline state. The ampicillin is then converted to sodium ampicillin with the crystallization, filtration, drying, milling and blending all performed under aseptic conditions in a specially designed sterile bulk processing area.

The sterile bulk ampicillin is then filled aseptically into vials in another specially designed sterile filling area. Here, all glassware, closures and supplies are sterilized and the sterile bulk sodium ampicillin is filled into the vials. These vials are then labeled and packaged and transferred to quarantine storage awaiting Quality Control release and certification.

Injectable ampicillin is extremely difficult to produce due to the necessary sterile specifications. It is tested for sterility, as well as other characteristics of identity,

strength and purity, at Bristol and is then submitted to the Food and Drug Administration for certification. Only after the FDA's testing is satisfied and its certification is issued may the ampicillin be marketed. This entire process----from fermentation to marketing-----requires approximately 30 weeks. That part of the process from ampicillin through sodium ampicillin to the market requires approximately 12 weeks.

Bristol's sterile bulk production facility at Syracuse performed normally through May 1973. However, on May 27, 1973, a microorganism problem was detected in Bristol's own testing of sodium ampicillin produced in the facility. This was completely unexpected, but is always a possibility in any sterile antibiotic production, which is of course the reason for the rigid sterility testing requirements imposed on every batch produced. Bristol promptly undertook to determine the source of this problem, but without immediate success. None of the sodium ampicillin produced from the time this problem was encountered was ever submitted to FDA testing or released for sale.

By September 1973, the microorganism problem had still not been completely eliminated. It appeared that no satisfactory solution could be obtained without a complete renovation of the sterile bulk antibiotic production facility, the FDA having taken the position on September 14, 1973 that they could accept no more product for certification from the Syracuse bulk sterile manufacturing location. Bristol therefore closed the plant and commenced a complete renovation.

Thus, operations in the sterile bulk manufacturing area were discontinued in September of 1973 to begin renovation of the facility and installation of new equipment. At that time we anticipated a start-up in six months. However, delivery of stainless steel equipment and doors was extended because of tight supply of materials and labor problems at some of the suppliers. Plastic components also were late in delivery as were the materials for the air handling equipment. All of this resulted in a delay of production start-up in the new facility until August of 1974, almost 12 months after the discontinuance of operations.

At the time of the closing of the sterile bulk manufacturing facility we had close to normal inventories of sodium ampicillin. We were unable to build further inventories because of the force majeure nature of these events. Shortly after the shutdown, we contacted other manufacturers and purchased quantities of sodium ampicillin. These purchases, along with our estimate of six months to renovate the sterile bulk manufacturing area, led us to conclude that adequate supplies would be available through the spring of 1974.

It is useful for present purposes to understand how Bristol Laboratories distributes sodium ampicillin to its customers. Bristol Laboratories sells directly to hospitals

or through pharmaceutical wholesalers. Most hospitals purchase their requirements directly. In 1973, 98% of Bristol's sodium ampicillin sales were direct to hospitals. Thus, as the shortage of sodium ampicillin developed, wholesalers had only very small quantities on hand, since they receive little demand from hospitals. Because of this, available supplies were limited to inventories carried by the hospitals, our company and other suppliers.

Many hospitals maintain limited inventories of products because of inadequate storage facilities or financial restrictions that do not permit the purchase of large quantities. For these reasons, the shortage developed rapidly.

In the early fall of 1974 when the shortage became apparent, pharmacists and physicians brought to the attention of our representatives situations which were felt to be critical. These were cases where sodium ampicillin was required because it was the treating physician's choice in serious infections. (There are effective alternate drugs available. See Medical Letter of November 8, 1974.) We have made every effort to react to such situations as they occurred.

At all times we maintained an inventory of sodium ampicillin to use for cases brought to our attention by hospitals, pharmacists or physicians.

Bristol's representatives also played a part in responding to shortages at hospitals within their territories by borrowing from one hospital to supply another with a more critical need. This happened frequently.

We also attempted to make the best use of all available dosage strengths of sodium ampicillin. On occasion we did not have available the size ordered but would recommend an alternative that met with the hospital's approval.

We are now processing sodium ampicillin at a level above the pre-shutdown period and plan to continue to do so until adequate inventory levels are established and demand is stabilized. It is now estimated that ample inventories will be established by the second quarter of 1975. We believe normal inventories will be achieved even more rapidly if hoarding does not take place.

To sum up, the basic cause of the sodium ampicillin shortage was the shutdown of the facility required in the manufacture. There has not been any shortage of the oral forms of ampicillin.

We recognize that a concern of the Subcommittee is whether any general lessons can be learned from the injectable

sodium ampicillin shortage. It appears to us that this was a unique event, resulting in the closing down of a major production facility. Bristol believes that it successfully met the problems that were presented, and that they are now ended. The reduction in inventory experienced seems unlikely to occur again in the foreseeable future.

Statement before the  
Senate Health Subcommittee on Dec. 5, 1974  
by Michael Bongiovanni  
President, U.S. Pharmaceutical Co.,  
E. R. Squibb & Sons, Inc.

Squibb has been asked to comment on resource shortages within the pharmaceutical industry and on the current shortage of Injectable Ampicillin specifically. Since Ampicillin is a product which Squibb makes and sells, we shall limit our comments principally to this problem.

Ampicillin is a semi-synthetic penicillin, with a relatively broad spectrum of activity. It is widely used in both oral and injectable forms. There are ample supplies of the widely used oral forms, but there is currently a shortage of the injectable form.

Ampicillin has been used by physicians for its breadth of activity, which includes many common infecting bacteria. Further, it is well tolerated and absorbed when given by mouth or parenterally. For these reasons it is convenient to use clinically.

However, within its spectrum of activity, there is no pathogen which is susceptible only to Ampicillin. There are other antibacterial agents which are equally effective to, or more effective than, Ampicillin against pathogens within the spectrum of activity.

These other agents have a different spectrum of activity from Ampicillin but all of them overlap Ampicillin at various points in the Ampicillin spectrum of activity. For example, by choosing carefully among the sulfonamides, the

cephalosporins, the tetracyclines, the erythromycins, the aminoglycosides (kanamycin, gentamycin, streptomycin), chloramphenicol and penicillin G, the clinical usefulness and intensity of activity of Ampicillin can be duplicated or exceeded.

In short, Ampicillin is an important choice to physicians for antibacterial therapy. But there is no disease for which it alone is specific. When used judiciously, there are highly effective alternatives. In fact, there are circumstances when some of the alternatives to Ampicillin exceed the intensity of its activity within its spectrum.

A review of published data on the Injectable Ampicillin market for calendar 1973 indicates that Bristol Laboratories held almost 60% of the market. Wyeth Laboratories held 23% while we at Squibb held 6%. Beecham-Massingill Pharmaceuticals followed with 4%; Ayerst Laboratories with 3% and Parke Davis & Company with 2.5%.

In early 1974, with no foreknowledge on the part of Squibb, Bristol ceased selling Injectable Ampicillin. Since Bristol had some 60% of the market, its action created the present shortage.

We at Squibb have reacted successfully to shortages before. Injectable Ampicillin, however, is difficult to make. Its manufacture requires highly specialized facilities. Squibb was at that time utilizing these facilities virtually 100%, leaving no excess capacity. With this type of drug, it is difficult to expand capacity significantly - quickly.

We did not seriously consider building a new facility - an extremely costly eighteen to twenty-four month undertaking - since we judged the shortage to be temporary.

We could, and did, shift some of our production facility from the manufacture of Injectable Penicillin to Ampicillin, but we wanted to be careful not to increase Ampicillin production at the expense of creating a shortage in other areas, particularly so when, as we have seen, other drugs can so often fill the need.

Squibb's specific response to the shortage was that for the first ten months of 1974 we shipped 62% more Injectable Ampicillin than we did in 1973. This was substantially above our 1974 forecasts.

However, the efforts of Squibb and other Injectable Ampicillin manufacturers failed to fill the void left by Bristol's continued absence from the market. Many of Bristol's customers started ordering from Squibb and the other suppliers. In August of this year, Squibb reached the point where we could not fill all of our orders promptly. A "first in, first out" order system was put into operation. In October, as the shortage worsened, we limited shipments to a maximum of 500 grams per hospital. We will continue on this basis so long as Injectable Ampicillin remains in short supply. It is reported that Bristol is again making deliveries, so it is reasonable to assume that there will soon be sufficient supplies to meet all requirements.

In summary, we believe that the impact on the public health from the shortage of injectable Ampicillin is not as serious as some have believed, particularly in view of the ready availability of substitutes. This latter thought was the dominant factor in all of our thinking and planning. We believe that the pharmaceutical industry has reacted in a sensible and responsible manner to overcome the problems posed by Bristol's temporary inability to supply the product.

Obviously, shortages of raw materials are an increasingly complex challenge. We have been faced for some time with shortages of petroleum derivatives and other materials which are vitally important to the manufacture of health-care products. To continue our production of these products, we have had to innovate to find alternate resources and to revise our manufacturing procedures. For instance, the shortage of acacia led to its partial elimination from some of our products through a process modification. We have switched from hard-to-get butanol to isobutanol in penicillin crystallization and through equipment changes we have reduced our consumption of acetone by over half a million liters per year.

Other items, like sugar, are now being watched carefully since Squibb uses 20-million pounds of sugar a year in its pharmaceutical operations.

Resource shortages are vital problems for the pharmaceutical industry - an area to which we continue to devote our fullest efforts.

I'd like to thank you for allowing me the opportunity to discuss Squibb's reaction to the Injectable Ampicillin shortage and to the natural resource shortage.

STATEMENT BY CORNELIUS W. PETTINGA, Ph.D.,  
EXECUTIVE VICE-PRESIDENT, ELI LILLY AND COMPANY,  
BEFORE THE SENATE HEALTH SUB-COMMITTEE  
AND THE SENATE COMMITTEE  
ON ADMINISTRATIVE PRACTICE AND PROCEDURE  
IN WASHINGTON, D.C., DECEMBER 5, 1974

Mr. Chairman and Members of the Committee:

My name is Cornelius W. Pettinga. I have been an employee of Eli Lilly and Company for more than 25 years and at the present time have the responsibility of executive vice-president.

We are pleased to be able to testify at these hearings today, which are examining the availability of pharmaceutical products in this country today. We hope that we can offer some useful insights into the balance of supply and demand. There is a growing demand for prescription drugs in the United States today, and we will spend some time discussing the way in which our company plans for and meets this increasing demand.

In addition, we will suggest an approach for improving the present process of voluntary industry-government communication and cooperative action to assure adequate supplies of medically strategic materials.

However, before discussing these general subjects, I would like to respond to the committee's request to make some general comments about heparin. The essence of this situation has been covered in considerable detail by other presentations today. Eli Lilly and Company plays a very minor part in the supply of heparin to the United States market. Therefore, our ability to supply substantial information about the availability of heparin is more limited than that of some other companies. However, our experience leads us to the following conclusions:

- The use of heparin is increasing, mainly because of the growth of the use of kidney dialysis and open-heart surgery techniques.
- The collection of hog mucosa and the supply of heparin are not without problems. However, appropriate action by pharmaceutical manufacturers, meat packers, and the F. D. A. is dealing with the situation constructively and positively.
- The outlook for future supplies of heparin is improving, given the fact it will require--and receive--special attention and effort. This work has already started. At the request of the F. D. A., a meeting of representatives

of organizations involved in the manufacture, distribution, and eventual use of heparin was held here in Washington on November 13. Its purpose was to explore ways of assuring future supplies.

- Our production of this product is increasing, but this will have little impact on the overall supply situation because, as mentioned earlier, our role is a very minor one.

Throughout the discussions of the current heparin situation, we have been impressed by the overall effectiveness of the information feedback system in operation between health professionals, pharmaceutical manufacturers, the meat packing industry, and the government.

For example, the meeting arranged by the F. D. A. and the U. S. D. A. on November 13 is a good demonstration that voluntary, constructive cooperation among interested parties can and does work in the public interest to assure adequate supplies of life-saving drugs.

A broader purpose of these hearings is to examine the question of availability of prescription drugs vital to the health of the American public. The question is an important one. People in this country rightly expect drugs to be available to them when needed. Pharmaceutical

companies, including Lilly, wholesale distributors, and pharmacies have the responsibility to supply these needs.

At this point, let me make it clear, Mr. Chairman, that I am speaking only on behalf of Eli Lilly and Company. It seems reasonable, however, that the experiences cited are not inconsistent with those of other leading pharmaceutical manufacturers.

There are several essential factors in making our pharmaceutical products readily available to those who need them.

1. Correctly anticipating the needs from one to three years, or even more, in advance.
2. Having necessary raw materials, energy sources, and packaging components available in the right place at the right time.
3. Having the facilities and trained personnel to produce needed supplies.
4. Using a distribution system that puts drugs at the disposal of 7,000 hospitals and 250,000 practicing physicians within hours.

Over the last ten years, the use of prescription medicines in this country has grown at a sizeable, but fairly steady and predictable, rate--something on the order of 6 percent a year. Thus, total usage has increased by 80 percent in the last decade, as measured by the number of prescriptions written.

This increase is a function of many factors. They include:

- The number of physicians has increased by 27 percent.
- The number of patient visits to physicians' offices has increased by 44 percent.
- The number of patients treated in hospitals has likewise increased by 26 percent.
- Advances in medicine have required more drug usage.
- Major drug discoveries have created chemotherapeutic treatment for diseases for which palliative drugs were formerly used. In addition, some chronic diseases are now being treated with long-term drug therapy which was not available earlier. Such diseases as arthritis, mental illness, hypertension, serious bacterial infections, and some forms of cancer are being treated by recent drug discoveries.

In general then, the use of drugs has increased because the means are at hand to treat a growing population with more effective therapeutic agents. No matter how exhaustive the research, no one in our business can say with certainty how medical practitioners will evaluate and use a new drug. Not too many years ago, we at Lilly committed \$40 million to building a new plant for one type of product several months before we had developed large-scale production techniques and nearly two years before the product was approved by the F. D. A. for marketing. My point is that anticipating demand also requires the willingness and ability to take action, including major financial risks.

At Lilly, we market over 700 pharmaceutical products. Once we arrive at a forecast, more than one year in advance, for each of these products and each package size, we then plan the usage of our production facilities to manufacture needed quantities at needed times.

Our planning system uses both historical data and market forecasts, taking into account trends in volume. It also includes seasonal demands for certain products. The system allows us to develop projected needs on a short-term basis as well as long-range forecasts for facilities, employees, raw materials, and packaging.

The final step in the process is the distribution system, whereby needed medicines are available to all pharmacies in this country, and through them to millions of patients.

To ensure adequate distribution, we must continually evaluate population trends by geographical areas, the size of pharmaceutical markets, and the number of retail pharmacies and hospitals.

Through our wholesale distributors, Lilly products are delivered to more than 50,000 retail pharmacies and 7,000 hospitals scattered throughout the country. These medicines are available, in fact, in virtually every county of the United States. Our wholesalers keep an average of about one month's supply of our products on hand. In addition, all pharmacies carry inventories on their shelves.

In order to strengthen and speed up our product delivery system, we have constructed four regional centers--in Indianapolis, Fresno, Dallas, and Atlanta--which serve our wholesale distributors on a regional basis. A fifth center is now being built at Enfield, Connecticut.

I would like to cite one example to show how this extensive planning, production, and distribution system works. It involves two drugs, Velban<sup>®</sup> and Oncovin<sup>®</sup>, which are used in the treatment of certain

forms of cancer. Both products are derived from Vinca Rosea, the periwinkle plant.

In order to assure continued and adequate supplies of these drugs, Lilly takes careful measures to purchase and store large quantities of the raw materials. The Vinca Rosea plant is not grown in the United States in commercial quantities, although experiments in cultivation are under way in this country. Present results indicate that we may be able to use these supplies as future raw materials for our Vinca alkaloids. Historically, we have purchased our supplies from Madagascar and Mozambique. In Indianapolis, we have a two-year supply of Vinca leaves, in addition to a 14-month inventory of the drugs in finished form.

Production planning for these medicines is complex because manufacturing time covers a span of 14 months. Very large amounts of the Vinca leaves are needed in production. Fifteen tons are used to produce one ounce of Oncovin<sup>®</sup>--more raw materials than for the production of any other medicine derived from a plant source.

We believe that our inventories and planning system are designed to provide a continuing supply of these anti-cancer agents, which have always been available when and where they were needed.

Essential to manufacturing, of course, are raw materials. We depend heavily on petrochemicals, natural products from agriculture and animals, and basic sources of energy.

Petrochemicals, derived from natural gas and crude oil, are critical to virtually every product manufactured by our company. Any disruption in our supplies of these raw materials would materially affect our ability to supply the drugs we manufacture to the American public.

Over two years ago, we foresaw problems in the supply of petrochemicals, and we set up special groups to assess our requirements and take action to secure necessary materials.

We intensified our activities to broaden our purchasing base, to prepare alternative manufacturing processes, and to improve product yields.

One of the petrochemicals in short supply was benzene, used as a solvent both in the isolation of natural products and for organic synthetic reactions.

- The original 1974 requirements were: 3,700,000 liters
- Actual 1974 needs are: 2,200,000 liters
- 1975 estimated requirements are: 1,000,000 liters

How did we accomplish these reductions? Essentially, through the elimination of benzene from one particular process and better recovery and recycling techniques. Similar conservation steps were successfully taken with other solvents that we utilize.

Even during the very critical period of petrochemical shortages from mid-1973 through mid-1974, Lilly products continued to be available to the consumer.

I don't wish to belabor what may appear to be elementary, but supplies of energy are vital to our industry, as all others. Without energy, we cannot synthesize drugs, we cannot ferment antibiotics, and we cannot run production lines. Without energy available to our suppliers, we cannot purchase from them the glassware, bottles, stoppers, and all the extensive packaging materials needed by a major drug manufacturer. To ship our merchandise, we need transportation throughout the country, and this is dependent on fuel.

The continued availability of raw materials, petrochemicals, and energy is essential to assuring plentiful supplies of drug products in the future. Any future government energy program which includes an allocation system must surely make adequate allocation to this sector.

In summary, I have attempted to outline the complex set of factors involved in this vital question of the supply of medicines to the

American public--future demand for products, availability of facilities and technical personnel, raw material supplies, actual production, and distribution.

As far as Eli Lilly and Company is concerned, I believe that the record speaks for itself. We fill immediately, without delay, more than 99 percent of the orders that we receive; and we have had no emergency requests in recent years that we have been unable to fill. To the best of our knowledge, no patient has been deprived of a Lilly life-sustaining drug because of a shortage.

While we continue to have problems with a number of materials from time to time, these problems have been manageable and have not resulted in a shortage of finished pharmaceuticals. Unless unforeseen events drastically change the situation, we believe the supply of raw materials will continue to support production of adequate quantities of critical pharmaceuticals.

Mr. Chairman, in my opening remarks I indicated that we would suggest an approach to further improve the already-effective process by which we anticipate and supply the growing needs for essential prescription medicines. Our proposal is based upon many years of experience in making sure that our prescription drugs are available

when needed and are used properly and only when needed. We believe this requires a process that is essentially educative and communicative. The physician, pharmacist, patient, and pharmaceutical company must first acquire appropriate information. Each must then fully and accurately communicate relevant information to the other. In many regards, the information feedback regarding heparin is encouraging evidence that this information process is working well.

However, these hearings have identified a need to further improve an already-effective system which is working well in a vast majority of cases. Our proposal is to build upon this system in the following ways:

1. We recommend that a representative group of participants from the pharmaceutical industry, health professions, and government be assembled as a task force to examine the broad question of raw material availability to assure adequate supplies of medically strategic materials. We believe that the nature of the problem, the complexities of multiple-supply sources, and the potential implications of government intervention and a generally effective supply system are far too significant to allow for hastily conceived proposals at this time. Rather, we

recommend that thoughtful study be given before any proposals are made and implemented regarding overall supply assurance.

2. Members of the industry and health professional organizations should, and I am confident will, consider it an essential responsibility to voluntarily alert suppliers, other health professionals, and the F. D. A. when situations are observed which have the potential for creating significant shortages in medically strategic materials. Such situations might include:

- a) Cut-off of our material supply by a foreign country.
- b) Breakdown of production facilities.

3. While our concept is admittedly general at this time, Eli Lilly and Company would be happy to work with other health organizations, government agencies, and your committee in order to develop a more specific proposal. It is essential, we believe, that any proposal be based upon the current system of

voluntary cooperation and basic responsibility among the various sectors of the health care industry and those government agencies involved with it.

The safeguards by which an adequate supply of medicine is furnished the American public are as intricate as they are vital. They require continuous monitoring and timely steps to assure the following complex set of factors are adequately managed:

- the future demand for products;
  - the availability of facilities and technical personnel;
  - raw material supplies;
  - actual production to quality standards;
- and
- effective distribution.

If there are any questions, Mr. Chairman, I would be pleased to try to answer them.

# # #

STATEMENT OF RICHARD LYNG  
President, American Meat Institute

presented to the  
Senate Health Subcommittee  
and the  
Senate Subcommittee on Administrative Practice and Procedure  
December 5, 1974

My name is Richard Lyng. I am President of the American Meat Institute in Washington, D. C. The Institute is the national trade association of the meat packing industry. Our membership is comprised of meat packers and processors doing business in all 50 states, as well as in international trade. We have, in addition, associate members who supply goods and services to our industry.

We are grateful for the opportunity to participate in this hearing on the current supply-demand situation of the anticoagulant drug heparin.

For hundreds of years, meat animals have been a source of by-products, such as hides and skins, gelatin and glue, natural casings, bone meal, and edible and inedible fats. These by-products have, in turn, been the raw materials for such consumer products as shoes, soaps, bone china, and animal and poultry feed. One of the least appreciated aspects of the meat packing industry is the supplying of raw materials for pharmaceuticals.

Many drugs, in addition to heparin, are made from animal sources. Beef and pork pancreas are both used in the production of insulin. Extracts are prepared from the parathyroid, pituitary, and thymus glands. Livers are used for various extracts in treating anemia and as an additive to vitamin preparations. Bones from the breastbone of young cattle are used in facial surgery, and adrenal glands are used for the production

of epinephrine and adrenal cortex extract. These are only a few of the many products from animals which make a vital contribution to human health.

It is our understanding that the anticoagulant drug heparin is prepared from a raw material called mucosa. Mucosa is removed from the small intestines of swine as a by-product in the preparation of natural sausage casings. Beef lungs are another source of the raw material for heparin, but pork intestines are the dominant source.

Two factors affect the available supply of mucosa. The first is the total supply of hogs. The following table shows the total commercial hog slaughter since 1970:

Total Commercial Hog Slaughter	
Year	In Thousands
1970	85,817
1971	94,438
1972	84,707
1973	76,795
1974	*82,100

\* AMI estimate

Source: Statistical Bulletin 522-ERS, USDA

Estimates of hog slaughter for 1975 should be available from USDA within a week. We anticipate that slaughter in 1975 will be down quite sharply.

The second major supply factor has been the growth of synthetic casings which have moved into a position of heavy usage in sausage manufacture. As a result of this, there has not been significant growth in the natural casing industry.

Others more familiar with the usage of heparin should discuss the demand for this important drug. The question for us to try to answer seems to be whether or not the supply of mucosa will be satisfactory to provide an adequate supply of heparin in the future.

Unfortunately, we are unable to completely answer this question because statistics are not available to us on either the total production of mucosa or the rate of increased usage of heparin. We can say with a fair degree of certainty that mucosa is not being saved in a large number of swine slaughtering operations. The market value of mucosa alone is too low to justify the labor cost of saving it. The available supply of mucosa, then, depends upon the demand for natural casings.

It is our estimate that mucosa is being saved from approximately one-third of the swine being commercially slaughtered. Theoretically, the total supply of mucosa could be tripled if all swine slaughtering plants were to begin to process for mucosa.

In order to increase the supply, mucosa would have to become the primary by-product rather than the secondary by-product of natural casings. This would mean a higher price for mucosa to give packers the necessary income to justify not only the cost of retaining the mucosa, but also a sufficient return to undertake a labor-intensive operation which also requires considerable capital investment. Furthermore, the packer would only be able to justify the investment required if he had some assurance from pharmaceutical firms that there would be a relatively long-term market for the product so that he would have a chance to at least recoup his investment and that he would not be faced with obsolescence at an early date. The fear of an available synthetic derivative within two years would stifle any capital investment in mucosa recapture.

To the packer the present value of mucosa is low. Here is an example. On November 30, 1974 a typical market weight hog had a value to the packer of \$89.19.

The hams from that hog could be sold for \$25.92. The belly, used for bacon, could be sold for \$14.64. The loins could be sold for \$20.16. The average yield of mucosa from that hog would be one and a half pounds, and the average price would be no more than 8¢ per pound. The gross return for mucosa from a single market hog would be 12.0¢. The gross return from the sale of small intestines as natural sausage casings would be approximately 45¢ or four times as much as the mucosa. Both products together represent approximately one-half of one percent of the wholesale value of an average market hog.

The meat packing industry has long understood that it has a special responsibility to the public to take advantage of the best possible use of every part of the meat producing animal it processes. We are concerned about the human benefits to be derived from all animal by-products. Our industry has the ability to provide for increased supplies of heparin from mucosa. If the demand is sufficient the meat packing industry will respond as it has in the past. We stand willing to cooperate with the pharmaceutical industry in improving the efficiencies of salvaging this essential by-product.

STATEMENT

BY

CHARLES R. ADAMS

VICE PRESIDENT & GENERAL MANAGER

RIKER LABORATORIES, INC.

SUBSIDIARY OF THE 3M COMPANY

BEFORE

THE

SUBCOMMITTEE ON HEALTH

SENATE COMMITTEE ON LABOR AND PUBLIC WELFARE

DECEMBER 5, 1974

Statement of Charles R. Adams, Vice President and General Manager  
Riker Laboratories, Inc.  
Subsidiary of the 3M Company

Subcommittee on Health  
Senate Committee on Labor and Public Welfare

December 5, 1974

Mr. Chairman and Members of the Committee:

I am Charles R. Adams Vice President and General Manager of Riker Laboratories, Inc., a subsidiary of the 3M Company. I am accompanied today by Mr. James L. Madison, Heparin Market Specialist, and Mr. Gary F. Lyons, Division Attorney. Riker is a manufacturer of a variety of ethical pharmaceutical drug products. One particular product of Riker's manufacture is Sodium Heparin Injection, U.S.P. Aqueous (Lipo-Hepin), an anticoagulant medication which is critical in the treatment of several life threatening conditions, and for which there is no known suitable substitute. We appreciate this opportunity to bring to your attention the facts, as we know them, concerning the current critical shortage of this important drug product.

We appreciate and understand the concern of this committee and many others, and we want to assure you that we and other manufacturers are successfully making every effort to see that no patient in need of the anticoagulant activity of heparin will be denied its use. Although we have not been able to meet the demand for heparin, and will not be able to do so for some months to come, we do feel we have been able to meet the critical need. To our knowledge there have been no reports of patients being denied heparin when the use of this anticoagulant was critical.

Mr. Chairman, in order that all may have a more complete understanding of the current situation, my statement will cover four major areas of concern. First, I wish to speak to some of the more important reasons for the current short supply of heparin.

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Second, we will discuss the total approach we have taken to date to help alleviate this problem. Third, we will give our best estimate as to what we see for the future, and discuss our forecasts for meeting future needs for heparin. We believe these assessments are fairly representative of the activities of most manufacturers of heparin.

Some of the major factors that have contributed to the heparin shortage are:

A. The most important factor has been the vastly increased medical uses of heparin. Primarily these are:

- 1) A tremendous increase in the number of kidney patients undergoing hemodialysis treatment.
- 2) An increase in the number of open heart surgeries.
- 3) The usage of heparin prophylactically to prevent post surgical deep vein thrombosis.

So that the committee might have a better appreciation of the impact these three medical uses have had on the demand for heparin the following information is of importance:

- 1) It is estimated that the number of kidney patients undergoing hemodialysis has doubled in the past 11 months. The latest estimate is that over 14,000 Americans undergo hemodialysis treatments two to three times each week. Each patient requires up to 30,000 units of heparin per treatment. The increased demand resulting from this one medical usage is more than 30 billion units of heparin annually.
- 2) Open heart surgery figures for 1974 are not currently available, but most who are knowledgeable on this subject state that there has been a dramatic increase in the number of open heart surgeries performed.

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We are informed that the minimum heparin requirement for each of these patients is twenty 10 milliliter vials containing 10,000 units of heparin per vial, or 200,000 units of heparin per surgery. Through November we have experienced a demand of over twice last year's for the same period of time for this particular size and concentration of heparin.

- 3) The relatively new and less critical usage of heparin prophylactically to prevent post-surgical deep vein thrombosis is just beginning. However, it has had and will have a dramatic impact on heparin needs in the future. Some authorities have recommended that all surgical cases should receive 5,000 units, two times each day, 1 to 2 days prior to surgery and 7 to 12 days after surgery.
- B. Another factor in the current shortage has been the stockpiling by some hospitals which has resulted in a maldistribution of heparin. This problem has continued to increase and is now evidenced by what we see as "panic" ordering of quantities which are sometimes double actual needs. This has been determined through discussions with hospitals requesting unusually large quantities of heparin as compared to past ordering.
- C. Another major factor and the one most often discussed by the media is the problem relative to the collection of sizeable additional quantities of raw material.

We believe this problem, although critical in meeting future needs, has been overstated and misrepresented. One fact that should be of interest to the committee is that Riker is currently producing heparin at twice the rate of just a year ago and

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we expect to more than double this rate by mid 1975. In order to eliminate the confusion regarding what constitutes our raw materials, and what factors are involved in our collection of this material, I would like to spend a few minutes discussing this subject.

Our raw material is hog mucosa and comes from the intestinal lining of the small intestines of hogs. This material (mucosa) is a by-product of the collection of sausage casings. In other words, the amount of raw material (mucosa) available to process into heparin is dependent upon the amount of sausage casings collected, so the limiting factor until now has been the production of sausage casings and not the size of the hog slaughter, since in the United States casings are collected from only a relatively small portion of the total hog slaughter. Unless used in the production of heparin this material (mucosa) would be a waste product since to our knowledge it has no other use. We do not compete with pet food processors for this material as has been reported.

Virtually all of the material available as a by-product of sausage casing collection is currently being used or is contracted for. Therefore, additional raw materials must come from making mucosa a primary product instead of a waste product, or by-product, of sausage casing collection. This, of course, means much more raw material is available if it can be made economical for the meat packers to collect it. There are two obstacles then to the expansion of the available raw material, costs and the time to bring these new sources into production within the realities of the meat processing industry.

Riker's efforts to alleviate the critical heparin problem have been many and varied. This problem has been made more complex by two separate needs. We consider our first obligation a moral one in that we must do everything in our power to insure that any patient who needs heparin will not be denied its use. Second, because we see the expanded use of heparin increasing at a rapid rate, we must secure long-term sources

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of raw material to meet future needs.

To help meet the immediate needs of hospitals, and more important, the needs of their patients, Riker initiated a program of manufacturing primarily those vials of heparin required for hemodialysis and open heart surgery patients. We also established a system of maintaining a backup supply of heparin to handle emergency needs for those hospitals whose prior sources had failed them temporarily. Our medical service representatives have worked with hospitals in switching inventories from one hospital to another and advising in the establishment of conservation measures.

An exhaustive search throughout the United States to secure more raw materials was and is being conducted by Riker people expert in this area. Their success in this area is evidenced by the fact that our current production rate is double that of a year ago. All of these programs have been successful, but they have not been enough to place us ahead of the increasing demand for heparin.

Our programs to prepare us for the increased future needs have been to literally search the world for additional sources of raw material. We have made good progress in this area, but a positive impact from these sources cannot be reasonably expected for at least a year. We have also intensified research efforts in other areas of anticoagulation therapy and into the nature of heparin itself.

We believe that everything that can be done has either been done, or is being done, and good progress is being made.

The trend is that of continued growth in the demand for heparin. We at Riker feel confident that the progress we have made in securing raw materials for immediate needs, as well as future needs, permit us to assure ~~this committee~~ that the critical heparin needs can and will be met. Our best estimates are that we will continue to experience a critical shortage

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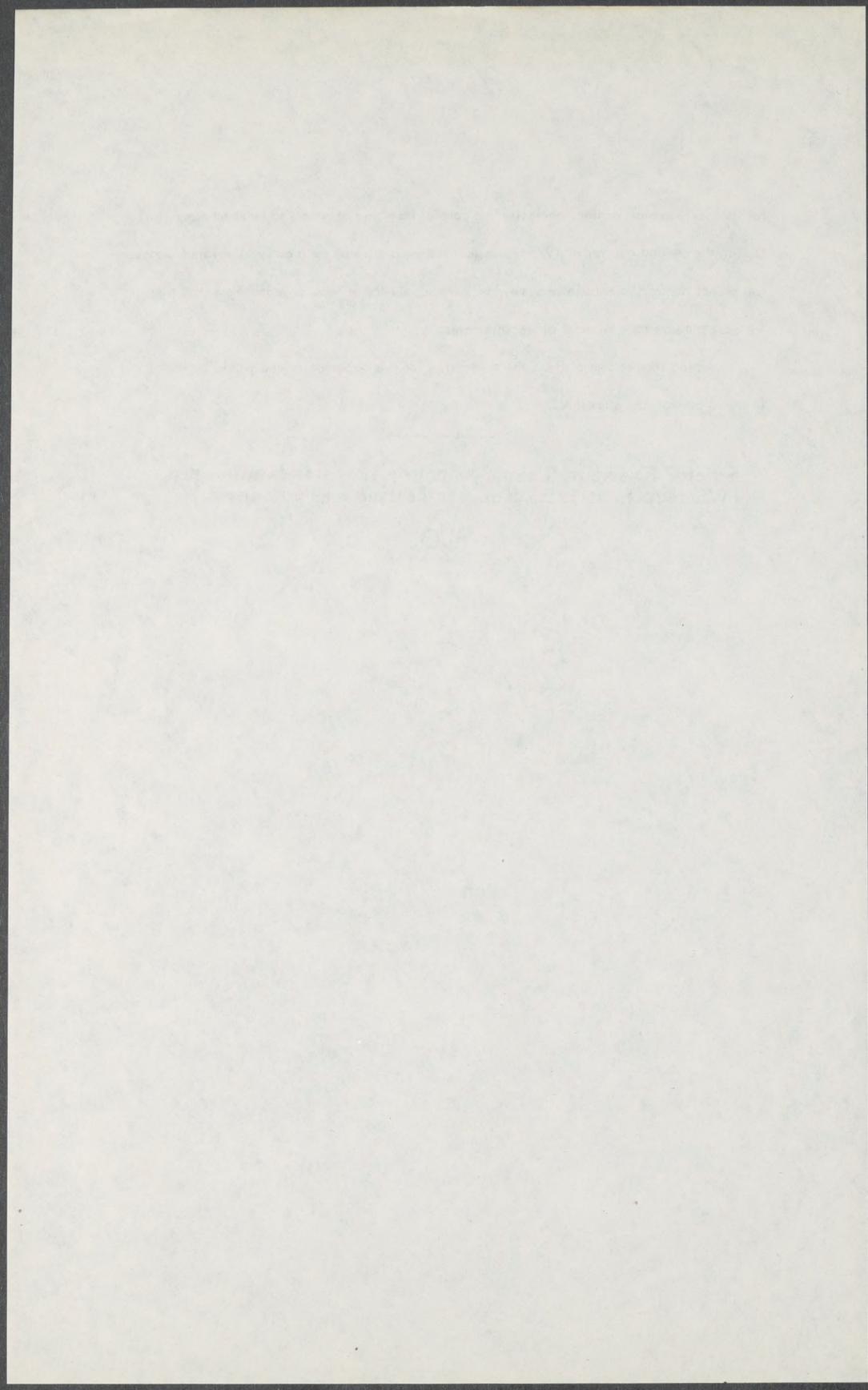
for the next several months, necessitating careful handling of orders to meet emergencies. During the second quarter of 1975 we expect the problem will be greatly alleviated although we expect heparin to remain in somewhat short supply for at least a year. Past that time we expect to be able to meet all requirements.

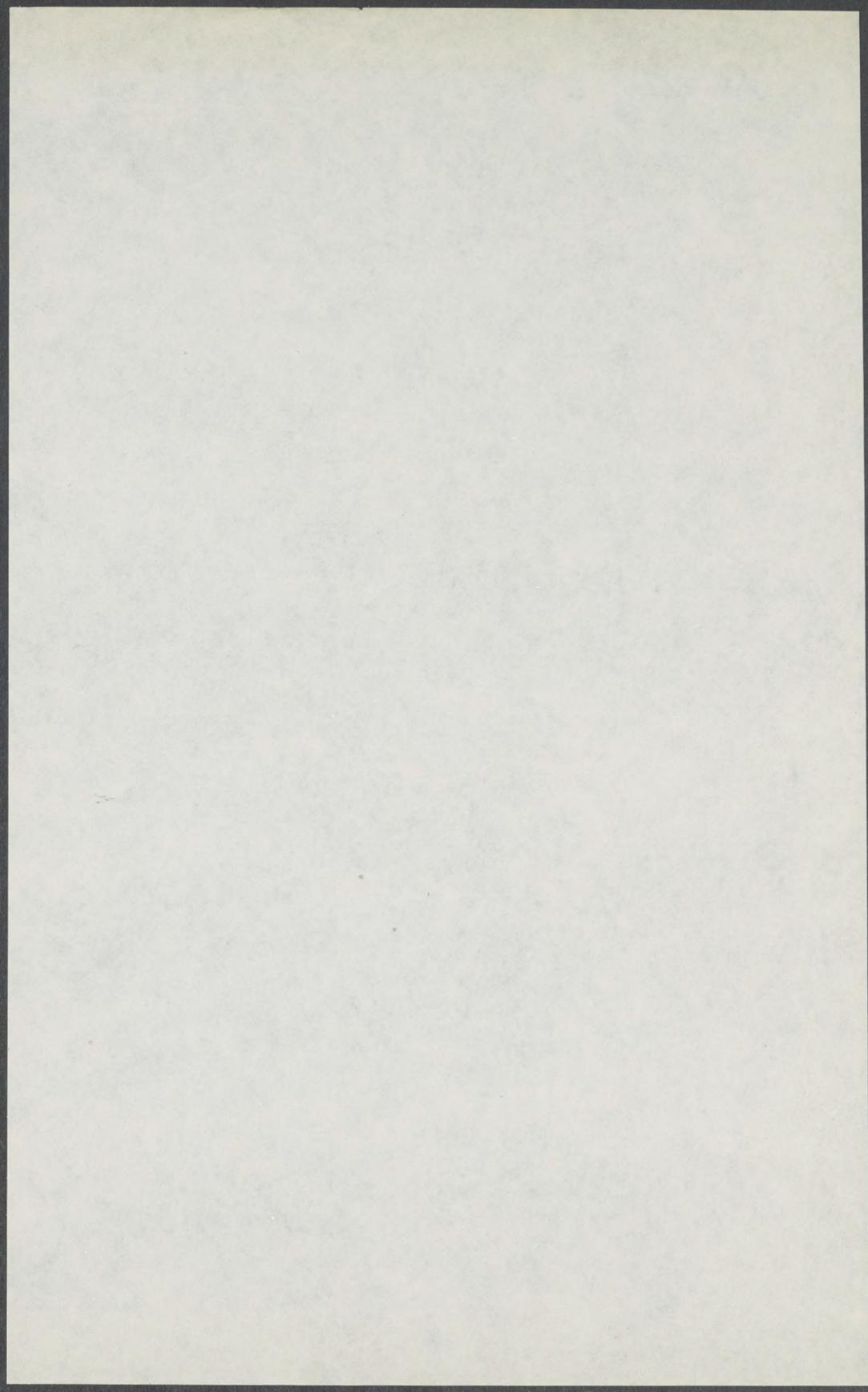
I would like to again thank the committee for this opportunity and would be happy to try to answer any questions.

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Senator KENNEDY. The subcommittee now stands adjourned.  
[Whereupon, at 12:25 p.m., the hearing was adjourned.]

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THE UNIVERSITY OF CHICAGO

DEPARTMENT OF CHEMISTRY

LABORATORY OF ORGANIC CHEMISTRY

REPORT OF THE DIRECTOR

FOR THE YEAR 1955

CHICAGO, ILLINOIS