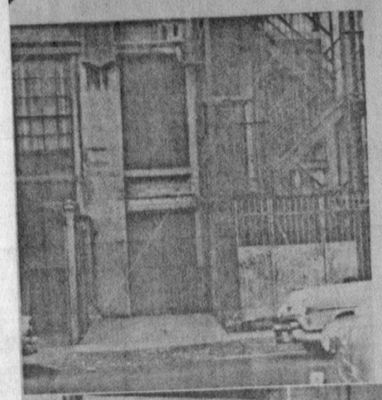
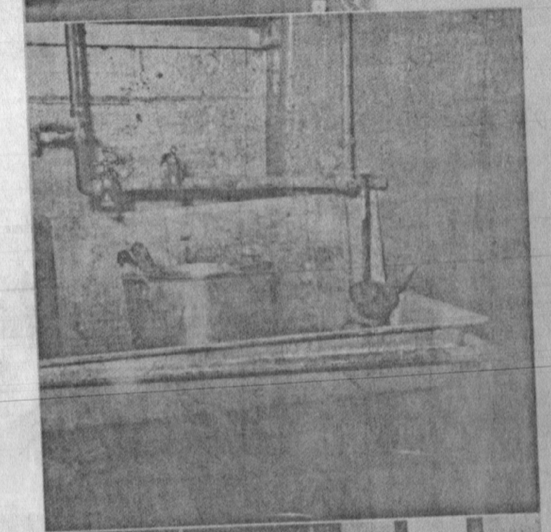
Journal of the American Pharmaceutical Association, Vol. 21, No. 8, pp. 470-471, August 1960

EXHIBIT A

adulteration, misbranding and illicit drug traffic



Taken shortly after the General Pharmacal Company was padlocked and its operators arrested, these pictures show the conditions under which drugs were being manufactured. The quotations used with each picture are taken from the 1959 catalogue issued by the company. At the left is the elevator entrance to the firm.



"All formulations kept strictly confidential . . . Products liability insurance carried."

"The C.F. number assigned to your formula assures you of a uniform product every time we make it."

Imagine—if you can—pharmaceutical houses using the following procedures in manufacturing drugs for the protection of public health.

Imagine enterprising men renting the top floors of a condemned building (away from the public eye), furnishing the area with tableting presses and producing a few drugs by generic name.

But, in addition to these drugs, picture these men producing many other drug articles. Their idea is to make them look exactly like items manufactured by reputable firms.

If you can project your imagination far enough you will realize that the least of this organization's worries are sanitary conditions, quality controls or actual content of the resulting bogus products. Then picture the hiring of "jobbers" to sell these products at "discount" priced repackaged samples.

An important element of this operation is a manually operated elevator. This can be easily lowered to admit friends to the field of operation. (If someone looks unfriendly—the elevator stays where it is.)

This whole fantastic scheme actually worked (reaping a reported $50,000 monthly) in New Jersey. Presumably no state drug inspector could possibly gain entrance.

But one day in June, the nightmarish operation ended when New Jersey drug inspectors and representatives of firms whose drugs were being counterfeited watched their chance and managed to get on the elevator belonging to the General Pharmacal Company of Hoboken, New Jersey.

Access was achieved when a familiar individual rang for the elevator. When it reach ground floor, a host of detectives swarmed into the elevator.

The undoing of the scheme actually began several months ago when personnel of the New Jersey Bureau of Food and Drugs learned from complaints filed by reputable companies that counterfeit drug products were apparently emanating from a source in New Jersey and were appearing in New York, Missouri, Illinois, Florida and other parts of the United States. They bore the same name and trademark as the legitimate products but the ingredients were not identical.

Because the offense involved more than drug adulteration and misbranding, Roscoe P. Kandle, state commissioner of health, notified Attorney General David D. Furman. State police were assigned to investigate.

Investigators said New Jersey was chosen for the operation because the state does not require the licensing of wholesale drug manufacturers as many other states do.

"A drug manufacturer who has to get a license would have to live up to much more stringent requirements and he would expect periodic examinations of his premises," one official of the state said.

Companies whose products were being counterfeited were Ciba Pharmaceuticals Corporation, Schering Corporation, Warner-Chilcott, Wallace Laboratories, Merck Sharp and Dohme, Smith Kline and French, and Wyeth Laboratories.

These companies have made every effort to assure the public and pharmacy that drugs purchased through legitimate and reputable pharmacy channels in regular sealed packages are genuine products.

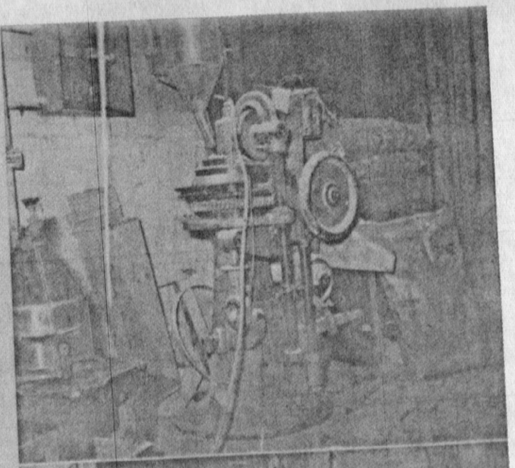
For example, Schering Corporation has sent a letter to pharmacists throughout the country explaining the situation. The Schering letter warns that "even though the General Pharmacal Company has been padlocked, there still may be substantial quantities of counterfeit tablets being peddled around the country in various bulk, unlabeled packages, often under the guise of 'repacked samples' or 'distress merchandise.'"

It asks pharmacists to help locate bootleg merchandise by contacting the corporation if anyone offers to sell unlabeled tablets as genuine products.

To this request APhA adds its own emphasis. It urges pharmacists to continue to protect the public health by exposing such illicit drug distribution methods.

The Association also reminds each pharmacist that regardless of his personal knowledge and intent, or responsibility of others, each pharmacist is independently liable under law for using any adulterated or misbranded product. This fact underscores the important professional task placed upon the pharmacist as purchasing agent for any pharmacy and its personnel. APhA urges the employment of only orthodox systems of drug procurement and cautions against "bargain" offerings. ■

"Uniform tablets from batch to batch. Laboratory controlled."



"We are equipped to handle large contract accounts. Your inquiries are cordially invited."

"All of our products are guaranteed to be in accordance with the Federal Food and Drug Act of 1906 or the Federal Food, Drug and Cosmetic Act of 1938; under the provisions of Section 404 or 405 of said Federal Food Drug and Cosmetic Act of 1938."

32-814 O - 74 (Face p. 10758)

REPORT TO THE CONGRESS

Problems In Obtaining And Enforcing Compliance With Good Manufacturing Practices For Drugs B-164031(2)

Food and Drug Administration
Department of Health, Education,
and Welfare

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

APPENDIX

HEARING DATES

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

WEDNESDAY, FEBRUARY 20, 1974

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

The subcommittee met, pursuant to notice, at 10:05 a.m., in room 6202, Dirksen Senate Office Building, Senator Gaylord Nelson [chairman of the subcommittee] presiding.

Present: Senator Nelson.

Also present: Chester H. Smith, Staff Director and General Counsel; Benjamin Gordon, Staff Economist; and John O. Adams, Minority Counsel.

Senator NELSON. The Subcommittee on Monopoly of the Senate Small Business Committee is today resuming its hearings on the efficiency, economy and rationality of the Federal agencies and departments in the procurement of drugs, as well as reimbursement under various programs of Government.

The subcommittee is particularly interested in finding ways in which competition can be promoted and the cost of drugs to Government can be reduced both in direct procurement of drugs and in reimbursement for drugs under medicare and medicaid. The witnesses have been asked to discuss: (1) efforts of Federal agencies to reduce the cost and to improve the procurement and supply of drugs in the Federal Government; (2) progress by Federal agencies in implementing the recommendations included in the Comptroller General's Report on Federal drug procurement dated December 6, 1973; (3) views of drug purchasing agencies concerning consolidation within the FDA of quality assurance activities relating to Federal procurement of drugs; (4) the efforts of the Federal agencies to: (a) promote the use of formularies and encourage the use of generic products, and (b) assure that only effective drugs are procured and used in Federal programs; (5) the relationship of FDA with other Government agencies in drug procurement and reimbursement; (6) the steps taken by the Food and Drug Administration to ensure a uniformly high quality for the Nation's drug supply.

Our witnesses today are Mr. Elmer Staats, Comptroller General of the United States and Dr. Alexander Schmidt, Commissioner of the Food and Drug Administration.

Mr. Staats, the Committee is very pleased to have you appear here today. We are well aware of the extensive work you and your agency have been doing in the field. We recognize it is a very valuable contribution to the problem that we are dealing with here.

Your statement will be printed in the record and you may present it however you desire. And would you identify, for the record, your associates so that the reporter will know who they are in the event they have some comment to make?[1]

STATEMENT OF HON. ELMER B. STAATS, COMPTROLLER GENERAL OF THE UNITED STATES GENERAL ACCOUNTING OFFICE, WASHINGTON, D.C., ACCOMPANIED BY GREGORY J. AHART, DIRECTOR, MANPOWER AND WELFARE DIVISION, GENERAL ACCOUNTING OFFICE; DEAN CROWTHER, DEPUTY DIRECTOR, MANPOWER AND WELFARE DIVISION; JAMES D. MARTIN, ASSOCIATE DIRECTOR, MANPOWER AND WELFARE DIVISION; AND PAUL SHNITZER, ASSOCIATE GENERAL COUNSEL, GENERAL ACCOUNTING OFFICE

Mr. STAATS. Thank you, Mr. Chairman. To my immediate right, Mr. Gregory Ahart, who is the Director of our Manpower and Welfare Division; to his right, Mr. Dean Crowther, who is Deputy Director of that Division; Mr. James Martin here to my immediate left is an Associate Director of that Division; and Mr. Paul Shnitzer, Associate General Counsel, of the GAO.

Mr. Chairman, in the interest of saving time for questions and for your next witness, I will try to summarize and paraphrase the statement which you have before you, and I will refer to it by page as we go along.

I believe we can cover the substance of the statement and speed up the process. We are going to be covering today in our testimony three subjects. One is our December 6th report on Federal procurement of drugs; second, the status of Federal efforts to promote the use of formularies and encourage the use of lower priced drugs, including generics; and third, the status of actions taken by the Federal agencies to assure that only effective drugs are procured.

On page 2, we point out that Federal expenditures and reimbursements for prescription drugs amounted to about $1.6 billion in fiscal year 1973, which is an increase of more than $44 million over the expenditures for 1972. And, more significantly, a $500 million increase since 1970.

This amount includes about $252 million in direct drug purchases by Federal agencies, and reimbursements of over $1.3 billion under federally sponsored health programs such as medicare and medicaid, which have increased some $430 million since 1970, thus accounting for more than 80 percent of the total increase. The increases in medicare and medicaid expenditures account for virtually all of the increases in the reimbursement programs.

Senator NELSON. What was that total increase?

[1] See information beginning at page 10497.

Mr. STAATS. These are figures since 1970.

Senator NELSON. What was the total?

Mr. STAATS. The total is $1.3 billion there—it is in my statement.

Senator NELSON. Yes, I see it. You said the increase was how much?

Mr. STAATS. This increase is about $430 million since 1970, thus it is about 80 percent of the total increase and virtually all of the increase in the reimbursement category is in the medicare and medicaid programs even though there are some other reimbursement programs, such as CHAMPUS. The increases indicated by going back to 1970 are much more significant than those indicated by the increases from 1972 to 1973.

Now if you turn to the next page, page 3, we point out here that about 84 percent of the total Federal expenditures for prescription drugs during fiscal year 1973 were indirect in that they consisted principally of the Federal share of drug costs provided to beneficiaries of health programs supported by the Government.

Medicare accounts for about $675 million, medicaid $605 million, the Federal employee health benefits program $41 million, and the CHAMPUS program $30 million.

We have a full table, Mr. Chairman, showing the increases in this program, both direct and indirect, beginning in 1969 and, if you agree, I would like to have that inserted in the record at this point. It just brings out the picture a little more clearly than I can in my summary here.

Senator NELSON. It will be printed in the record at this point.

[Testimony resumes at page 9926. The material referred to follows:]

ESTIMATED FEDERAL EXPENDITURES
FOR PRESCRIPTION DRUGS

	Fiscal year expenditures (in millions)				
	1969	1970	1971	1972	1973
TOTAL FEDERAL EXPENDITURES	$ 999.5	$1,065.9	$1,331.1	$1,527.9	$1,572.3
TOTAL DIRECT PURCHASE	203.2	177.3	268.7	275.0	252.0
Department of Defense Depot[1]	103.2	71.4	105.6	103.1	91.4
Veterans Administration Depot and Local	30.4	21.3	35.4	46.3	49.9
Federal Supply Schedule	57.4	60.4	75.2	77.0	78.2
Public Health Service[2]	12.2	6.4	18.3	20.0	13.6
Agency for International Development[3]	NA[4]	14.0	11.0	19.2	10.4
Small Federal Programs[5]	NA	1.5	21.6	7.2	8.5
Office of Economic Opportunity	NA	2.3	1.6	2.2	NA
TOTAL REIMBURSEMENT PROGRAMS[6]	796.3	888.6	1,062.4	1,252.9	1,320.3
Medicare, Part A	460.7	482.2	541.2	616.8	674.0
Medicaid, Institutional	131.0	154.2	202.6	257.6	264.8
Medicaid, Ambulatory	158.1	206.0	252.8	308.8	340.5
Federal Employees Health Benefits[7]	22.9	22.5	31.3	40.9	NA
CHAMPUS, Institutional	12.4	13.0	18.6	21.4	25.1
CHAMPUS, Ambulatory	2.8	3.6	3.8	4.7	6.1
VA Hometown Pharmacy	2.6	1.4	3.2	NA	4.1
OEO Vendor Program	2.4	2.4	0.6	NA	NA
Public Health Service	1.7	1.2	5.8	NA	2.5
Federal Employees Compensation	1.7	2.1	2.5	2.7	3.2

Sources: Estimates for fiscal years 1972 and 1973 were made using data supplied by individual departments and agencies responsible for the programs and activities listed above. Data for fiscal years 1969 through 1971 were obtained primarily from the Prescription Drug Data Summary published by the Department of Health, Education, and Welfare.

[1] Data concerning non-Federal Supply Schedule local procurements made by DOD activities data is not available. These local procurements may approximate 18 percent of depot procurements.

[2] Excludes data for St. Elizabeths Hospital, National Institutes of Health, and National Institutes of Mental Health. For fiscal year 1973, $6.2 million of the $12.0 million was procured for the Communicable Disease Center by the VA under special Federal Supply Schedule contracts but is not included in the $78.2 million procurements under Federal Supply Schedules.

[3] An undetermined amount of AID-furnished drugs are procured from DOD or VA depots.

[4] Not available.

[5] Includes expenditures for U.S. Bureau of Prisons, Peace Corps, Coast Guard, D.C. Government, Job Corps, and several other small programs. For fiscal year 1971 data includes expenditures for unspecified small Federal programs.

[6] Estimates for reimbursement programs include costs of drug dispensing.

[7] Amounts represent estimated expenditures for drugs in the Federal contribution to employee's health insurance premiums.

Mr. STAATS. Now on page 4 we point out, in the first full paragraph, that pending legislation which would increase Federal participation in health care activities, suggests that Federal expenditures for drugs may increase in the future, and perhaps very substantially.

During the first session of the 93rd Congress, numerous bills were introduced which dealt, in part, with drug purchases under the medicare program. Most of these bills included provisions to extend medicare to cover the costs of certain drugs to be dispensed to eligible recipients on an outpatient basis, and used to treat specified chronic illnesses.

The Social Security Administration estimates that such an extension of Medicare coverage would cost about $1.1 billion a year.

Now on the next page, we point out that several national health insurance proposals are currently under consideration. The passage, obviously, of a national health insurance plan would represent a major upward impact on Federal outlays for drugs.

Now, turning to our December 6th report, we discussed the effectiveness of Federal agencies' administration of programs and activities relating to the direct procurement and supply of drugs.

This matter has been a subject of interest since at least 1963 when Federal agencies began studying the possibility of a single agency having Government-wide responsibility for managing pharmaceuticals. In February 1971, the General Services Administration, and the Department of Defense, agreed to assign medical material to DSA—that is the Defense Supply Agency—for integrated management, but the assignment was deferred pending the outcome of a comprehensive study proposed by the OMB in June of 1971.

Now this study was started in January of 1972, just 2 years ago.

Senator NELSON. What was the outcome of the discussions involving the proposal to have all purchasing concentrated in just one agency?

Mr. STAATS. I come to that a little bit later, if that is all right. I believe it is covered.

As of December 1973, no final agreement had been reached as to whether a single manager for drugs would be established. Our report supports the need for coordinated action in procuring and supplying drugs.

In summary, we concluded that significant savings and other advantages could result from greater coordination and cooperation between the agencies in procuring drugs, such as consolidating requirements, making joint procurements, and reducing small-quantity local purchases by authorizing use by any Federal agency of any centralized Government supply source.

Second, there should be increased use of specifications for drug products to encourage greater competition and central management of drugs to reduce costs.

Third, better reporting of drugs bought locally and better use of related reports would improve selection of items for central management.

Fourth, responsibility for all quality assurance activities relative to Federal purchase of drugs should be assigned to the Food and Drug Administration.

Turning to page 7, to improve the direct procurement and supply of drugs by Federal agencies, we recommended that the OMB take the lead in developing policies and procedures, including consolidating requirements, to increase agency cooperation in buying drugs, and achieving substantial savings through large-volume buys. Field installations should be authorized to obtain their drug requirements from any centralized Government supply source.

The VA should develop specifications for all new drugs which it decides to manage centrally and centrally managed drugs, for which it currently has no specifications.

Third, the Department of Defense should revise its policy to ensure that drugs will be obtained centrally whenever savings would result.

Fourth, Defense and VA should develop specifications which would satisfy all Federal agencies' requirements.

Fifth, Defense should develop, for reporting local drug purchases, a uniform reporting system aimed at requiring all military activities with individual drug purchases exceeding specified criteria to report their purchases; and require centrally managed drugs purchased from other than a central manager to be reported.

Sixth, the VA should require that its central office supply service prepare lists of summary and exception data from the information reported; require local field stations to report their purchase data correctly and consistently; and see that all vendors report detailed sales data when required, by contracts.

Seventh, Defense and VA should consider using a standardized coding system, such as the National Drug Code, for identifying local purchases of drugs not having Federal stock numbers.

Eighth, Defense, HEW and VA should review the frequency and type of inspections required and the related changes needed to transfer to FDA of all quality assurance responsibilities pertaining to purchases of drugs by Federal agencies.

Mr. Chairman, this is a fairly long report, but it seems to us it might be useful to have it inserted in the record.

Senator NELSON. It will be received for the record.

Mr. STAATS. This is a very brief summary of that report.

On page 9 we point out that the OMB—and this gets to your question of a few minutes ago—in commenting on our final report, by letter dated January 14, 1974, stated that the study group had completed its report and had made recommendations which are currently under review by the principal agencies involved. The OMB stated also that the findings and recommendations of its study closely paralleled those of the GAO report.

Mr. GORDON. Are there any differences between your recommendations and the recommendations of the OMB report?

Mr. AHART. I think, Mr. Gordon, that the recommendations of their report would be somewhat more specific than ours, because they made an in-depth study of the various agencies concerned, and probably went much more deeply into it.

As the Comptroller General indicated, OMB has stated that the recommendations are parallel to ours and are in line with our objectives.

Mr. STAATS. In the next paragraph, we point out that the Defense Department also, in commenting on our report, indicated general agreement. In the last sentence of that paragraph, they are indicating that a clarifying policy adapting medical items for central procurement is expected to be released in about 60 days.

And, in the Veterans Administration's letter dated January 16, 1974, they also indicated general agreement with the report and indicating that its marketing centers and supply depots would accept orders from DOD field installations.

VA will initiate a control system with DOD to assure that drug specifications are either developed jointly or coordinated; and it is willing to rely on FDA to provide quality assurance for VA drug purchases, provided that FDA makes the necessary data available in a timely manner.

Now we point out here also that HEW likes the idea of a single agency plan for quality control, and it is indicated that the Food and Drug Administration is therefore currently developing an initial concept for that consolidated program, based on its assessment of quality assurance requirements.

Now, turning to page 11, we turn to the second topic of our testimony, dealing with reducing drug costs through the use of formularies, and encouraging the use of lower priced drugs, including generics.

The military medical regulations require that Pharmacy and Therapeutic Committees be appointed by the commanders of U.S. military hospitals.

Among the primary functions of the P. & T. Committees are the development and periodic review and revision of the hospitals' drug formularies. In making decisions concerning the addition or continuation of formulary items, the P. & T. Committees consider the relative costs of therapeutic alternatives.

In addition to the general use of formularies by the services, the Surgeons General and subordinate administrative levels issue monthly newsletters or special letters to health facilities highlighting comparative prices of drugs maintained in central inventories and encouraging the use of less expensive drugs when they are considered to be therapeutically equivalent to the more expensive items.

Prescriptions written by military physicians and filled in military hospitals for brand-name products may be filled with generic equivalent products except when the physicians specifically require that such substitutions not be made.

The DOD has not established regulations requiring the use of formularies in the CHAMPUS program, and has not encouraged the use of generic drug products for either the inpatient or outpatient portions of the CHAMPUS program.

The Veterans Administration requires that each of its medical facilities have a P. & T. Committee which develops and maintains

a drug formulary. This formulary generally consists of monographs on those products selected by the P. & T. Committees for use in the facility.

Generally, prescriptions will not be filled for drug items not included in the formulary. However, exceptions may be made with special permission.

These monographs include the nonproprietary names of the drug, therapeutic classification, dosage, and instructions regarding product usage. The VA has also instructed its physicians that generic identification of prescribed medications is preferred to the use of brand names.

The HEW agencies that provide direct patient care, such as the Indian Health and the Federal Health Program Services of the Public Health Service, require that all field installations be serviced by P. & T. Committees responsible for the development and maintenance of current formularies of accepted drugs.

The formularies are required to list drug items by their official generic, or nonproprietary names, and only formulary drugs are authorized for routine use by HEW installations providing direct patient care.

Among the items the P. & T. Committees are required to consider in developing their formularies are comparative efficacy of formulary drugs with other drugs intended for the same use, evaluation of the benefit/risk of formulary drugs, and cost effectiveness.

Under part A of the medicare program, drugs are paid for by the Social Security Administration, through fiscal intermediaries, as part of the eligible recipients' total hospital bills.

Under part B of the program, Federal coverage for physicians and related services are provided through organizations known as "carriers".

Coverage of drugs under part B is limited to those drugs which are commonly furnished in physicians offices and which cannot normally be self-administered.

The regulations for medicare state that in order for a drug to be covered under part A, it must represent a cost to the institution in rendering services to the beneficiary, and either be included or approved for inclusion in specified drug reference volumes or approved by a P. & T. Committee—or equivalent—for use in the participating hospital.

In order to be covered under part B, costs of eligible drugs, like those of other medical services, must be accepted by the carrier as reasonable and necessary.

Under this system, SSA generally is not provided detailed information concerning the specific drugs that are being prescribed under medicare. SSA advises that there are currently no regulations which encourage the use of generic drug products.

Under the medicaid program, which is administered by State agencies with Federal guidance and reimbursed in part by the Social and Rehabilitation Service, the use of formularies and generic products is optional.

The applicable Federal policy states that "where either is employed, there must be standards for quality, safety, and effectiveness, under the supervision of professional personnel."

Although SRS discusses the use of a formulary system as a means of reducing overall drug costs, the use of formularies is not required. Presently 20 States use some type of formulary.

SRS, in its Medical Assistance Manual, points out the arguments for and against the use of generic drugs, but does not emphasize their use.

Although the States generally accumulate data concerning the specific drugs being dispensed under the medicaid program, the data is not normally provided to SRS.

As you know, Secretary Weinberger recently announced that HEW will be publishing regulations for public comment which, if adopted, would limit drug reimbursements under programs administered by the Department to the lowest cost at which the drug is generally available, unless there is a demonstrated difference in therapeutic effect.

The reimbursement policy is intended to result in major savings in the cost of providing prescription drugs under medicare and medicaid. The announcement prompted the Chairman of the Senate Subcommittee on Health, Committee on Labor and Public Welfare, to hold another hearing on February 1, 1974, to provide representatives of the administration and the drug industry the opportunity to clarify their positions concerning this significant new HEW policy. To date, the proposed regulations have not been published.

Now, thirdly, and finally, we turn to the status of actions taken by the Federal agencies to assure that only effective drugs are procured with Federal funds.

During our last appearance before this subcommittee, we commented on actions taken by DOD, HEW and VA with respect to the FDA's pronouncements on drug efficacy. FDA has categorized drugs as "effective", "probably effective", "possibly effective", and "ineffective" for one or more therapeutic indications claimed on the drug's labeling.

Legal action was brought against FDA in an effort to expedite FDA's completion of its determinations of drug efficacy under the Drug Efficacy Study Implementation, which is known as DESI.

In October 1972, the Federal District Court for the District of Columbia ordered the FDA to meet specific target dates for various phases of DESI and to submit 6-month status reports to the court concerning its progress.

It required the FDA to make final determination on drug efficacy or to rule on drug sponsors request for hearings, by October 1976.

Senator NELSON. Let us see, who initiated the lawsuit? You say the Federal District Court ordered the FDA to do certain things? Who was the complainant?

Mr. STAATS. I will have to ask one of my colleagues, Mr. Chairman.

Mr. AHART. Mr. Chairman, the information I have is it was a

joint suit by the American Public Health Association and the National Council of Senior Citizens.

Senator NELSON. That was, I take it, to specifically implement the provisions of the 1962 amendment.

Mr. AHART. I think the thrust of the suit was to require FDA to speed up the effort and to require the publication of the National Academy of Sciences evaluational report on drug efficacy.

Senator NELSON. All right, thank you.

Mr. STAATS. As of January, 1974, FDA's initial ratings on all but one of the more than 4,000 drug products included in the study have been published in the Federal Register.

However, in accordance with the procedures of DESI, FDA has revised its ratings for specific drugs as new information is submitted by the drugs' sponsors.

We inquired into the status of Federal agency actions to insure that only effective drugs are purchased with Federal funds and noted that, in general, definitive actions taken have been limited to direct Federal health care programs.

We testified in May, 1972, that as of November 18, 1971, the Defense Medical Materiel Board had initiated action to stop further procurement and to eliminate from the supply system all items that FDA had then pronounced "ineffective" or "possibly effective." Also, the surgeons general of the military departments had emphasized through instructions to medical organizations the DOD policy on such drugs, which became effective January 21, 1971.

This policy provided that remaining stocks of "ineffective" drugs withdrawn from the market were to be destroyed or other appropriate action was to be taken to remove them from the inventory. For items categorized "ineffective," but awaiting final determination of FDA, further use of remaining stocks was suspended until the final status was announced by FDA. P. & T. committees were required to question all prescriptions for "possibly effective" items, but local procurement of such items could be made if no alternative means of therapy was available.

On June 11, 1973, DOD announced a revised policy which is a bit less stringent with respect to the use of "ineffective" and "possibly effective" drugs. According to DOD, the original policy was revised because the completion schedule for the DESI had been substantially extended from that originally anticipated and because some of the FDA's more recent drug classifications would be revised following only minor changes in labeling or formulation of certain widely-used items.

The revised policy provides that procurement of items classified by FDA as "ineffective" and ordered withdrawn from the market continues to be prohibited. However, for items which FDA classified as "ineffective" but has permitted to remain on the market pending final resolution of the items' classification, the policy permits the Defense Medical Materiel Board, in conjunction with the Surgeons General, to determine whether centrally-procured stocks are to be discontinued .

Additionally, the policy authorizes the services to make similar decisions concerning locally-procured drugs in this category or to delegate their authority to local P. & T. committees.

The policy also authorizes the procurement of "possibly effective" drugs when no alternative means of therapy is available and final determinations on their efficacy are expected to require a long period of time. However, both central and local procurements of these items are to be minimized to take into account the possibility that they may be finally determined by FDA to be "ineffective" and ordered removed from the market.

Shortly after June, 1973, the military departments included the revised policy in their instructions for field installations, together with up-to-date consolidated listings of FDA drug safety and effectiveness data for use by military medical personnel.

The CHAMPUS program places no restriction on the drugs that may be prescribed, and is not supplied detailed data concerning the specific drugs that are being paid for. Therefore, DOD could be paying for drugs under CHAMPUS which would not be procured for its direct care activities.

Since December, 1970, the VA's policy has continued to be that all "ineffective" drugs must be removed from VA hospitals except where special approval of the Central Office Executive Committee on Therapeutic Agents has been obtained. Also, VA's policy concerning "possibly effective" drugs continues to require that consideration be given to using an alternative product having a higher FDA effectiveness classification.

To strengthen the policy's implementation, the VA is furnishing a list of drugs ordered to be withdrawn from the market to the P. & T. committees at each VA facility which buys or dispenses drugs. Further, a current statement of VA policy on the use of drugs is now being developed by the Central Office Executive Committee on Therapeutic Agents for distribution to all VA facilities.

HEW's policy has been that Federal funds shall not be spent for "ineffective" drugs except under approved clinical research projects, or for "possibly effective" drugs except under similar projects or when alternative means of drug therapy are not available.

In October, 1971, HEW agencies involved in direct patient care were instructed to stop procurement and use of such drugs and to advise their contract physicians of the Department's policy. These instructions remain in effect.

I think I can skip over the next paragraph.

We sent a letter to the Administrator, SRS, in May, 1972, bringing the matter to his attention and asking him to advise us concerning SRS plans for implementing the Department's policy. In June, 1972, the Administrator told us that a draft of regulations implementing the Surgeon General's 1970 policy had been cleared in SRS and was being prepared for transmittal to the Secretary for publication as a proposed rule. The regulation was not published.

Now, we recently initiated a survey of the administration of the

medicaid drug program, and have already observed that States are continuing to pay for "ineffective" and "possibly effective" drugs.

For example, in 1 month, September 1973, three States paid an estimated $692,000 for such drugs. Also, we contacted officials of two additional States—which were included in our 1972 review—and were informed that these States had not changed their policy concerning payment for ineffective and possibly effective drugs and would not do so until SRS issues its final regulations concerning this matter.

Now, we have again brought this matter to the attention of HEW in a letter to the Secretary dated February 15, 1974, which we will be happy to have included in the record at this point.

Senator NELSON. We would like to have the letter for the record.

[Testimony resumes at page 9939. The material referred to follows:]

UNITED STATES GENERAL ACCOUNTING OFFICE
WASHINGTON, D.C. 20548

MANPOWER AND WELFARE
DIVISION

B-164031(2) FEB 15 1974

The Honorable
The Secretary of Health,
Education, and Welfare

Dear Mr. Secretary:

During our survey of the administration of the Medicaid drug program, we found that the three States included in the survey (California, Ohio, and Texas) were expending significant amounts of funds (portions of which are reimbursed by the Federal Government) for prescription drugs that have been declared ineffective or possibly effective by the Food and Drug Administration (FDA). The Department of Health, Education, and Welfare (HEW) has not issued regulations prohibiting the use of Federal funds for the purchase of ineffective and possibly effective drugs under the Medicaid program. We believe that HEW should expedite the issuance of such regulations.

BACKGROUND

The 1962 Amendments (P.L. 87-781) to the Federal Food, Drug and Cosmetic Act required that drugs be effective before they can be approved for marketing. Under these amendments, FDA began evaluating the effectiveness of all drugs that it had approved for marketing under a safety criteria in force before the amendments. After analysis by the National Academy of Sciences/National Research Council of the available data relating to the effectiveness of a drug, FDA publishes in the Federal Register a notice of its initial classification of the drug as being effective, probably effective, possibly effective, or ineffective.

If a drug is not classified as effective, a notice of an opportunity for a hearing is also published. If interested parties justify, on the basis of new evidence, the need for a hearing, one is held. After the hearings FDA publishes its final determination of the effectiveness of the drug and declares it to be either effective or ineffective.

The criteria for the initial classifications are: (1) effective meaning that the drug has the purported therapeutic effect; (2) probably effective meaning that the effectiveness of the drug is probable, but additional evidence is required before it can be declared effective; (3) possibly effective meaning that there is little evidence of effectiveness; and (4) ineffective meaning that there is no acceptable evidence of effectiveness.

On December 11, 1970, the Surgeon General requested all agencies within HEW to establish procedures within 45 days to prohibit the use of Federal funds for the purchase of drug products classified as ineffective or possibly effective by FDA. Two exceptions were noted:

--Ineffective and possibly effective drugs could be purchased for use in approved clinical research projects.

--Possibly effective drugs could be purchased when no alternative means of therapy with drugs in the probably effective or effective categories is available.

On October 8, 1971, HEW issued a regulation prohibiting expenditure of Federal funds under its direct care programs for ineffective and possibly effective drugs except under the two conditions listed above. However, regulations prohibiting such purchases under Medicaid have not been issued.

PRIOR GAO REPORT ON EFFECTIVE DRUGS

On May 9, 1972, we issued a letter report to the Administrator, Social and Rehabilitation Service, HEW, in which we recommended that regulations to preclude the purchase of ineffective and possibly effective drugs under Medicaid be issued without further delay. We stated that about $196,000 had been expended in Ohio during January, April, July, and October 1970, for 38,000 prescriptions for 106 ineffective drugs, and that about $99,000 had been expended in Illinois and New Jersey in July and October 1970, for 21,000 prescriptions for 16 ineffective drugs.

In his reply, dated June 13, 1972, the Administrator stated that a regulation precluding expenditures for ineffective and possibly effective drugs under Medicaid was being prepared for transmittal to the Office of the Secretary, HEW, for publication as a proposed rule. The proposed regulation has not yet been published.

B-164031(2)

STATES STILL PAYING FOR INEFFECTIVE AND POSSIBLY EFFECTIVE DRUGS

We found that the three States in our current survey were expending significant amounts for ineffective and possibly effective drugs. The costs and number of prescriptions of ineffective and possibly effective drugs purchased under each of the three States' Medicaid programs are presented in the table below. The data for California and Texas is for September 1973. Because data was not available for Ohio for September 1973, the data presented is the average monthly figures for the period September 1972 through August 1973.

	California	Ohio	Texas
Ineffective:			
Cost	$104,754	$25,700	$ 81,264
Number of prescriptions	(note a)	6,700	15,816
Number of drugs	27	80	93
Possibly Effective			
Cost	169,767	45,500	264,921
Number of prescriptions	(note a)	8,300	36,863
Number of drugs	77	174	211
Total cost:	$274,521	$71,200	$346,185
Percent of Total Medicaid Drug Costs	4.4%	6.6%	11.9%

Note a: Data not obtained

Expenditures at these monthly levels represent annual costs of about $8.3 million for ineffective and possibly effective drugs in the three States.

Neither Ohio nor Texas have procedures for removing drugs classified as ineffective or possibly effective from their Medicaid drug formularies. California has a procedure for removing drugs which have been finally determined by FDA to be ineffective--a State employee reads the Federal Register to determine which drugs have been finally classified as ineffective and provides this information to the California Medical and Therapeutics Committee which has them removed from California's Medicaid

drug formulary. This procedure is apparently not fully effective, however, because California paid for three drugs in September 1973 which FDA had finally declared ineffective in March and May 1973.

We also contacted officials in Illinois and New Jersey, which with Ohio were the States included in our prior review, who informed us that neither State had changed its drug payment policies. The officials told us that their States would continue to pay for drugs which had been classified as ineffective and possibly effective, until HEW made its final determination on this matter and issued regulations.

CONCLUSIONS

It has been more than 3 years since the Surgeon General requested HEW agencies to prohibit the use of Federal funds for the purchase of ineffective and possibly effective drugs, but regulations have not been issued for Medicaid. Such regulations should result in more effective utilization of Federal funds and improved health care of individuals included under Medicaid, through the substitution of drugs having evidence of effectiveness for drugs having little or no evidence of effectiveness.

Since evaluation of specific drugs by FDA also applies to identical drugs and may be applied to related or similar drugs[1], HEW should prepare and distribute a list of all drugs which are identical, related or similar to drugs declared to be ineffective or possibly effective.

RECOMMENDATIONS

SRS officials told us that a draft of a regulation precluding the use of Federal funds for ineffective and possibly effective drugs under Medicaid will be sent to your office shortly for your approval and publication as a proposed regulation. We recommend that you expedite publication of the proposed regulation and that, after comments are received, final regulations be published without delay.

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[1]An identical, related, or similar drug includes other brands, potencies, dosage forms, salts, and esters of the same drug moiety as well as of any drug moiety related in chemical structure or known pharmacological properties.

B-164031(2)

We recommend also that you direct the Administrator of SRS, in conjunction with the Commissioner of FDA, to establish procedures for providing to States and drug providers, lists of drugs declared to be ineffective or possibly effective, and lists of all identical, related, and similar drugs.

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We are sending copies of this report to the Chairmen, House and Senate Committees on Appropriations; the Chairmen, House and Senate Committees on Government Operations, the Chairman, House Committee on Ways and Means; and the Chairman, Senate Committee on Finance. Copies are also being sent to the Director, Office of Management and Budget.

Sincerely yours,

Gregory J. Ahart
Director

Mr. STAATS. This concludes my prepared statement.

Senator NELSON. Thank you, Mr. Staats.

You stated that the DOD spent $91,400,000, and the Veterans Administration about $38,100,000 in their central purchasing. They spent maybe $84 million for drugs at much higher prices through the Federal Supply Schedule, and more through local purchases at even higher prices.

Why is it, or is it necessary at all, to spend such a large percentage of the drug purchases, of money on drug purchases at such high prices?

Mr. STAATS. Mr. Ahart will respond.

Mr. AHART. I think there are several reasons for that, Mr. Chairman.

In some cases, the volume used of a particular drug product would not be sufficient to justify the expense involved in bringing it into a central management position in a procurement center. You do have transportation costs involved in shipping it out to the local station when you bring it in centrally, and the economics of it call for it to be a local purchase or a supply schedule item.

Secondly, you have certain——

Senator NELSON. Well, on that point, we have lots of examples, and have had for several years off and on, of smaller purchases being charged at a unit price much lower than large purchases.

Let me read from a speech given last summer by Mr. Vincent Gardner, Chief of Drug Studies Branch, Division of Health Insurance Studies, Office of Research and Statistics, U.S. Social Security Administration.

Now Mr. Gardner says—and I shall just read an excerpt from one page of this speech:

> A recent pilot study by the Social Security Administration of drug product costs to non-government hospitals showed a wide variation in prices for similar quantities of the same product. The cost to the hospitals for one manufacturer's antibiotic varied from $29.85 to $92.68 for quantities of 500. The price of an anti-infective from another producer varied from $85 per 1,000 to $216 per 1,000. Or, take another anti-infective from a major producer which ranged in price from $9 to $43 per 1,000 tablets. Contrary to the conventional wisdom, industry claims and economic theory, little relationship was found between order size and price to the hospitals. In addition, in instances where there were price differentials paid for different quantities, the differential was often much greater or smaller than would normally be expected on the basis of usual quantity discounts or different packing and shipping costs. For example, in the case of an antibiotic, one hospital paid $39.50 for bottles of 500 in purchasing a total of 2,000 capsules, whereas another hospital paid $52.50 for bottles of 500 in purchasing 1,500 capsules. So you had a differential in quantity of 500 capsules, and yet one was, the one who brought 2,000 capsules paid $39.50 and the one who brought 2,000 capsules paid $52.50. Excuse me, the one buying 2,000 capsules paid $39.50; the one buying 1,500 capsules paid $52.50. The differential is not explicable on the economic theory.
>
> This from the same producer or hospitals in the same area.
>
> On this basis, it could be concluded that the first hospital received a discount of $62.60 per 100, simply for purchasing one bottle more than the second hospital. Or, to put it another way, one hospital paid $157.50 for 1,500 capsules, while another paid 50¢ more for an additional 500.

Now, there are lots of these examples.

Here is an example of a purchase by the Defense Supply Agency in which they bought a product at the unit price of $13.89 on a

bid; then buying the same drug off the Federal Supply Schedule from the same supplier, they did not pay $13.89 unit price, they paid $47.64.

Is there any reasonable explanation for a differential that huge?

Mr. AHART. Such examples are certainly well documented in these series of hearings. And as you know, Mr. Chairman, there are a lot of differentials in prices given to different hospitals. And in our review, certainly we found differences in prices given to the Veterans Administration vis-a-vis the Department of Defense for like quantities of the same item in relatively the same time frame.

I think the explanation for this in the hospital situation that you mentioned just a moment ago and the DOD situation is partly attributable to just a different degree of aggressiveness in negotiating prices on the part of the various hospitals and on the part of the Veterans Administration and DOD.

A certain amount of it is certainly due to the use of competitive contracting by one agency and non-competitive procurements by another agency for the same items.

We did make a comparison of 13 sets of purchases between the Veterans Administration and DOD, where one of them had gone competitively and the other had gone negotiated with the sole source, and in 11 of those cases there were significant differences in the prices paid—favoring, of course, lower prices when competition was obtained in the procurement.

But I do not think we are in a position to explain all of the differences which you have put on the record, particularly between one hospital and another hospital when the buys were made from the same manufacturer. I think part of that is explained by a different degree of effectiveness in negotiating with the manufacturer to get the best price that they can.

Now, we did include in our report, on page 37 of our report, the comparison that we made of purchases under the Federal Supply Schedule, with those that were purchased on a central basis. And the range we found is in some cases a very slight difference between the price paid centrally versus the Federal Supply Schedule; but the range went all the way up to about 360 percent higher on the Federal Supply Schedule for certain items, with an overall average, I believe, of about 74 percent differential.

Senator NELSON. Well, I am looking at another DOD example: for nitrofurantoin 100 milligram tablets ordered from the same company in bottles of 1,000, the same product from different companies. On bid the unit price for these tablets, 100 milligram—a bottle of 1,000 was $11.65. For exactly the same compound, brought from the Federal Supply Schedule, the unit price was $170.

Well, it is just inconceivable that you could have that much difference in the unit price accounted for by packaging, shipping, and individual handling. It is a differential of almost $160.

Now, would you not suppose that a substantial purchaser, such as the DOD's Defense Supply Agency, when they had a successful bidder, could also make an agreement right then that if they needed some supplementary supplies, that it could be purchased at some reasonable markup?

Can you think of any way to justify a markup of $11.65 unit price to $170?

Mr. AHART. Offhand, the difference is quite striking. I really would not know how to explain it or how to justify it. It is possible that if it is a truly competitive situation, the manufacturer might find it to his advantage to discount rather drastically off the catalog price in order to get the additional business which, if he does not get it, will go to someone else. The manufacturer is not really in the same kind of a situation as when his products are listed in the Federal Supply Schedule since there often is no competition for the items included in the schedule.

But again I would say that is a rather startling differential, and I think it would be very difficult certainly for us to explain it or for anyone else to explain that differential at this point.

Senator NELSON. All right.

Now, here are two interesting cases: One is a purchase of erythromycin tablets, same company; off the Federal Supply Schedule, the unit price $8.90, locally purchased the unit was $7.79. That is totally illogical, isn't it?

Mr. AHART. Well, I am not familiar with the details of the local purchase, Mr. Chairman, or what might have been involved in it. It does seem contrary to the logical situation.

Senator NELSON. Well, here is one for tetracycline: Off the Federal Supply Schedule the price is $27 unit price; locally purchased, same company's product, $13; so they are paying less than half as much for local purchase as they are paying off the Federal Supply Schedule.

There has got to be something wrong with that, does it not?

Mr. AHART. Well, I am really not in a position to comment on it, except it does not seem to be consistent with the logic of the Federal Supply Schedule System.

Senator NELSON. They ought to be able to purchase locally the whole thing and give up the purchasing agency if they are going to pay twice as much.

Mr. STAATS. I might interject here and say that we see great problems in the Federal Supply Service, generally beyond the area of Federal drug procurement. We have studies going on now in our Procurement Division, looking at the operation of the Federal Supply Schedule. We think there are very serious problems.

Senator NELSON. Well, to me it is just incredible to end up paying twice as much off the Federal Supply Schedule as you would have on the local purchase where the highest price logically should be.

Mr. STAATS. There has been a general presumption—and this is the substance of the issue that we are looking at—that an item on the Supply Schedule which normally carries a 10 or 15 percent discount is a good buy. In many instances we think you can get a much better buy by competitive bidding; and this is the issue that we are looking at generally with respect to the GSA's procurement supply program.

Senator NELSON. Are you also looking at the question of the specifications that will be drawn in competitive bidding by the Federal

agencies, Defense Supply Agency, and the Veterans' Administration, in which if you draw up the specifications in a particular way, there is only one bidder or only one person to negotiate with.

I think it is an important point to look at because you can sit there and draw your specs, such as in the buying of tetracycline. If you are drawing up specs with some variations for tetracycline, you can end up getting a very expensive brand name of the compound tetracycline that has some modifications in the way it is compounded although it may have the same therapeutic effect. If you put the specs right, there will be only one company that can meet it; and that issue has been raised before. I think it is worth looking at.

Mr. STAATS. Ten to 15 percent discount may or may not represent a very significant discount in relation to what you might be able to get by developing specifications and then going for a broader-based competition in procurement.

Senator NELSON. Now, what, if any, arrangements have been made between the DOD and the VA to coordinate and establish requirements prior to negotiation of drug contracts?

Mr. AHART. This is one of the things we commented on in our report, Mr. Chairman. At the time of our work in this area very little was being done to coordinate requirements into joint purchasing arrangements even though that seemed to be the appropriate way to go.

Now, hopefully, as a result of our report and our recommendations and the general agreement of the agencies with those recommendations, and the corresponding OMB study, and the implementation of what came out of that study, that there will be much better coordination, determination of requirements, and consolidated purchasing for the total Federal needs as opposed to each agency going out on its own and doing its own job.

Senator NELSON. As of now they have not reached such an agreement? Or are they in the midst of negotiating some agreement or coordinating their activities?

Mr. AHART. Well, as the Comptroller General mentioned in his testimony, the OMB study is with the various agencies for comment now; and hopefully within a short period of time they will reach agreement on just what is going to be done in this area.

Senator NELSON. And then, what actions, if any, have been taken to transfer the quality assurance program to the FDA?

Mr. AHART. It is my understanding that all three agencies are in general agreement with the proposition that one agency could do a better coordinating job in this area. The Food and Drug Administration, I believe, has requested certain information from both the Veterans Administration and the Department of Defense, and should be, within a fairly short period of time, able to define conceptually what they are going to do in this area and start implementation.

Senator NELSON. Will that mean that the program for assuring quality will be exclusively within the Food and Drug Administration, or will we continue to have duplication with the Veterans

Administration and the Defense Department, with their own inspectors and so forth?

Mr. AHART. Well, I think if the intent of our recommendation is carried through, it will mean that the quality assurance function will rest solely with the Food and Drug Administration.

Senator NELSON. Well, does it appear that they are proceeding to implement a policy of that kind?

Mr. AHART. Every indication that we have is that they are moving in that direction and are trying to reach the agreements necessary and move toward the consolidation of that function. Yes, Mr. Chairman.

Senator NELSON. The GAO has no doubt that the FDA has the capacity to guarantee or the capacity to carry out an effective quality assurance program?

Mr. AHART. Well, I think certainly if they are not now in a position to meet the requirements of the Department of Defense and VA——

Senator NELSON. If they are what?

Mr. AHART. If they are not now in a position to do all of the things that DOD and VA feel are necessary to meet their requirements, I feel certain that the potential is there for them to acquire that capacity and to carry it out.

Senator NELSON. What does that mean?

Are you suggesting that the VA and the Department of Defense carry on a quality assurance program that is somehow superior to what FDA now does?

Mr. AHART. No. What I am suggesting, Mr. Chairman, is that the Department of Defense does have quite a number of specific requirements that go beyond the requirements for drugs which are now available to the general public in terms of——

Senator NELSON. Well, what kind of requirements?

Mr. AHART. In terms of color tolerances, indication of deterioration of the drug, packaging requirements—these types of things that will have to be built into the FDA program if they are going to meet the specific requirements of the Department of Defense.

Senator NELSON. Well, I guess we will be going into that later; but do those requirements have anything to do with the effectiveness of the drug?

Mr. AHART. Well, I think we are talking here about meeting the specific military requirements which are above and beyond what would be suitable for the general public.

Senator NELSON. I cannot quite understand what you mean above and beyond. Every witness we have had from the medical and science fields have stated that if you are meeting USP standards, that is as high a quality—as high as there is.

What quality would they have specified that is super-duper?

Mr. AHART. Mr. Crowther has some examples to illustrate what I am talking about, Mr. Chairman, that might help clarify the situation.

Mr. CROWTHER. Mr. Chairman, in a couple of cases, particularly one that the military brought to our attention—it was called co-

caine penicillin C for aqueous injection, 300,000 units. The original technical requirements were the FDA and USP monographs. There was a field complaint that arose in DOD that involved the syringeability problem. It was reported the material could not be aspirated from the bottle or could not be injected from the syringe. Additionally, there were some vials that were overfilled.

In order to avoid this they had to have a higher degree of consistency. For example, they added a standard that when the drug was reconstituted, each milliliter of the resulting suspension would contain not less than 280,000, not more than 380,000 USP penicillin units, and when reconstituted and shaken for 30 seconds it should flow freely without binding with the contents of the final containers or aspirated through a 22 gage hypodermic needle using a suitable syringe.

They found a particular problem with the drug in their use. Now, whether this had to do with the specific locations, temperatures, many other things, it is not obvious. But nonetheless, in their field use they did identify these kinds of problems that required a higher degree of consistency and more specific tolerances.

Senator NELSON. So you are not talking about the question of the quality of the drug. You are talking about problems that may arise from being shipped to different parts of the world, or shelved in a tropical climate versus a moderate one, or subjected to much rougher handling.

Is that the kind of thing that we are talking about?

Mr. CROWTHER. Generally that is the kind of specific requirements that they would have to include rather than ones dealing with effectiveness.

Mr. GORDON. Mr. Chairman, may I ask a question at this point?

Senator NELSON. Yes.

Mr. GORDON. In your report of March 29, 1973, you stated that, "FDA has not always enforced aggressively compliance with good manufacturing practices by many drug producers."

In fact, an employee of the Department of Defense, Mr. Max Feinberg and also Mr. Stetler of the Pharmaceutical Manufacturers Association, have used quotations from your report to show that the FDA cannot be depended on to insure that only high quality drugs are produced.

In this connection, then, can you tell us if the recommendations in your March 29, 1973, report have been accepted and are being followed by the Food and Drug Administration?

Mr. AHART. To our knowledge, Mr. Gordon, all six of the recommendations we included in that report have been accepted by the Food and Drug Administration, and action has been taken to implement those recommendations.

So I think the Food and Drug Administration is in full agreement with the need for improvement in those specific areas.

Mr. GORDON. And they are doing something about it?

Mr. AHART. They have implemented all six of the recommendations. I think there is one that, just because of the timing of it, will not be in full implementation until about April; and that is the

registration requirement. But beyond that there is total agreement between the Food and Drug Administration and ourselves on the need to take these actions, and FDA has taken actions.

Mr. GORDON. HEW's Secretary Weinberger said that his Department will adopt the policy for reimbursement for drugs under medicare and medicaid at the lowest generic price available. Do you see any reason why this same policy should not be applied by the DOD to its CHAMPUS program—that is, the DOD's home program—or the VA to its home program?

Mr. AHART. Well, I think certainly the principle involved in the Secretary's policy decision would be applicable to the CHAMPUS program and to the Veterans Administration's home town pharmacy program, even though they are both smaller volume programs than the programs the Secretary is dealing with. But in principle, the same policy should be applicable.

Senator NELSON. I guess that is all the questions I have.

Thank you very much for you very valuable testimony, Mr. Staats.

Do you have any questions, Mr. Adams?

Mr. ADAMS. Just one, Mr. Chairman. Thank you, Mr. Chairman.

Mr. Staats, it appears from your testimony that neither DOD, HEW, or Social Security Administration require that formularies list drug items by their official, generic or nonproprietary names, while in some cases they are preferred or recommended.

Would you share with the committee your thoughts as to whether you think this is a wise course of action, or whether the use of the generic, nonproprietary name should be mandatory, where possible, in this program and other Federal programs?

Mr. STAATS. In general we do favor this, and we have previously testified here to that effect. As to whether it could be made mandatory or not at this point in time I would like to ask my colleagues to express a judgment on that point.

I think that would come down to a question of practicability. But in general, we do support the concept.

Mr. AHART. Yes. I think many formularies in use in hospitals do use both the generic name in all cases and the brand names if applicable; and certainly, I think we would, as the Comptroller General has stated, agree with that principle, that the generic identification of the drug should be included in the formularies.

Mr. ADAMS. On page 19 you discuss the fact that DOD has placed no restrictions on drugs that may be prescribed under the CHAMPUS program. I take it then that under this program DOD could and probably is paying for drugs already determined to be ineffective or possibly ineffective by the FDA.

Is that an accurate understanding?

Mr. STAATS. That would be correct. That would be a correct interpretation of our statement, yes, sir.

Mr. ADAMS. And one last question.

On pages 4 and 5 you discuss pending legislation that deal with medicare and medicaid and the possible future passage of a national health insurance plan. Later on in your testimony you point

out that under the Social Rehabilitation Services program the States accumulate certain data regarding specific drug usage, but this data is not normally provided to the SRS.

Would you recommend that in contemplation of additional Federal health programs and their being administered by the State, that the State begin now to set up a reporting scheme to provide this kind of information on specific drugs to the Social Rehabilitation Services group and to other Federal agencies?

Mr. AHART. Well, I think any information of this type that you can get back to the Federal program managers will be useful. I think it is particularly important at this point in time, based on the survey we are doing in the medicaid program, where you have a state of transition involved in getting "ineffective" drugs off the market, that the Federal Government be apprised and take such steps as it can take to make sure that it is not reimbursing for drugs which have been determined to be "ineffective" by the Food and Drug Administration.

Now, whether you could justify economically a very detailed reporting system by all of the States, I think we would have some serious question on that as a long-term proposition.

Mr. ADAMS. I just wanted to make sure that I have it right. As it currently stands, the States do not report this. And if I can understand the testimony correctly, you mentioned that the total Federal drug bill may increase in excess of $1 billion; and it is that $1 billion expenditure and keeping track of the drugs that are being paid for, especially the ineffective drugs, about which I am concerned.

I am simply suggesting that perhaps before we reach that crunch we set up some kind of mechanism whereby the States can report, and out of necessity, detailed information.

Mr. AHART. Perhaps Mr. Crowther would like to comment in more detail on that.

Mr. CROWTHER. Let me add to that just a little bit. There are several ways actually that you could set up a control mechanism to avoid the problem. You can set up as a condition of participation by each hospital, for example, under the medicare and medicaid program, that such drugs will not even be included in the hospital formulary or in the hospital pharmacies. So if they are not in the hospital at all, they cannot be administered to medicare and medicaid patients. That is probably one of the best means of control.

A second would be to provide some system of reporting and control, or at least testing of the controls at the State levels, particularly in the State programs of the medicaid type. Rather than have all of that type of information come centrally into Washington somewhere and, in effect, create just a deluge of paperwork here, an effective control system and mechanism should probably be implemented at the hospital level or at the State level where the administration of the care is actually carried on. There are several means by which that can be done, and I am sure they are under consideration at this point, rather than necessarily reporting all of that data. For programs as large as these, this would be just a huge amount

of data being reported into Social Security Administration or the Social Rehabilitation Service.

Mr. ADAMS. I see.

Then that control should be in the field. Is that what you are suggesting. But it still should be controlled.

Mr. CROWTHER. Yes. It still should be controlled.

Mr. ADAMS. Thank you, Mr. Chairman.

That's all I have.

Mr. STAATS. Mr. Chairman, may I just say this before we conclude. As you can see from the figures we have presented here today, the growth in the Federal costs involved in drug procurement has been very dramatic over the last few years. The potential is here for additional expenditures such as the inclusion of payment for certain drugs under the medicare program and the possibility of national health insurance.

This subject takes on even greater significance than it has had in the past, so we commend you for your interest in this area. We want to continue to do work in this field. We think some real progress has been made since we last appeared before your committee.

We think also there is a great deal of potential for savings here and improved quality of drug care.

Senator NELSON. There have been, as you know, proposals made and amendments offered on the floor that would cover all drugs in medicare, medicaid, or other proposals to cover in a more limited fashion drugs that are used on a continuing basis.

But in any event, if you would cover them all, you are looking at figures estimated at a couple of billion dollars. Have you done any studying or made any computations to indicate how much money would be saved if you achieved the ideal of purchasing all drugs at the lowest price of that compound, whether it was brand or generic name—the lowest price of that compound that was available?

Do you have any notion as to what that might mean in the program of the size we are now involved in? I realize it is a growing program.

Mr. STAATS. We can do it for individual drugs, but to take the whole universe, it would be a very, very major undertaking to try to develop anything like a reasonable estimate.

Mr. Ahart or Mr. Crowther may have something to add to that.

Mr. AHART. No. We have not really tried to come up with any figure like that; and I am not sure it would be possible, Mr. Chairman. As you indicated by some of the statistics on individual transactions that you have put on the record here, sometimes you really have a difficult time even finding out what is the lowest price at which a particular product might be available.

Mr. STAATS. I personally think if you can take several good examples, the point is made without having to go through the effort to come up with an overall total.

Senator NELSON. I suppose we do not even know what amount—or do we—what amount of money is spent under Federal programs for the, or, 25 or 40 most widely prescribed drugs.

When we are looking at the amount of money spent on Federal programs, do we know what drugs it is being spent on?

Mr. AHART. That information could be developed for the direct Federal procurements. I think it would be very difficult, because of some of the considerations Mr. Crowther spelled out, to develop it for the indirect procurements that the Federal Government participates in.

Mr. STAATS. This would, I think, be a useful exercise on the direct procurement. I think that would give you some indication then, by extrapolation, of what you could save on the indirect procurements.

Senator NELSON. When you refer to direct procurement, you are talking about procurement by negotiation, procurement by bids, and also procurement of drugs at the local level by a veterans hospital or a military hospital in one part of the country from a local supplier to supply some need they have. If you have that breakdown, it might be of some significance.

Mr. STAATS. Let us explore that, if we may, and let you know what we think would be a feasible analysis.

Senator NELSON. It would be interesting to see. I do not know if you could extrapolate from that. But we know what the 50 most widely prescribed drugs are. There might be some correlation between what the Government buys directly of the 50 most widely prescribed drugs and what is purchased locally under medicare and medicaid programs, by prescription of a local physician filled by a local pharmacist. I do not know, but it might not be too difficult to figure that out.

Well, thank you very much, Mr. Staats.

Mr. STAATS. Thank you very much.

Senator NELSON. Our next witness is Dr. Alexander Schmidt, Commissioner, Food and Drug Administration.

Dr. Schmidt, the committee is pleased to have you appear here today. You may present your statement and your material however you desire.[1]

STATEMENT OF HON. ALEXANDER M. SCHMIDT, M.D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION, ACCOMPANIED BY J. RICHARD CROUT, M.D., DIRECTOR, BUREAU OF DRUGS; BERNARD T. LOFTUS, DEPUTY DIRECTOR, OFFICE OF COMPLIANCE, BUREAU OF DRUGS; AND ROBERT C. WETHERELL, ACTING DIRECTOR, OFFICE OF LEGISLATIVE SERVICES

Dr. SCHMIDT. Thank you very much, Mr. Chairman.

We are delighted to be here this morning to appear before you on a topic which, of course, is extremely important to the Food and Drug Administration.

I would like to introduce my colleagues here with me. On my immediate right is Dr. Richard Crout, Director of the Bureau of Drugs. To his right, is Mr. Bud Loftus, Deputy Director of the Office

[1] See information beginning at page 10638.

of Compliance in the Bureau of Drugs. To my left is Mr. Bob Wetherell, who is in charge of our Office of Legislative Services. Mr. Peter Barton Hutt, our General Counsel, who usually accompanies me on these occasions, could not be here. He will try to get here later, but is now attending another Senate activity.

My statement is a little long. As I go through, I will try to summarize some areas, if that is acceptable to the committee.

Senator NELSON. You go ahead and present it in any way you wish. We have the time if you desire to read it, and we shall have some questions to ask as you proceed.

Dr. SCHMIDT. All right.

We are pleased to discuss our drug quality assurance programs and the effect these programs may have on other Government agencies involved in drug procurement and reimbursement.

Let me begin by stating that the pharmaceutical industry must bear the primary responsibility for assuring the production of high quality drugs. The Food and Drug Administration's role is to assure that manufacturers meet their responsibility. We do so by setting appropriate standards for the manufacture of drugs and by carrying out surveillance activities such as factory inspections and analyses of selected products. When firms do not meet their responsibilities, the Federal Food, Drug, and Cosmetic Act provides us with authority to take certain measures to bring about correction and/or to remove offending products from the market.

Our quality assurance programs for drugs are aimed at providing optimal assurance of drug quality to all physicians and consumers. These programs employ a major portion of our field manpower available for drug work and range in approach from continuing surveys of the manufacturing practices of selected drug firms to intensified targeted programs such as certification of specific products or plant inspection and analyses involving a certain product with identified problems.

The Federal Food, Drug, and Cosmetic Act requires inspection of every drug firm at least once every 2 years. In fiscal year 1973, we inspected 2,700 registered human drug establishments and made some 7,000 inspections of registered and related drug establishments.

Senator NELSON. Doctor, you mentioned 2,700 establishments. How many are there in the United States that manufacture drugs?

Dr. SCHMIDT. Well, counting all registered establishments of all kinds for all drug products, about 14,000 have registered during the biennium of 1971 to 1973. This is a very inclusive number, however.

Senator NELSON. Are these both prescription and nonprescription establishments?

Dr. SCHMIDT. Yes, sir. These include companies of all sizes that make prescription drugs, nonprescription drugs, food and bulk drugs, animal drugs, and so forth.

Senator NELSON. Do you inspect only those that manufacture prescription drugs, or do you inspect those that manufacture both prescription and nonprescription?

Dr. SCHMIDT. Well, as I just said, the requirement is, as you know from various speeches and remarks that have been made, the requirement is that we inspect all firms at least once every 2 years.

We find it necessary to set up a priority system and pay most attention to those firms that produce most of the drugs in the country. At the top of our list are those large firms that produce 95 percent of the prescription items in the country.

The number of inspections that I mentioned includes inspections of 100 percent of the firms in the country with business over $10 million a year that produce prescription drugs.

Senator NELSON. What do you mean, inspection 100 percent? The law requires you to inspect them all once every 2 years, does it not?

Dr. SCHMIDT. Yes, sir.

Senator NELSON. Do you meet that requirement?

Dr. SCHMIDT. No, sir, we do not, and I do not think that we ever could for a number of reasons. Certainly, we would miss one firm every 2 years, and, therefore, we would not meet the statutory requirement, by definition.

We must have a flexible policy of priority inspections. When we do identify a very large problem in an important drug, we must be free to make as many inspections of one particular plant or one group of plants in a year as might be needed to correct the problem.

A good example of this, for example, is the large volume parental industry that had a problem with manufacturing sterile products. This is, of course, a critcal problem, and we mounted an intensive program in this particular industry. We inspect many of the plants five or six times in 1 year if necessary, and some we do not get to, within the 2-year period.

Senator NELSON. Let me put it another way.

What percentage of the prescription drugs that go into the marketplace, what percentage of those drugs do you inspect once every 2 years?

Is it 95, 98, 90 or some other percentage?

Dr. SCHMIDT. Our best estimate is 95 percent, sir.

Senator NELSON. You are saying that companies producing 95 percent of all of the prescription drugs that go into the marketplace are inspected at least once every 2 years?

Dr. SCHMIDT. Yes, sir.

Senator NELSON. What about that other 5 percent? Are those producers never inspected, or inspected once in 3 or 4 or 5 years? Do you have any figure on it?

Dr. SCHMIDT. Well, they are programed by our field force for inspection as soon as can be done. We have established, partially in response to the GAO report you just heard discussed, a system in which we monitor all firms and notify the field of those that have not been inspected within 1½ years, then 2 years, then about 2½ years, so that when a firm is not inspected within the 2-year period, it will move to the top of the priority listing of our inspectors.

Senator NELSON. So it will get inspected within what period?

Dr. SCHMIDT. Within 2 years.

Senator NELSON. Two years after the expiration of the first 2 years?

If I understood you, you said that when one has not been inspected within the 2 years, they go into top priority.

Dr. SCHMIDT. We would then put it at the top of the priority list and inspect it immediately.

Senator NELSON. Well, then I do not——

Dr. SCHMIDT. The result of this is that all firms should then be inspected within the 2½-year period. We would estimate that for these firms that we are talking about, the system will pick up 100 percent of them within a 2½-year period. Our aim is to hit them all within a 2-year period.

Senator NELSON. So you are saying that within a 2½-year period, you inspect the firms that produce 100 percent of the drugs in this country?

Dr. SCHMIDT. Yes, sir.

Senator NELSON. Do your records show the names of the firms in all of the United States and that at least once every 2½ years, every single one of them which produces prescription drugs is inspected by the FDA?

Dr. SCHMIDT. The firms are all on a computer system, and a computer can kick out for us the firms that have not been inspected within a 2-year period, and then within the immediate 6-month period, then, we would move to inspect all firms.

The concern that has been expressed by the PMA, and my concern, frankly, is that there may be some small, vary small firms that might need inspection more than some of the large quantity firms, and that we might be missing some of these firms. Our data show that of the very small firms—and we classify those as being firms doing less than $500,000 business a year—we are only seeing about half of those within a 2-year period. We will now do better with these firms.

Senator NELSON. All right.

Please proceed.

Dr. SCHMIDT. We really wish to determine whether drug manufacturers are following what the law refers to as current good manufacturing practices. And as you know, GMP's are spelled out in our regulations and serve to guide our inspectors when they review plant operations.

In addition to providing routine surveillance on a scheduled basis, GMP inspections may be made on a selective basis, as I mentioned a minute ago. We often schedule inspections as a result of information obtained from our own product analysis or other reports that come to us of defective products. A pending New Drug Application or a request for certification of an antibiotic by a firm may also trigger an inspection, since a determination of compliance with GMP's is a required condition for approval.

Senator NELSON. You mean this is a request from a company for certification to produce the antibiotic?

Dr. SCHMIDT. Yes, sir.

Senator NELSON. All of its production would subsequently be batch tested by the FDA anyway?

Dr. SCHMIDT. That is correct.

Senator NELSON. But you require a prior certification of good manufacturing practices before you even permit the company to produce an antibiotic?

Is that correct?

Dr. SCHMIDT. That is correct, and this inspection is a very thorough inspection of their actual manufacturing practices.

A second basic approach to assuring the quality of drugs is a monitoring program involving the sampling and analysis of marketed drugs to determine their adherence to compendial standards, as well as standards established in the NDA's.

Criteria used in selecting drugs for examination include: Their therapeutic significance; the complexity of compounding—for example, some drug may have just a very small amount of the active ingredient in its final form; the history of that particular drug product.

The objectives of the program are to: Identify defective batches of drug products and remove these from the marketplace; help determine the reasons for batch failures and assure that the manuturing procedures are corrected to eliminate these problems; provide a means for measuring changes in the quality of drugs and the relationship of such changes to actions that the FDA might take; and provide a statistically valid evaluation of the quality of selected drugs under study.

The analytical work for this program is carried out in our St. Louis laboratory or in one of our 18 field laboratories. Where feasible, drugs of similar composition are assigned to one laboratory for analysis. This increases laboratory efficiency by permitting the use of specialized and mass production techniques.

During the last fiscal year, we analyzed over 9,000 human drug samples. During the current fiscal year, we programed for analysis of 15,000 samples of human drugs. In general, we have found that only a small percentage—and by small we mean 1 to 1½ percent overall—of the drugs analyzed are defective. And by defective, we mean that they do not meet all of the compendial standards.

Now, those that are defective are followed up by our field officers to remove them from the market and to ascertain the cause of the defect. Also, we publish the results of our drug quality surveys in the FDA Drug Compliance Information Letter, and with your permission, I would like to submit a copy of this letter for the record.[1]

When our monitoring activities reveal problems with an entire class or type of drug, specific intensive programs are established. Our recent efforts to assure digoxin content uniformity and dissolution and sterility of large volume parenteral solutions are examples of such programs.

In 1970, to assure digoxin content uniformity, we established an industrywide voluntary certification program. Until a firm demonstrated that it could consistently manufacture digoxin in compliance with standards, it had to obtain a batch-by-batch analysis and FDA release prior to marketing.

When we later received information concerning variation in bioavailability—as opposed to the earlier content problem of digoxin manufactured by different firms and a new U.S. Pharmacopeia, or USP, dissolution rate standard was adopted, we instituted a certifica-

[1] See pages 10657–10672.

tion program similar to that employed in the content uniformity problem.

We put forth new regulations pertaining to the marketing of digoxin which became effective on January 22, 1974. And once again, with your permission, I would submit a copy of these regulations for the record.[1]

The regulations require batch-by-batch certification of digoxin until the firm demonstrates that its product consistently meets the new USP dissolution standards. These regulations also require that all firms intending to continue the marketing of digoxin must present evidence of bioavailability within 180 days after filing such notice of intent.

Senator NELSON. Are you able to assure that all digoxin now going into the marketplace meets the USP standards, the new USP standards?

Dr. SCHMIDT. Yes, sir, we feel so. We worked with the industry to recall the defective products over the last few weeks, and we believe that the new program will give every assurance that the digoxin being marketed will meet the new standards.

Senator NELSON. How many digoxin products were in the marketplace when this issue was raised about lack of content uniformity and bioavailability?

How many firms were in the marketplace?

Dr. SCHMIDT. Dr. Crout was on top of this.

Dr. CROUT. If you would allow me a little leeway with the numbers——

Senator NELSON. Yes. And if you want to submit for the record a correction and the names of the companies and the names—the trade names of those that had trade names—I would like to have it for the record at this point.

But you go ahead and off the cuff tell me.

Dr. CROUT. Fine.

The problem with inconsistent tablet uniformity was discovered in 1969, and at that time there were, as I recall, 44 firms manufacturing digoxin.

[The information referred to follows:]

DIGOXIN MANUFACTURERS

American Pharmaceutical Co., Hillside, N.J.
Banner Gelatin Products, Chatsworth, Calif.
Barr Laboratories, Inc., Northvale, N.J.
Bell Pharmacal Corp., Greenville, S.C.
Burroughs Wellcome Co., Inc., Triangle Park, N.C.
Blueline Chemical Co., St. Louis, Mo.
Cord Laboratories, Inc., Detroit, Mich.
J. Davis Laboratories, Inc., Palisades, Park, N.J.
J. W. S. Delavau Co., Philadelphia, Pa.
Endo Laboratories, Inc., Wilmington, Del.
Halsey Drug Co., Brooklyn, N.Y.
Heather Drug Co., Cherry Hill, N.J.
E. W. Heun Co., St. Louis, Mo.
KASCO-EFCO, d.b.a. E. FOUGERA, Hicksville, N.Y.

[1] See page 10673.

Ketchum Laboratories, Amityville, N.Y.
Lakeside Labs., formerly Davies-Rose-Hoyt, Needham, Mass.
Lannett Co., Philadelphia, Pa.
Lederle Laboratories, Pearl River, N.Y.
Marshall Pharmacal Corp., South Hackensack, N.J.
Parke, Davis & Co., Detroit, Mich.
Park Laboratories, Inc., Fredonia, Wis.
Premo Pharmaceutical, South Hackensack, N.J.
Philips Roxane Labs, Columbus, Ohio.
Rexall Drug Co., St. Louis, Mo.
Rondex Laboratories, Gutenberg, N.J.
Stanley Drug Products, Inc., Portland, Oreg.
ICN Pharmaceuticals, formerly Strong Cobb Arner, Cincinnati, Ohio.
Tablicaps, Inc., Franklinville, N.J.
Towne Paulsen & Co., Inc., Monrovia, Calif.
Vale Chemical Company, Allentown, Pennsylvania.
Vita-Fore Products Co., Ozone Park, N.Y.
Vitarine Co., Springfield Gardens, N.Y.
West-Ward, Inc., Bronx, N.Y.
Wyeth Labs, Philadelphia, Pa.
Zenith Laboratories, Inc., Northvale, N.J.

STATUS REPORT DIGOXIN CERTIFICATION PROGRAM—APRIL 9, 1974

On January 22, 1974, Regulation 21 CFR 130.51, "Digoxin Products for Oral Use; Conditions for Marketing" was published in the *Federal Register* setting forth FDA's position regarding the conditions for the continued marketing or oral digoxin products. The regulation, which became effective on the date of publication, has the following requirements for oral digoxin products:

1. Declared all oral digoxin products to be new drugs.
2. Requires submission of ANDA, including bioavailability tests for all oral digoxin products.
3. Requires a *mandatory*, FDA certification program based on dissolution testing by NCDA. No oral digoxin product may now be released without FDA approval.
4. Requires recall of any previously marketed batch of digoxin tablets found to fail USP dissolution specifications.

A meeting was held on January 21, 1974, at the Parklawn Building prior to publication of the *Federal Register* announcement to advise the industry of the status and importance of the program and to enlist their cooperation for its success.

The current status of the certification program is as follows:

PREVIOUSLY MARKETED BATCHES

1. One hundred and fourteen (114) previously marketed batches of digoxin from twenty-seven (27) manufacturers have been tested for dissolution and the results reported to the manufacturers.
2. Thirty-four (34) manufacturer batches representing fifteen (15) manufacturers and fourteen (14) distributor batches representing ten (10) distributors have been found to fail the requirements of the *Federal Register*, statement and removed from the market place by recalls.

BATCHES SUBJECT TO PREMARKETING CERTIFICATION

1. Thirty-four (34) digoxin manufacturers are involved in the program.
2. Twenty-one (21) batches from five (5) manufacturers have been certified by FDA and released for marketing.
3. One (1) manufacturer has submitted four (4) consecutive passing batches for each of its three (3) digoxin dosage strengths and has been temporarily released from the certification program.
4. One (1) manufacturer has submitted four (4) consecutive passing batches for its one (1) dosage strength and has been temporarily released from the certification program.

BATCHES REJECTED FOR CERTIFICATION

Five (5) batches from three (3) manufacturers have been denied certification for failure to meet USP and/or F.R. requirements.

Senator NELSON. So there were 44 digoxin products in the marekt-place by 44 different companies?

Dr. CROUT. They were all making an identical product. They were making 0.25 milligram tablets, and there were, as I recall, 44 manufacturers.

Senator NELSON. How many of those had brand names and how many of those were generic?

Dr. CROUT. Well, the most prominent brand name is Lanoxin made by Burroughs-Wellcome. I am not aware of any other brand name for digoxin. I think the other 43 were sold under the generic name of digoxin.

Senator NELSON. Do you have the names of the companies that were manufacturing this drug?

Dr. CROUT. We can submit that.

Senator NELSON. Would you submit names of those companies for the record?

Dr. CROUT. Yes, sir.

Senator NELSON. And there was only one that met the standards?

Dr. CROUT. No, by no means. Well, beginning back in 1969, the firms that had tablets out of compliance, from the standpoint, remember, of content uniformity, they had mixing problems—some tablets had more digoxin than was supposed to be in the tablets, some had less—entered into a voluntary certification program.

Several firms dropped out of the business at that time, and we ended up with something on the order of 30 to 35 firms making digoxin between 1970 and now. The tablets entering the market from 1969 through now have met the USP standards for content uniformity.

In 1970, I believe, 1970 or 1971, a new problem appeared with digoxin. The discovery was made that certain of the tablets lacked bioavailability; that is, that the blood levels in patients receiving those products were not up to standard, even though the tablets themselves were meeting USP specifications at that time.

So between 1971 and late 1973 a number of things happened in the research scene. The Food and Drug Administration, and the USP, went to work to develop a dissolution rate test for digoxin. When that became available in late 1973, we published our new regulations and said all manufacturers must meet the new USP dissolution rate specification.

Senator NELSON. Was there a direct correlation between the dissolution rate and the bioavailability?

Dr. CROUT. If you will allow the word "direct" to be interpreted a little broadly, yes; there is a pretty good correlation.

We then tested almost all the products that were on the market in late 1973 for the new dissolution rate standard. We tested about 30 manufacturers' products. There may be a few more, but we tested 30 manufacturers. Twenty of those passed, and the other ten were recalled.

Now, everybody must do a couple of things at this point. They must enter a certification program, and they must submit to us an ANDA stating that they are going to do bioavailability testing within 180 days. We do not know yet how many manufacturers are going to submit ANDA's, but we would assume that it is on the order of at least 20.

Senator NELSON. What do they have to put into the abbreviated NDA?

Dr. CROUT. I beg your pardon?

Senator NELSON. What do they have to include in their abbreviated NDA?

Dr. CROUT. They have to include evidence of bioavailability. They have to include their specific procedures for making digoxin. They have a plant inspection and so on, which is part of the usual procedure of approving an ANDA.

Senator NELSON. What about your batch testing?

Dr. CROUT. Batch testing will go on for as long as necessary, but we assume that as the bioavailability data come in and as manufacturers demonstrate repeatedly that they can make a good batch, they will drop out of this certification program. So we view this certification program as a transient and not a permanent phenomenon on the digoxin scene.

Senator NELSON. You stated you discovered the problem in 1969.

Dr. CROUT. Yes.

Senator NELSON. The Defense Personnel Support Center state they learned about the problem in 1965. They have no record of ever having informed the FDA about that.

Do you have such a record?

Dr. CROUT. No, and I am not certain what the problem could have been, because the problem discovered in 1969 required a methodology by which you could analyze individual tablets.

That methodology was not available in 1965, so whatever problem you are referring to was not the problem that I am discussing.

Senator NELSON. Because the technique was not available?

Dr. CROUT. The technique was not available in 1965.

Senator NELSON. Since it is a very important drug and its availability may very well be critical to patients, should the Defense Supply Center not have notified the FDA of whatever problem it was they said they discovered at that time?

Dr. CROUT. I would have thought so. As you know, I was not at the agency in 1965. I do not know what the communication channels between the two agencies were at that time.

Senator NELSON. Well, has any system now been established which would require any agency that discovered a problem with any drug to notify the Food and Drug Administration, which has the most significant responsibility for assuring quality?

Dr. CROUT. I think there are several systems established which the Commissioner deals with in his testimony coming up.

Dr. SCHMIDT. I might say that when we heard of some criticism by the Agency, we took a look at the communications link, and I asked

a team from the FDA to visit that Agency, which they did. And I made sure that there will be effective communication henceforth, at least out of our Agency.

Senator NELSON. All right.

Go ahead, Doctor.

Dr. SCHMIDT. Well, if I might, I would like to just make one point about digoxin. You have heard much about bioavailability problems, and the digoxin story is such a nice example of an important drug in which problems arose. The first problem turned out to be content; the second problem turned out to be a dissolution problem.

We have instituted a program to handle the problem. In recent months and years much has been learned about bioavailability problems, even though it is a young field. And we can now say that these problems are manageable, and I think that the digoxin story is a kind of case history that demonstrates the bioavailability problems very well.

Mr. GORDON. Dr. Schmidt, I just want to go back to another problem that the Chairman was talking about just a few minutes ago, that is, about your contacts with the DOD.

The DOD stated in material given to us that there is a close working relationship between Defense Personnel Supply Center (DPSC) and the personnel of the FDA. As far as I can see, there is no such thing as of now, anyhow.

Would that be correct?

Dr. SCHMIDT. Well, I do not believe we had a close working relationship in the last few years with the DPSC. At least it does not meet my definition of close.

Senator NELSON. But you do now?

Dr. SCHMIDT. Well, very recently, we do, because I sent a team up there. I was intrigued by Mr. Feinberg's speeches, and it stimulated me to get a closer relationship.

Senator NELSON. Please proceed.

Dr. SCHMIDT. Thank you.

In my prepared statement I use another example of this problem, the large volume parenteral problem which I mentioned, and I would skip over that since we have talked about them.

Another program we have for monitoring drug quality is a joint effort involving the various pharmaceutical associations, the USP and FDA. Under this program, pharmacists across the Nation report apparent product defects or problems to the USP. Copies of these reports are furnished to the manufacturer or other distributor of the product in question and to the FDA. Based on the evaluation of these reports, we issue investigatory assignments to the field when indicated, or in some cases institute special programs or surveys.

During fiscal year 1973, we received 2,750 program reports. The program, while still young, is expanding at a very rapid rate as demonstrated by the fact that we have already received 2,350 reports for the first half of this fiscal year. We find in looking very recently that our reports now are coming in at the rate of about 1,000 a month, so that we believe this will be an extremely productive information gathering source.

I include an example on page 7 of the problem that came up with

nitroglycerin. We learned about this through the program and were able to take appropriate measures to solve the problem.

Now, in conjunction with the total quality assurance program, the Agency conducts a number of programs which help assure a uniformerly high quality Nation's drug supply, including establishment and product inventory.

All drug manufacturers must register annually with the FDA. During the past 2 years, we have improved our data systems, and we continuously review our official establishment inventory list of registered firms to verify its accuracy and to insure that all registered firms are active.

This was another point made in one of the GAO reports and we agreed with their recommendation and are moving to comply with it.

The Drug Listing Act of 1972 authorizes us for the first time to require information that will result in a comprehensive inventory of all marketed pharmaceutical products. We are currently processing submissions under this act and expect this file to be active within a few months. This will provide an important resource for other agencies as well as for us and will enable us to use in other areas field manpower formerly needed for gathering information on drug products.

Now, another important drug quality assurance mechanism is the new drug approval process, the NDA process, and I believe this is so well known to you that I will not detail it now.

Another important measure that, again, you have heard about already this morning from the previous testifier, is our drug efficacy study implementation that is going on now. The DESI program rates the effectiveness of drugs and seeks evidence of their safety and efficacy.

Under this program, some 5,600 ineffective drug products have been removed from the market, ineffective indications for use have been deleted from drug labeling, and where drugs have been shown to be only possibly or probably effective, manufacturers have been provided an opportunity to supply the data that will establish their effectiveness.

In addition, manufacturers of many products not previously covered by NDAs have been required to submit abbreviated NDAs.

Senator NELSON. My copy does not have your figure. You say there are 6,000 ineffective drugs that have been removed from the market?

Dr. SCHMIDT. To date, 5,600 is the figure I gave. This is, within a few drugs, an accurate figure.

Senator NELSON. That is based on the National Academy of Sciences-National Research Council studies?

Dr. SCHMIDT. Yes, and our subsequent evaluation of their recommendations and our grading of the drug.

Senator NELSON. You mention almost 6,000 ineffective drugs. That includes, I assume, those that were found to be "possibly effective" by the NAS–NRC, and subsequently the company could not produce substantial evidence that they were, in fact, effective, so they became classified "ineffective?"

Is that correct?

Dr. SCHMIDT. If there are any in that category, it would be extremely small, and there may be none as yet at all.

Senator NELSON. What I am trying to get at is a definition. When you say almost 6,000 ineffective drugs have been removed from the marketplace, I take it that there are a number of drugs that were classified "possibly effective," and FDA has required in accordance with the statute, that the manufacturers submit substantial evidence of effectiveness. And if they cannot do so, that drug that was classified "possibly effective" then becomes classified "ineffective."

Is that correct?

Dr. SCHMIDT. Well, yes, sir. Generally where we are now in the process is that the clearly ineffectives for which there were no data supplied have generally been removed from the market. We are now in the process of evaluating data submitted to us by firms for drugs that have been classified as possibly or probably effective.

In most instances—and this point relates to an earlier thing you heard about, and that is the delay in our implementing the study and the court order that we are currently under—there are a number of mechanisms that come under the heading of due process that caused delay in our taking action against drugs.

For example, we would propose to remove drugs from the market. This proposal may be challenged, and, indeed, we will probably have to run a great number of hearings and probably then be in court a number of times before we can finish up this job.

Senator NELSON. You mean the issue involved will be a difference of opinion between the manufacturer and the FDA as to the adequacy of the evidence to support the claim of efficacy?

Is that what you are saying?

Dr. SCHMIDT. Partly the argument should be scientific, and partly they will be procedural. But in general we are going down a carefully constructed path that will include hearings before we remove some of the drugs that are in these intermediate categories for which conclusive data of efficacy has not been submitted.

Senator NELSON. Please proceed.

Dr. SCHMIDT. I mntioned that many products not previously covered by NDAs have been required to submit abbreviated NDAs, and as Dr. Crout has just mentioned, before such applications are approved, we require compliance with GMP regulations. As in the case of NDA submissions, this is determined by a very thorough plant inspection. This program has greatly increased our inspection activities in small and medium-size firms in the past and has resulted in substantial improvement in compliance with the requirements of GMP regulations.

The DESI program has also improved and promoted the exchange of information between FDA and other health agencies regarding drug efficacy status and does have an influence on purchasing policies of various Government agencies. The impact of the program is remarkably broad. You heard some of it earlier from the previous testifier.

The Secretary of DHEW has directed that Federal funds will not be expended for the purchase of drugs classified under the DESI

program as no greater than "possibly effective" for use in certain of the Department's programs, such as the direct care programs, contract care programs, and Federal grant programs.

With the Drug Enforcement Administration, which now includes the former Bureau of Narcotics and Dangerous Drugs, we have established procedures for implementing the large-scale DESI review follow-up action against amphetamine-containing drugs not in compliance with current requirements.

These drugs are under the jurisdiction of both the Drug Enforcement Administration and the FDA. Although this cooperative action has not as yet been completed, some 1,755 amphetamine-containing drugs manufactured by 351 firms have been effectively removed from the market. This regulatory action involved 549 drug recalls and five seizure actions under the FDC Act. With cooperating State health officials, a high degree of success has been achieved in the removal of these violative drugs from pharmacy shelves throughout the country.

Liaison for exchange of DESI program information has been established with the Chief Pharmacy Officer of the Public Health Service. In addition, we have received numerous communications from State, foreign government, and United Nations health officials about drug status under the DESI review program. And we routinely forward copies of the DESI announcements to several Government agencies.

The Federal Food, Drug, and Cosmetic Act requires that samples of each batch of antibiotics and insulin be tested and certified by FDA before these products are released for sale. Batch certification is also imposed for other products when it is needed to assure uniform quality. And as we have just previously discussed, digoxin has been subjected to batch certification since our drug surveillance program revealed significant variances from official standards.

The FDA regulations set standards for the facilities and conditions under which drugs are manufactured. Because good manufacturing practices should be "current" and change as drug technology changes, these regulations are periodically updated. The regulations were last revised in 1970 and are currently under further revision. Among changes being actively considered is a requirement that all drug products bear an expiration date based on adequate stability data, and also addition of GMP regulations for specific classes of products such as large volume parenterals.

Now, to return to the bioavailability or the bioequivalency problem, it has been shown in recent years that in a few instances chemically equivalent drugs, even though they meet all official standards, produce significantly different blood levels in man, and this is referred to as either bioavailability or, the drugs lack bioequivalency.

To assure the bioequivalency of chemically equivalent drugs, we are taking three steps. First, we will shortly publish in final form regulations describing standards and procedures to be followed in conducting bioavailability studies.

Second, we will shortly publish proposed regulations requiring bioavailability studies for all drugs of certain kinds; for example,

those for which the precise dosage is particularly critical and where a bioavailability problem would create a health hazard—and digoxin was certainly an example of that kind of drug; and also those formulations with previously documented bioavailability problems.

And last, we will also publish in the near future a notice concerning the procedures we will follow in calling for and reviewing data about the potential for bioavailability problems with other drugs; that is, those without previously well-documented bioavailability problems.

Mr. Chairman, in my opinion, the issue of bioequivalency is currently being overdrawn. As we have learned more about nonequivalency problems, it has become clearer that they are limited in number and are manageable. And, again, I think the digoxin story is a classic example of the problem.

If I may speak for a moment to our relationship with other Government agencies. Many Government agencies are involved in the procurement of drugs. An organization called the Intra-Governmental Professional Advisory Council on Drugs and Devices was established to provide these agencies with a forum for the timely interchange of medical-technical information, and, through cooperative efforts, to improve the quality of drugs furnished to the agencies. Types of information exchanged include specifications, standards, and those involving quality control and inspection. The FDA is a charter member of this council.

Working groups have been established within the council for in-depth exploration of appropriate subjects and areas. These groups meet every 4 to 6 months, which provides an opportunity for informal contact and exchange of information of mutual interest.

The FDA supplies the DPSC with copies of FDA daily action reports identifying all seizures, prosecutions, injunctions, and recalls involving drugs. Since September of 1973, we have also been supplying DPSC with unevaluated copies of all notices of observations, the form supplied to all drug firms by our inspectors at the end of inspections. These documents represent the individual inspector's raw and unreviewed observations.

Representatives of the Bureau of Drugs maintain frequent contact with the various Federal purchasing agencies and continually respond to inquiries, both written and by telephone, from DPSC, Defense Medical Material Board, Veterans Administration, GSA, and Public Health Service Stock Pile Management, concerning firms and products. These inquiries generally involve such matters as the adequacy of labeling, "new drug" status of drugs, FDA inspectional and laboratory results, and tests, procedures or other data in New Drug Applications that have been submitted to us.

In addition, when a drug is to be recalled from the market and we determine from distribution reports that the firm has supplied the drug to DPSC, VA, or other Government agency, we notify that agency of the recall. It is then the responsibility of that agency to insure appropriate recall of the drug under its control.

When we receive a report through our Drug Defect Reporting System, the DPSC is notified whenever the report originated from

a Federal hospital or other Federal installation, and also where a Federal stock number is part of the labeling of that product.

Again, as you heard earlier, we have completed actions to implement the recommendations of the March 1973 GAO report on Enforcement of Good Manufacturing Practices for Drugs. We have developed a monitoring system to identify, first, new drug firms that require inspection; second, existing drug firms that fail to reregister for a current year; and three, firms that require inspection to fulfill a statutory requirement for biennial inspection, as we discussed a few minutes ago.

In addition, FDA has revised the Administrative Guideline for GMP's to provide more specific guidance to FDA personnel in determining the need for regulatory action subsequent to a GMP type of inspection. Now, that guideline is under current consideration for further revision.

The more recent GAO report in December of last year on Improving the Federal Procurement of Drugs recommended that the separate quality assurance activities of the DOD, the Veterans Administration, and the FDA, should be consolidated into a single organization. We believe this to be a sound recommendation that will enhance the efficiency of the Federal quality assurance efforts.

Senator NELSON. Is that recommendation being implemented?

Dr. SCHMIDT. Yes, sir. We have begun, we have proceeded perhaps a little further with the Veterans Administration, in part I think because it is a smaller operation. We have a general agreement with the Veterans Administration to have us provide for them drug quality assurance. Indeed, with the VA we have been doing drug analyses for them for a long time.

With the Department of Defense, we have been talking with officers of the Department, and I believe have secured general agreement that the FDA can and will provide quality assurance. We do not have specific details worked out as yet. However, I will put it in the category of a general agreement to agree.

Senator NELSON. It is your expectation that the responsibility for quality assurance for the DOD will be assumed by the FDA?

Dr. SCHMIDT. We believe this is a proper thing to do. We believe we can do it, and we believe that the DOD agrees.

There are probably two principal areas that I will wish to see adequately spelled out before I will be happy with any arrangement we might come up with. The first area regards purchasing. I think that we should and can and will see to the quality assurance, but I want to be assured that we do not get involved in the actual purchasing of the drugs and the setting of purchasing specifications, which I think is kind of another question.

The second area is one that you have already touched on, and that has to do with the special requirements that Mr. Feinberg mentioned in his speeches. I am cautious in this area because I feel, first of all, I do not know enough about the special requirements to speak comprehensively and wisely to them. In general, we feel that the quality of drugs and the safety of drugs is the same thing for the military as it is for the civilian population. And if

indeed there are requirements over and above our present compendia or other requirements for drugs that are laid down by the DOD, and these are legitimate, then we should make the requirements for drugs that are issued generally to the population.

Senator NELSON. Well, do you have any indication that the DOD has any standards or requirements that exceed the compendial requirements?

Dr. SCHMIDT. I just have a series of questions about whether or not the requirements really reflect on the quality of the drug or not, or reflect on some more or less arbitrary requirements that are laid out by the DOD for some special purpose of their own.

Now, there may well be, I suppose, some packaging requirements for shipment of drugs to Timbuktu or wherever, that really do not have to do with the quality of drugs. But in general I do not see the need for two standards of drugs, one for the military population and one for the civilian.

In short, we feel that the FDA is the most logical focal point for the quality assurance responsibility of the Federal Government, and I mentioned we have been talking to the VA and the DOD recently about consolidating these efforts, and we requested from the Department of Defense and the Veterans Administration information as to precisely what resources they now expend for drug quality assurance. We expect that within 30 days of receipt of such data, as well as data involving any particular quality requirements they may have, we can prepare and circulate a program in both agencies that will give them the assurances that they can legitimately require that we can in a timely fashion meet their needs.

At the present time, we direct essentially all of our human drug budget, which is approximately $43 million to $44 million to assuring that the drugs in the marketplace are safe and effective. During the last 2 years we have analyzed thousands of drug samples in both certification and surveillance programs and have inspected 97 percent or 100 percent of those manufacturers of human prescription drugs who are responsible for about 95 percent of the marketed drugs.

We believe that the impact of our quality assurance programs on the drug industry has made that industry one of the most quality control conscious industries in the country. This has resulted in a drug supply for this Nation that we believe to be of the highest quality in the world.

We plan to take any necessary measure to strengthen further our quality assurance program in the months ahead. We know we will find problems in the future. Indeed, this is to be expected. When they are found, however, we will correct them, and thereby take one more step toward the goal of a consistently and uniformly high quality drug supply.

Mr. Chairman, we will be very happy to respond to any questions that you or the staff members may have.

Senator NELSON. Thank you, Dr. Schmidt.

As you know, for quite some time a representative of the DPSC, Mr. Max Feinberg, has made public statements which, if true,

would tend to cast doubt on the quality and vigor of FDA's quality assurance program. The Pharmaceutical Manufacturers Association has widely quoted Mr. Feinberg's statements and relied heavily on them in opposing Secretary Weinberger's proposals for drug reimbursement costs.

Mr. Feinberg has testified before State legislative bodies in opposition to the repeal of the antisubstitution laws. This subcommittee has asked the DOD for material to support Mr. Feinberg's charges. This material will be placed into the record of these hearings at the appropriate place. A copy of this material was also given to the FDA and others for comment and analysis.[1]

In addition, members of the office of compliance of the Bureau of Drugs visited the DPSC in Philadelphia to ascertain precisely what kind of data could have been the basis of Mr. Feinberg's many speeches and articles.

We would like to have you discuss this matter and these data in detail. For example, Mr. Feinberg stated that: "We develop definitive product specifications which often exceed official or commercial standards."

On the basis of the material submitted to you, would you please tell us the significance of these so-called extra requirements and the kind of drugs to which they are applied. Have any complaints about drugs or their manufacturing plants been submitted to the FDA by the Defense Department in the past 5 years?

Have they ever resulted in FDA action? In other words, has DPSC ever given you information sufficient to bring about an action on your part?

Given the information you have about DOD from the data they submitted to us and your examination of data in Philadelphia, how would you compare DOD's quality assurance program in size as well as quality with the FDA's? How significant really are DOD's activities in this field?

Would you mind commenting on that?

Dr. SCHMIDT. Mr. Chairman, I might make first just some general comments, and then if there are areas that you wish to explore in a more detailed fashion we can double back on it.

I myself became aware of these particular speeches by reading them, and it may be that my scientific background helped me in evaluating them as I read them. But I was not particularly alarmed or upset by the speeches myself, because they were general. There were no specific figures or times or any solid evidence contained in the speeches.

Mr. GORDON. Excuse me, Dr. Schmidt. There were some specific figures with respect to rejection of drugs and manufacturing plants.

Dr. SCHMIDT. Well, again, I guess I began by saying that perhaps my having read scientific literature for 20 years or more kind of helped me with this, because if I see a figure that says 43 percent, and it does not say 43 percent of what, I generally skip to the next article.

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[1] See page 9978.

Three, as you know, is 60 percent of 5. And 300 is 60 percent of 500. And there is a difference of several hundred there. And in general this does explain why I was not alarmed by what I read. I was somewhat alarmed, however, that the PMA and others began quoting from and basing testimony on what I considered to be quite insubstantial grounds. And I think that any critical reader of the speech or anyone knowledgeable in the area would realize that you really cannot say too much definitive on the basis of this.

For example, it is stated that we do not inspect 100 percent of drug firms every 2 years. And of course we do not. We cannot. There is no way we can.

Senator NELSON. But you do 100 percent in 2½ years?

Dr. SCHMIDT. Well, we do do that. We do 100 percent of inspections of those firms that manufacture 95 percent, at least of prescription drugs. We do many more inspections of those drug firms in which we know there are problems. So that the main question I have in regard to what Mr. Feinberg says is, what relationship does all that he says bear to the quality of drugs.

You mentioned early on his making the point of their standards exceeding compendial standards. Well, fine. My question is, what relationship do the standards they set, exceeding compendial standards have to do with the quality of the drug. And from what I have seen of their standards, they either do not relate to the quality of the drug at all or they may relate to packaging or some legitimate need of the military.

I did send a team to visit the establishment and Mr. Feinberg was generally cordial and helpful to our team in reviewing what he does and how he does it. And I think perhaps, was a little embarrassed after he had information provided to us that there were inaccuracies in his speech. He still did not change the speech. He apparently had some secretarial problems that prevented the speech from being retyped.

The inspections, the big point about GMP's, I think, failed to find evidence to support his charges, and he has failed to provide us with evidence that support the charges in his speech that his inspections demonstrate our failure to maintain quality. The number of analyses of drugs done there is very small, and the principal analyses are done, not on production runs of drugs, but on special runs of drugs done by a new company wishing to make the drug, in many instances a company that has never made it before. And his 45-percent rejection rate is of a relative handful of drugs on a nonproduction run by companies, some of which have never made it before and have never sold drugs to DOD before.

Mr. GORDON. Dr. Schmidt, may I interrupt for a moment?

Here is the kind of statement the public has been hearing—I am going to quote from his speech:

> The rejection rate on DOD plant inspections is 45 percent, and the rejection rate on precontract award samples inspections is 42 percent.

It does not say percentage of what or anything. Now, when a lay reader sees this, he is going to be alarmed, do you not think, when he sees this?

Dr. SCHMIDT. Well, an uncritical reader may very well be misled by those statements.

Mr. GORDON. Here is another statement:

> Based on my experience of drug plants, it is my firm conviction that the primary problem lies in the fact that many producers in the business today are in gross violation of FDA's good manufacturing practices regulations. Those same firms are manufacturing drugs on a daily basis.

Here is another quote:

> We have seen totally unacceptable housekeeping conditions involving dirt, filth and rodents. We have reviewed production records that showed noncompliance with the company's own standards. We have found instances where ingredients in finished products are not adequately tested.

If a person reads or hears this, I would think he would be alarmed. I certainly would.

We asked the DOD for evidence to support these statements. We submitted the information to you.

And what do you have to say about it?

Dr. SCHMIDT. Well, many, many of the inspections that they have done, I think principally the inspections that he is quoting from there, were not done when the company was in full production. I really do not know on what basis the author of those statements is convinced. He would have to speak for himself in those matters.

I think it is true, I could go into the kitchen of the home of every individual in this room and shut it down for being unsanitary. I made a specialty of that when I was in the service, and I think that as the GAO found out I could probably go into drug firms today and find some violation of GMP in some plant at some time.

If we find major and serious GMP violations we take corrective actions immediately on these.

Part of his statement, and I think part of what he was able to put together with other things to convince him, was the statement in the GAO report that in some instances we have not taken action when a "critical" GMP violation was discovered. We had a problem with the GAO and the definition of the word "critical." We supplied the GAO with proper definition of the word "critical" which did not mean in that report what it sounded like, that we were ignoring critically important GMP violations.

It is true that we make informed judgments and wise judgments, hopefully, from time to time not to shut down a plant for any GMP violation. We could readily shut down every pharmaceutical plant in the United States if we went in, as I would in your kitchen if I wanted to find dirt. So that, you know, there is an element of truth in some of these statements. But again, the relationship of these statements to the quality of drugs is inapparent to me, and many of the statements are unsupported totally by any evidence, either in the paper or by any evidence that he has provided to us.

I mention the sampling; the program includes, as you know, drug sampling and inspections, and the numbers of these both are small, and when these are done raises a question, because some of the inspections are not done when the plant is in operation, and therefore would have no meaning to the quality of the drug produced.

As far as the statements he makes about bioavailability, we spoke of one or two or those already, and I will just say that he has really provided us with no specific special evidence of bioavailability problems that he has that we do not have. The drugs that he mentions as having bioavailability problems generally everybody knows and has known about the problems, and indeed, we have moved to correct the majority of those problems.

Mr. GORDON. Concerning the "definitive product specifications" he talks about, he says they often exceed official or commercial standards.

Now, on the basis of the material submitted to you, would you tell us the significance of these so-called extra requirements?

He makes a big deal out of this.

Dr. SCHMIDT. Well again, I would just divide them into two categories. There may be some that are required by the Department of Defense that do not relate to drug quality, but rather relate to shipping problems or maintenance problems in an extremely hot, humid atmosphere or some such. We would need to look at those carefully, and I think work out with their purchasing people the kinds of specs that are legitimately required by the DOD which do exceed compendial standards.

There is another group as I look at them, and I will ask Dr. Crout or Mr. Loftus to comment on this in a moment, that do not seem to us to relate to drug quality at all.

Do you have a comment?

Dr. CROUT. Yes. If we have to base an answer to your question on what was submitted to us through you, then it is quite clear that most of the violations of GMP's as we see them are relatively trivial and unrelated to the quality of the drug. It is quite clear that these specifications relate to the needs of a purchaser, rather than to a general assurance of quality. I think we are hesitant only in that, as Commissioner Schmidt mentioned before, our communications with DPSC have not been strong through the years. We are in many respects still in contact with them on the issue of what is it exactly they do.

I do not mean to quote back to you something that you already know about. But I think we can all read down here and read descriptions of violations. You know, washroom was not clean; no receptacle for used towels; a loose, slightly soiled roll of towels was available for drying hands; paint had flaked from the ceiling on many locations; dust and refuse was found on the floor in work areas.

Again, these are true. But an in-depth GMP inspection is quite a different thing. One is really interested in the recordkeeping of a firm; evidence of repeated weighings, of two people weighing something carefully and checking each other; evidence of analytical procedures at various steps along the way; evidence that the temperature during a cooking procedure was indeed maintained for the right number of minutes at the right temperature. Those are the kinds of information you get out of a GMP inspection.

Now, there is not anything like that in anything here. This is a superficial look in and glance kind of an operation. We are not say-

ing that the DPSC does not do a good GMP inspection. But if you ask the question on the basis of this piece of paper that you have supplied to us, the answer is "no" in our view.

Mr. GORDON. Well, that is what they supplied to us in response to our request.

Now, Mr. Loftus was in Philadelphia. Perhaps he might tell us what they are doing there and the significance of what they are doing.

Mr. LOFTUS. Yes, sir. Mr. Chairman, when I got these answers I sent wires out to six of our field district offices and I said, the Department of Defense has furnished us this information. DPSC has furnished us this information. They furnished it to the Nelson subcommittee, and we sent it out to you. What did you do about it? What did you think of it in your judgment?

These people are professionals. They have been in Food and Drug a long time. They are management people. They have been in a lot of drug firms. And I have wires back from four of those districts, and I have telephone reports from the other two. I believe there are 25 of these reports here, and I think I have 18 or 19 reports back. Some of them we never got. One involved a foreign firm that we did not inspect.

But what comes out of it is that in one instance the district said in response to a recent inspection that was reported to us by DPSC, yes, Mr. Feinberg was right. We have documented what he said and we are going to do something about it. You will get a regulatory recommendation of some sort. I got that telephone report.

In the main, they said, we either made an inspection as a result of the report or we had already made an inspection or we evaluated it, and in our opinion it was either not a GMP problem at all, or if it was, it was a minor GMP problem.

What I am saying to you is that representatives of six different field districts of the Food and Drug Administration—I am talking about management people who have been in the Food and Drug Administration a long time—arrived at value judgments that in the main—not in every case, but in the main—these are relatively minor things.

Now, I do not want to put this, or take this thing out of perspective. Nothing, nothing is completely minor. What we aim for, Mr. Feinberg aims for, is absolute perfection. Absolute perfection does not exist in a drug firm. It does not exist in this room. It does not exist in my home or yours. But we aim for it. We do not minimize and we do not belittle what Mr. Feinberg has reported to us. We are glad to get it.

As a matter of fact, when we make an inspection, at the end of that inspection our inspectors do precisely what Mr. Feinberg's inspectors do. They write down on a piece of paper a last of everything they find wrong in their opinion with the firm, including, if it is so, an unscreened window that has been locked for years. They will report that, too, for the edification and the knowledge of the management, a goodwill gesture. We do this. We are not required by law to do it. We do it as a simple gesture of goodwill toward the industry, here is what our inspector found. Look to it.

But when it comes to whether or not the law has been violated and the law says that drugs must be manufactured under current good manufacturing practice, and the courts have held that this current good manufacturing practice is articulated in the regulations under part 133 in the Code of Federal Regulations, title 21, what we call GMP regulations.

If there is—I hate to use these adjectives, because they get us in trouble—but if there is a significant deviation from GMP, if a reasonable man who knows something about drug manufacturing would be led to believe or would believe that something is going on in that firm might cause that drug to become adulterated, FDA has an obligation, a duty to act and act now. Our position is that we do.

The allegation of Mr. Feinberg's speeches—and it is throughout many of his speeches, throughout the years—that many drug firms in the United States operate under gross violation of FDA's GMP's is his own private, personal opinion. He believes this. I have had conversations with him that convinced me he believes this deep in his soul.

I do not agree with him, nor do our people in our Washington headquarters or in the field.

There is a situation which DPSC follows—I have no quarrel with it—the military sets its own rules. We do not interfere with them—in which for some reason a firm that wants to bid and is not on a bidders list must pass a pre-award survey inspection. The preaward survey inspection requires absolute perfection. I do not understand this, but I do not quarrel with it.

For some reason, again that I do not understand, once a firm has a contract to manufacture drugs, the rules change and the absolute perfection parameters disappear. Proof of this is the fact that samples that they analyze—what do they call them, first production —or samples that they analyze of drugs when a—first article samples—when a production just starts under contract are 20 percent defective. These are their own figures.

I do not know how they could be 20 percent defective while they are under inspection by the Department of Defense—they call it DCAS inspector—if they have absolute perfection. It does not make sense.

Again, I do not want to, and the Commissioner has tried very hard not to deprecate the requirements of as much perfection as you can possibly get. This is what we are working for. We are not trying to pooh-pooh good housekeeping. We want good housekeeping in drug firms.

Senator NELSON. But if I understand your testimony and that of the Commissioner: One, that you have considered their criticisms on good manufacturing practices in the main to be insubstantial; two, that if there was any violations of good manufacturing practices that affected the quality of the drug, you would consider that a major, important matter, and if they did not affect the quality of the drug, you may require them to correct it, but that you do not consider it a substantial matter.

Is that a roughly correct statement?

Mr. LOFTUS. I would only qualify it, sir, to say that might, in our judgment, affect the quality of the drug. If it is established that the quality of a drug is affected, there is no question but that we would take action.

Dr. CROUT. May I add one other point that I think we are making. And that is we think that based upon the man effort that goes into an inspection, the DPSC, like everybody else must rely on the FDA inspector for the indepth inspection of plants for GMP's.

Senator NELSON. Because they do not have the personnel to do so?

Dr. CROUT. And simply do not put the time into it, based upon—they have one inspector in a plant for a couple of days. You cannot figure out whether an enormous operation is making drugs by GMP's with one man in a couple of days. It just takes more work than that in a big plant.

Senator NELSON. What is the dimension of this inspection made by FDA? I realize it varies, but one man in 2 days could not inspect a major operation. If it is a major operation, what do you generally consider a necessary commitment of time and personnel to make an adequate inspection?

Dr. CROUT. This has varied from time to time depending on the inspectional program; but let Mr. Loftus speak to that, and I think maybe the IDIP program would be a good model.

Mr. LOFTUS. Yes. It would vary, sir, depending on the size of the firm and the type of the operation. Are they making tablets, are they making a particular type of tablet. For instance, the problem, the GMP problem, the manufacturing quality control problems with regard to meprobamate manufacture or aspirin manufacture would be considerably different from the manufacturing problem involving digoxin or prednisone or something like that, where the ratio of active ingredient to inactive ingredient in the one case is extremely high and in the other case is extremely low.

You would have tablets in both cases, but one inspection you might do in a couple of days, another inspection might take a week.

You get into a manufacturer of parenterals. Whether you are talking about large volume parenterals or small volume parenterals, these are the type of inspections you do not make in a couple of days.

Dr. Crout alluded to what we call the IDIP program. We had a few years ago a program, as we call it, the indepth inspectional program of the entire prescription drug manufacturing industry. I say entire, but I do not deal in absolutes. I think there were a few that we missed, but we got most of them. And some of those inspections lasted as much as 6 months, and we did not leave those firms until—any of those firms—until our district people were satisfied insofar as human beings can be satisfied that those firms were actually producing prescription drugs under proper GMP conditions.

I have years ago been an inspector myself, and it was nothing to spend a week or 2 weeks in a parenteral plant, to spend several days or a week in a tablet plant, depending on the size. You certainly would not spend 2 weeks or a week in a little mom and pop

drugstore that works up some sort of a little salve for the local business.

I am told, or we are told by Mr. Feinberg and his colleagues, we were told this when we visited them in January, that DECAS has some 20 full-time drug inspectors. I checked that in one of his speeches that he made in 1972, and he used the figure 20. More recently, in my dealings with Colonel Huyck and others of the Pentagon, I have been told that figure is a little higher.

But they have some 20 full-time drug inspectors, 5, 6, or 7 of whom, depending on day-to-day problems, I suppose, are what they call resident inspectors. For instance, Lilly might have a resident inspector full-time in the plant. I do not know if that is so. But Lilly might have a resident DECAS inspector full time.

But in the main, their drug inspectors spend very little time on—it is pretty obvious that they spend very little time in drug plants, because you cannot stretch 20 inspectors very far.

Senator NELSON. How many does FDA have?

Mr. LOFTUS. FDA has—do you know, Dr. Crout?

Dr. CROUT. I might comment on the scope of our programs, yes. There is in the Bureau of Drugs headquarters for fiscal year 1974 an assigned 1,026 people. In the field the drug programs involve 839 people.

Senator NELSON. 839 who are inspectors?

Dr. CROUT. Inspectors and analysts.

Senator NELSON. And analysts?

Dr. CROUT. And analysts and chemists. Now, inspectors will be about a third of it, I suspect.

Mr. LOFTUS. About half.

Dr. CROUT. About half.

Senator NELSON. About 400 plus?

Dr. CROUT. And we would consider of all of these people that roughly, I would say, one half of the whole Bureau's programs are in the quality assurance area, another 40 percent perhaps are in the drug review area; and there is some spinoff, as you recognize, and some linkage between the drug application review and quality control areas. So really, 80 to 90 percent of everything we do is in one of those two areas. And——

Senator NELSON. You mean the whole Agency?

Dr. CROUT. The whole Bureau of Drugs.

Senator NELSON. Oh, the whole Bureau of Drugs.

Dr. CROUT. And the other things——

Senator NELSON. With over 1,000 people in the Bureau?

Dr. CROUT. The other things involve medical communication, or adverse reactions reporting. They are small, and they pick up about 10 to 20 percent of our resources.

So we are talking about a total operation of 1,800 people; something like 40 to 50 percent of that entire effort is in the quality assurance area.

Now, the DPSC, as we understand it, is something on the order of 20 to 30 people. We are talking about a difference of 50 fold or something between us. That is why I say there is no question that

simply on a resource basis the primary inspectional mechanism of the Federal Government that monitors the drug supply in this country is in the Food and Drug Administration.

Mr. GORDON. How about laboratory facilities—that is, testing of samples and so forth—how would you compare DPSC? DPSC claims it does not have any M.D.'s. Now, the FDA has M.D.'s, pharmacologists, pharmacists (many at the doctorate level), toxicologists, chemists, biochemists, all kinds of specialists—does it not?

Dr. CROUT. Correct.

Mr. GORDON. Now, compare that with what DPSC has.

Dr. CROUT. Well, I think you have enumerated what we feel to be our resources. I cannot compare that because I personally do not know exactly what the personnel of DPSC are.

Mr. Loftus, do you?

Mr. LOFTUS. The DPSC—neither DECAS nor DPSC has any pharmacologists, toxicologists, medical people, these kind of thing.

Mr. GORDON. Or M.D.'s?

Mr. LOFTUS. Or M.D.'s. The DMMB, Defense Medical Materiel Board I believe is what they call it—this is composed of the Surgeons General of the three services—have advised DPSC to rely on FDA for bioavailability information and support. We are told this by Mr. Feinberg.

I believe you have also been told this by the Department of Defense in answers that they submitted to you.

That laboratory—DPSC has a nice little laboratory in Philadelphia. It is a good lab, and they have got good professionals there; but they have from 8 to 9 analysts, one of whom is a microbiologist working on human drugs.

Now, I do not know how much of their time is spent on drugs, but let us say all their time is spent on drugs. They also work on medical devices and other medical things.

Mr. Feinberg told us when we were there in January that that laboratory—Mr. Feinberg and/or his staff told us in his presence that that laboratory analyzed from 600 to 700 samples of drugs in fiscal 1973. Of that 600 to 700, more than 600 involved preaward sample analyses and first article sample analyses.

So what this tells us is that that laboratory analyzed somewhere between 0 and 100 finished product samples in fiscal 1973. We do know from information that your committee obtained from the Department of Defense that there were something more than 400 samples analyzed in fiscal 1973 on contract by other persons other than their own lab.

But it all comes down to a rather miniscule effort. Again, it represents a difference in philosophy between the approach that FDA takes to quality assurance, and the approach that the military takes.

I am not faulting it or criticizing it in any way. But the approach is that when they are satisfied that a particular drug firm can make drugs well, then everything is fine. If they have an inspector in the plant fulltime, which is the case with very few or part-time—and I do not know what that part-time comes down to—

once that inspector is satisfied that the output of that firm is fine, that is it; they accept the drug.

I have no quarrel with that either, because we, too, have to rely on the drug firm. But it would seem, and it is FDA's position, that a good quality assurance program operated by Government has to take into account post-manufacture analysis of finished product. It just has to be.

Mr. Feinberg said in one of his speeches that the inspector has the right and the duty to utilize the drug firms' laboratory facilities to make whatever laboratory analyses he thinks are indicated.

I said I have difficulty with this, because I know in my own experience that when I was a drug inspector I would have been thrown out of the plant if I tried to use somebody's laboratory facilities to do analyses. He agreed, and he said no, they do not do assays. They do not do content uniformity. They do not do sterilization. But they watch the professional in the firm who does.

We asked them what happens if a piece of equipment is out of calibration. Obviously, the results are going to be wrong. What check have you here? And he says, we will be wrong, too.

Okay. I was satisfied with that, but it does not help.

Senator NELSON. But your inspectors check the calibration, do they?

Mr. LOFTUS. Well, they may or they may not, but they certainly do check the finished product.

Senator NELSON. Well, do they have the qualification to check the calibration of the material?

Dr. SCHMIDT. Mr. Chairman, I think the point here is we do not rely on their laboratories at all; and that is not whether the issue is in or outside of calibration. What we do is take the drug, take it to our own laboratories where we know the calibrations are accurate, and do the analysis of the finished product.

The point is that he is relying on their labs but we do not. We rely on our own laboratories.

Mr. LOFTUS. The qualifications of analysts vary. The way to check that is to check the output of those analysts.

Dr. CROUT. Again, if you are interested in a comparative size figure, I can supply or will supply a more precise one. But we run on the order of 10,000 drug analyses in a year.

Senator NELSON. Is this against the 800?

Dr. CROUT. One hundred, as I understand. This is on marketed products.

Senator NELSON. They do about 100, and you do about how many?

Dr. CROUT. Ten thousand.

Senator NELSON. And these are done in your own labs?

Dr. CROUT. Yes.

Mr. GORDON. Do I understand correctly that they do not do any testing of finished products?

Dr. CROUT. Again, I think we have to keep in mind that our objectives are somewhat different. We run a monitoring system designed to assure to the extent possible that drug manufacturers are making a quality drug product. They are running a system

designed to see that the drugs the military buys meet whatever standards they choose to set up.

Now, one of the things they do is say to a manufacturer if you want us to buy your drug, submit us a sample of what you can make. And the manufacturer may never have made it before. He may not be marketing that drug. And those are the ones they apparently, as far as we can tell, put most of their laboratory investment into testing. And therefore, they are dealing with a different population of drugs than we are dealing with. That is why they get defect rates orders of magnitude different than we see. Their testing is done for a different purpose.

Senator NELSON. I take it from your comment, Dr. Schmidt, on page 14 then, that you agree with Dr. Edwards' statement made on February 1st before the Health Subcommittee: "Nevertheless, based upon present knowledge, I believe that with very few exceptions any drug prescribed in this country will give the same therapeutic results as any other chemically equivalent product. . . . we regard this issue as limited, well recognized, and manageable."

Do you agree with that?

Dr. SCHMIDT. Yes, sir. I do.

Senator NELSON. Then you stated on February 1st yourself, you estimated that there may be "10, 12 or 14 drugs" which may have bioavailability problems.

Is that correct?

Dr. SCHMIDT. Yes, sir.

Senator NELSON. Can you give us the number of drugs which in the opinion of the FDA present bioavailability problems at this time?

Do you have them along? If not, can you submit their names?

Dr. SCHMIDT. Yes, sir. My comments were based on a comprehensive analysis of list of drugs that have been mentioned in articles, drugs that are in our own files, and so on, that are purported to have bioavailability problems.

I need to take a moment to define carefully this list, because the proper assessment of the bioavailability problem includes answering the questions about precisely what drug one is talking about.

We ask the question in how many cases have two or more drugs which contain the same active ingredient, the same chemical, which would include the same salt which is in the same dosage form, that is, in pills as opposed to one pill and one capsule, in the same amount—that is, the same amount of the ingredient—in which dosage form meets all official compendium standards.

Now, I think it is only fair to say that there are bioavailability problems with a drug when one can say that he is dealing with two things that are the same salt, in the same amount, and the same dosage form, both of which meet compendium standards.

When we analyze then the drugs that there have been shown bioequivalency problems with that meet those requirements, we come up with a list of 12 or 13, which include—would you like me to read the list?

Senator NELSON. Sure.

Dr. SCHMIDT. Acetazolamide, acetylsalicyclic acid in two forms. This list is 13 drugs, and 2 of them are acetylsalicyclic acid in 2 different forms.

Ampicillin, chloramphenicol, both of which, of course are antibiotics; digoxin, which we have mentioned; diphenylhydantoin pediatric suspension form; nitrofurantoin; oxytetracycline, which is another antibiotic—these, of course, are batch-tested; phenylbutazone.

Senator NELSON. Not tetracycline itself, but oxytetracycline?

Dr. SCHMIDT. I am sorry. Would you say that again?

Senator NELSON. You mentioned oxytetracycline. You did not include the parent drug, tetracycline.

Dr. SCHMIDT. The antibiotics we are batch testing, as you know.

Senator NELSON. You mean this one teracycline——

Dr. CROUT. No. Tetracycline is also on the list. We are coming to it.

Dr. SCHMIDT. I mentioned oxytetracycline, then phenylbutazone; riboflavin sugar coated tablets; then tetracycline hydrochloride, which is a plain tetrachloride; and then finally, trisulfapyrimidine, another pediatric suspension.

Now, I would again hasten to add that digoxin and the antibiotics and so on are batch tested, so that while there have been substantiated bioequivolency problems, we feel these problems are being managed.

When I said in my testimony that I felt that the bioequivalency area is being overdrawn, what I mean by this is that a lot of enthusiastic people are in the field hunting up names of drugs that have been suggested that might have bioavailability problems or whatever.

I think that one must be precise, and logical, and scientific in his thinking about such problems. And I have been unsuccessful in finding any large mysterious problem area that people hint at in their testimony about drugs.

Mr. GORDON. Well this has become a WPA project for many people. It puts them to work to try to dig up these drugs.

Excuse me, Commissioner. Did you say that these drugs that are on the market—say tetracycline—may present a bioavailability problem. Those that are on the market, however, are bioequivalent, are they not?

Dr. SCHMIDT. Well, this list is a list of drugs which we feel meet our requirements for having had a genuine bioequivalency problem. This is not a list of current problems.

Mr. GORDON. Oh, not a list of current problems.

Senator NELSON. Is it feasible for chemists, pharmacologists, scientists, to make an educated guess in advance, about what kind of a compound and what kind of a form might likely present the bioavailability problem?

Dr. SCHMIDT. Yes. And I think very importantly we have in our regulations—and again, I mentioned that we will deal with this problem—dealt with this issue—perhaps I could ask Dr. Crout very briefly to——

Dr. CROUT. Yes. I think the answer is yes. And there is increasing data in that area. It is a little easier, I think, to specify the kinds

of drugs which are perhaps unlikely to have a bioavailability problem than it is those which are likely to. And in general, the water-soluble compounds and those which go into solution readily in the stomach, do not have bioavailability problems.

I would like to, as a general principle, state something that I think has caused a lot of confusion. There are two issues that I think are being mixed up at the moment by a number of people; and they should not be mixed up for us to properly consider public policy.

One issue is are there lots of examples of a drug in different dosage forms, in different crystal sizes, and so on, and different salts, which produce different blood levels? The answer to that is yes. There is an enormously expanding literature to the effect that the same active molecule, if you compound it differently and put it in the form of a different salt, if you put it with different binders in a tablet and so on, that you may get different blood levels. Now, that is being done purposefully by people in biopharmaceutics who are experts, for the purpose of identifying the principles of how to compound a good tablet.

Now, you cannot mix that literature up with another problem. The other problem is: If there are already well-known standards for the manufacture of a drug, and if two manufacturers are trying to make the identical thing, absolutely identical—same salt, same dosage size, same tablet, everything—how often—excuse me—and the products they make meets all the compendium standards, how many examples are there then that unsuspectingly those two products were different?

Now, that is the issue in public policy. And that is the short list which the Commissioner just gave you.

Now, I think there are some—they include both the Pharmaceutical Manufacturers Association and the Academy of Pharmaceutical Sciences—who are tending to mix up those two issues and tending to take the large literature, demonstrating a lot of differences between drugs when they are in slightly different dosage forms, and say that is relevant to the second issue, which is two manufacturers trying hard to make a drug, and they both meet identical standards. And those should not be mixed up.

I want to make it very clear, because otherwise the list we gave you is subject to attack. But we do not think it is subject to attack if the attackers will stick by the ground rules we just gave you—namely, identical product, identical salt, made by—all meeting compendium standards, and the difference between them is unsuspected.

Senator NELSON. Is there not a further question, and that concerns a drug that achieves a different blood level at a different rate, but that this difference has no therapeutic significance.

Dr. CROUT. Yes. That is possible; indeed, it happens all of the time. And that is a matter then of judgment on whether these two different forms are identical. But that is a judgment of man that applies to all issues, if you will, and indeed, to all drug issues besides bioavailability.

We have to make those kinds of judgments, for instance, on clinical data or on efficacy also.

Senator NELSON. Well, you had the case of chloramphenicol.

Dr. CROUT. Correct.

Senator NELSON [continuing]. In which the brand name product Chloromycetin achieved a higher peak level much more quickly than all of the others, with the blood level dropping off much more quickly. When you look at the charts, one of the other products looked like a bell curve while the other one went up quickly—with a high peak and went down precipitously.

Dr. CROUT. Yes.

Senator NELSON. Now, at the time the FDA required the other companies to comply with the blood level achieved by the Chloromycetin; and there has been no evidence, and I have heard of none since, that the Chloromycetin was more effective therapeutically than the others. But since it had been in the marketplace for many years; physicians had dealt with it; and it was an effective drug for the purpose for which it was indicated, therefore you required the others to achieve the same blood level.

If it had been the other way around, that the Chloromycetin had a bell curve level and the others achieved a higher level and went down, I assume you would make the same decision, make them meet that same blood level—not based upon the evidence that one was more efficacious than the other, but based upon the fact that you knew one was effective and had been in the marketplace.

Is that correct?

Dr. CROUT. Correct.

Mr. GORDON. Concerning the extra requirements that the DPSC has for some of the drugs which you examined, would it be fair to say that some of the requirements there, which may not have medical significance, tend to undermine competition? For example, the use of certain expensive equipment, which may not have any medical significance, would at the same time exclude many small companies from supplying drugs to the DPSC?

Dr. SCHMIDT. In looking over the requirements I would think that some of them would have the effect of limiting those that could meet the standards, yes.

Mr. GORDON. Even though they may not have medical significance?

Dr. SCHMIDT. Yes.

Senator NELSON. Thank you very much, gentlemen, for your very valuable testimony.

Dr. SCHMIDT. Thank you, sir.

(Whereupon, the hearing in the above-titled matter was recessed at 1:05 p.m., to be reconvened the following day, Thursday, Feb. 21, 1974, at 10 a.m.)

[Testimony resumes at page 10163. The information referred to by Senator Nelson follows:]

MATERIAL SUPPLIED BY THE NELSON SUBCOMMITTEE TO THE FDA AND OTHERS FOR COMMENT AND ANALYSIS

ALAN BIBLE, NEV., CHAIRMAN
JOHN SPARKMAN, ALA. — JACOB K. JAVITS, N.Y.
GAYLORD NELSON, WIS. — PETER H. DOMINICK, COLO.
THOMAS J. MCINTYRE, N.H. — EDWARD J. GURNEY, FLA.
SAM NUNN, GA. — J. GLENN BEALL, JR., MD.
J. BENNETT JOHNSTON, JR., LA. — JAMES L. BUCKLEY, N.Y.
WILLIAM D. HATHAWAY, MAINE — WILLIAM L. SCOTT, VA.
JAMES ABOUREZK, S. DAK. — WILLIAM V. ROTH, JR., DEL.
FLOYD K. HASKELL, COLO.
DICK CLARK, IOWA

CHESTER H. SMITH,
STAFF DIRECTOR AND GENERAL COUNSEL

United States Senate
SELECT COMMITTEE ON SMALL BUSINESS
(CREATED PURSUANT TO S. RES. 58, 81ST CONGRESS)
WASHINGTON, D.C. 20510

January 17, 1974

The Honorable James R. Schlesinger
Secretary of Defense
Department of Defense
The Pentagon
Washington, D. C.

Dear Mr. Secretary:

The Monopoly Subcommittee of the Senate Small Business Committee has been studying various aspects of drug procurement by agencies of the Federal Government. In connection with our study we would be very grateful if you would send us the information requested on the attached sheets.

The Subcommittee would appreciate receiving the requested information by January 30, 1974.

If there are any questions, please contact Benjamin Gordon at the office of the Senate Small Business Committee 225-8489.

Sincerely yours,

GAYLORD NELSON
Chairman
Subcommittee on Monopoly

Attachments

DEPARTMENT OF DEFENSE

1. On what percent of contracts awarded do you do a "pre-award survey" just prior to a specific award?

2. What percent of pre-award surveys are done by DPSC? By DSA?

3. On what percent of contracts awarded do you do laboratory analyses of pre-award samples?

4. How many man-years/devoted in FY 1969, 1971 and 1973 to the inspection of drugs by DPSC? By DSA?

5. What percentage of man-years of inspection time was devoted in the same years to:

Pre-award surveys?
In-process inspection?
Acceptance of product inspection?
Other?
In-store (Depot) surveillance?

6. For FY 1969, 1971 and 1973 how many man-years of laboratory work went into support of the inspection process?

Please breakdown the total laboratory Man-years into:

DPSC laboratory
Contract laboratories
Other (specify)

7. For Fiscal Year 1973 please give the number of people in:

DSA -- overhead assigned to DPSC
Medical Material
DCAS -- Medical Material Support for drugs
Other medical [illegible]

DPSC —

Medical Directorate
Supply Operations
Technical Operations
Laboratory
Overhead
Procurement Directorate
Medical Division
Drugs
Other

8. For Fiscal 1973 give total manpower of laboratory personnel

Chemists
Pharmacists
Support (Specify)
Overhead
Other

9. Please give total DOD annual budget involved in inspection of drugs for Fiscal 1969, 71, 73.

10. Who evaluates the clinical effectiveness data you require from some suppliers?

11. How many M.D.'s are there on the DPSC staff?

Of these, how many are pharmacologists?
Same information for DSA staff.
Do you contract for these types of services? (to determine clinical effectiveness)?

If yes, please name the contractor and drugs studied for years 1969, 1971, 1973.

12. Please list all technical division personnel who have a scientific degree of Master or PhD?

13. For the 150 top drugs -- by dollar volume -- bought by DOD:

Which pharmaceutial companies supplied the information which was incorporated into each specification?

For each of these drugs, give the names of pharmaceutical companies who have been successful bidders on DPSC contracts for each product since original specification was first written. Please give stock numbers, and established and trade names of each product.

14. Number of drug contracts in Europe for the past year? Number of DOD representatives in Europe that inspect drug facilities.

15. In the past several months Mr. Feinberg of the DPSC has publicized certain problems for which the Subcommittee is very anxious to secure additional information. His statement and our questions are as follows:

(a) "The rejection rate on DOD plant inspections is 45 percent and the rejection rate on pre-contract award sample inspections is 42 percent."

Would you please explain exactly how these figures were derived?

(b) "Based on my experience of drug plants, it is my firm conviction that the primary problem lies in the fact that many producers in the business today are in gross violation of FDA's good manufacturing practices regulations. Those same firms are manufacturing drugs on a daily basis."

Will you please supply: (1) the names of the firms; (2) the dates of the "gross violations" of FDA's good manufacturing practices regulations; (3) were

these were reported to the FDA and other government purchasing agencies, and if so, when and in what detail; (4) the exact description of the violation (not a general statement like "poor housekeeping," etc).

(c) "We have seen totally unacceptable housekeeping conditions involving dirt, filth, and rodents. We have reviewed production records that showed noncompliance with the companies' own standards. We have found instances where ingredients and finished products are not adequately tested."

As in the previous question, please supply the names of the companies involved, dates on which violations were found, were these reported to the FDA and other government agencies, and if so, when and how, and the exact description of the violation.

(d) With respect to problems of digoxin tablets -- "This was no surprise to the drug specialists in DPSC because we know of many other examples demonstrating that compliance with laboratory standards is not necessarily indicative of clinical effectiveness."

When did the DPSC drug specialists first learn about the problem with some digoxin tablets on the market?

Was the FDA informed of this problem by your organization and if so, when and how?

Which of your drug specialists first became acquainted with the problem?

-4-

Please name the "many other examples" mentioned. Was the FDA informed? When and how? Give name and title of drug specialists who discovered these problems?

(e) "We develop definitive product specifications which often exceed official or commercial standards."

Please name each product for which such specifications have been developed; the significance for each product of these extra requirements; and the medical purpose served by these extra requirements;

16. Please state deviations from FDA's good manufacturing practices regulations which the DOD considers significant, and which are not considered significant by the FDA? Please identify where there is a difference of opinion.

Who in DPSC makes the determination whether the raw observations are significant?

What criteria does DPSC use?

Does DPSC relate the violation to a particular product? In other words, does the violation, for example, contribute to the contamination of the product?

-3-

RECEIVED JAN 31 1974

ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, D. C. 20301

HEALTH AND
ENVIRONMENT

30 JAN 1974

Honorable Gaylord Nelson
Chairman
Subcommittee on Monopoly
Select Committee on Small Business
United States Senate
Washington, D. C. 20510

Dear Mr. Chairman:

This is in response to your letter of 17 January 1974 in which you requested certain information pertaining to the procurement of pharmaceuticals within the Department of Defense.

Selected manpower and cost data pertaining to prior years was not readily available. Additionally, our accounting system does not provide for a separate breakout of inspection manpower staffing and costs by commodity. The appropriate activities within the department are engaged in obtaining the desired data and it will be furnished to you in the near future.

You will note that enclosure 1 does not contain a response to the question regarding clinical effectiveness data. The following response is provided:

> "The Military Medical Services rely upon the evaluations of clinical effectiveness data as accomplished by the Food and Drug Administration pursuant to applicable Federal Regulations (i.e., New Drug Applications, etc.). There are, however, some exceptions such as drugs developed primarily for military uses, i.e. antidotes for chemical warfare agents, certain anti-malarials, etc. Additionally, on an infrequent basis, the Services have been asked to evaluate studies presented by the Defense Personnel Support Center (for example, bio-availability/clinical effectiveness studies on a few drugs). In the case of these exceptions, the bio-availability/clinical effectiveness data related thereto has usually been evaluated by the appropriate expertise among the professional staffs of all three Surgeons General's Offices."

It is hoped that the information provided will be of assistance in the conduct of your study. If there are any additional questions regarding this matter please contact Lt. Colonel Theodore D. Wood in my office (Tel. 695-4938).

Sincerely,

George J. Hayes
Major General, MC USA
Principal Deputy

Enclosure (1)

QUESTIONNAIRE

INFORMATION REQUIRED BY SENATOR NELSON FROM DEPARTMENT OF DEFENSE

1. QUESTION:

On what percent of contracts awarded do you do a "pre-award survey" just prior to a specific award?

ANSWER:

A pre-award survey is an evaluation by a contract administration office of a prospective contractor's capability to perform under the terms of a proposed contract. Such evaluation shall be used by the contracting officer in determining the prospective contractor's responsibility. The evaluation may be accomplished by use of (a) data on hand, (b) data from another Government agency or commercial source, (c) an on-site inspection of plant and facilities to be used for performance on the proposed contract or (d) any combination of the above. Pre-award surveys shall be conducted in accordance with Appendix K, Pre-Award Survey Procedures. A pre-award survey shall be required when the information available to the purchasing office is not sufficient to enable the contracting officer to make a determination regarding the responsibility of a prospective contractor.

Defense Personnel Support Center (DPSC) obtains Defense Contract Administration Services (DCAS) on-site facility surveys on approximately 10% of the contracts awarded.

2. QUESTION:

What percent of pre-award surveys are done by DPSC? By DSA?

ANSWER:

100% are performed by DCAS. DPSC may elect to participate and does send technical personnel as part of the pre-award survey team.

In FY 73 DCAS conducted 206 pre-award surveys. Of these, DPSC participated in 100. DCAS man-hour expenditure was about 9,000 (about 5,000 in quality and about 4,000 in production). Of this total, approximately 5,000 man-hours were expended by DCAS for drug pre-award surveys (about 3,000 quality assurance and about 2,000 nonquality assurance). The remaining man-hours were expended for other Medical Materiel.

Enclosure 1

Information Required by Senator Nelson
from Department of Defense

3. QUESTION:

On what percent of contracts awarded do you do laboratory analyses of pre-award samples?

ANSWER:

For Medical Materiel, pre-award samples are evaluated on approximately 9% of the contracts awarded. For drugs the rate is closer to 5%. Laboratory analysis of pre-award samples is performed in order to supplement the currently available information and/or pre-award survey and assist the Contracting Officer in determining if a prospective contractor is responsible. The need for samples is predicated upon the available quality history of the prospective contractor and/or the item being procured.

4. QUESTION:

How many man-years were devoted in FY 1973 to the inspection of drugs by DPSC? By DSA?

ANSWER:

DPSC - Approximately 6 man-years of the technical personnel assigned to the Quality Assurance Branch, DPSC were devoted to the inspection of drugs.

DSA - DCAS personnel devoted to the inspection of drugs not readily available, and will be provided in second increment.

5. QUESTION:

What percentage of man-years of inspection time was devoted in the same years to:

Pre-award surveys?
In-process inspection?
Acceptance of product inspection?
Other?
In-store (Depot) surveillance?

Information Required by Senator Nelson
from Department of Defense

5. ANSWER: *

Domestic Pre-Award Surveys	
- Preparation, on-site DPSC Participation and Report Preparation	16%
- Requesting, Evaluation, and Report Preparation where DPSC did not participate	27%
Foreign Surveys	17%
In-Process Inspection	--
Acceptance of Product Inspection	3%
Other	
Quality Audit	17%
Pre-Award Samples	5%
Misc (Supervision, Review of Protocol, Special Inspection Requests, Contract Review, etc.)	11%
In-Store (Depot) Surveillance (Quality System Management Visits only)	4%
	100%

* Percentages apply to DPSC man-years of inspection time only. DCAS percentages not readily available, and will be provided in second increment.

6. QUESTION:

For FY 1973 how many man-years of laboratory work went into support of the inspection process? Please break down the total laboratory man-years into:

DPSC laboratory
Contract laboratories
Other (specify)

ANSWER:

Laboratory work in support of the inspection process for Fiscal Year 1973 covering Pre-Award Samples, Contractual Samples, Pre-Acceptance Samples and samples submitted by the QAR for verification is as follows:

Information Required by Senator Nelson
from Department of Defense

6. ANSWER: (Cont'd)

DPSC Laboratory: 9 Man-Years

	Samples	Cost
Contract Laboratories	*8	$ 845.00
Other Laboratories:	*213	$4,819.55
Walter Reed	*144	$3,101.00
U.S. Army Medical Research Lab., Ft. Knox	*69	$1,718.55

* Man-year data not available.

7. QUESTION:

For Fiscal Year 1973 please give the number of people in:

DSA -- overhead assigned to DPSC Medical Material
DCAS -- Medical Material Support for drugs & other medical material
DPSC -- Medical Directorate
Supply Operations
Technical Operations
Laboratory
Overhead
Procurement Directorate
Medical Division
Drugs
Other

ANSWER:

Fiscal Year 1973 manning was as follows:

DSA - overhead assigned to DPSC Medical Materiel 0.

DCAS - Medical Materiel Support for drugs & other Medical Materiel -- not readily available. Data will be provided in second increment.

Information Required by Senator Nelson
from Department of Defense

7. ANSWER: (Cont'd)

DPSC	TOTAL	DRUG	OTHER
Medical Directorate	*482	83.5	398.5
Supply Operations	115	12	103
Technical Operations	168	32.5	135.5
Laboratory Branch	(22)	(9.5)	(12.5)
Provisioning Branch	(9)		(9)
Procurement	163	35	128
Overhead	36	4	32

* Includes 22 military personnel.

DPSC Overhead 130 (Includes 3 military)

8. QUESTION:

For Fiscal 1973 give total manpower of laboratory personnel

Chemists
Pharmacists
Support (Specify)
Overhead
Other

ANSWER:

Total manpower for the Medical Materiel Laboratory for Fiscal Year 1973 is as follows:

Chemists	7
Pharmacists	1
Microbiologists	1
Engineers	6
Engineering Technicians	4
Clerical Support	3
Laboratory	22

Information Required by Senator Nelson
from Department of Defense

9. QUESTION:

Please give total DoD annual budget involved in inspection of drugs for Fiscal 1973.

ANSWER:

Data not readily available, and will be provided in second increment.

10. QUESTION:

Who evaluates the clinical effectiveness data you require from some suppliers?

ANSWER:

Not applicable - Will be answered by the Defense Medical Materiel Board.

11. QUESTION:

How many M.D.'s are there on the DPSC staff?

Of these, how many are pharmacologists?
Same information for DSA staff.
Do you contract for these types of services? (to determine clinical effectiveness)?

If yes, please name the contractor and drugs studied for years 1969, 1971, 1973.

ANSWER:

The DPSC Medical Materiel Directorate and the HQ DSA staff do not have an M.D. or a Pharmacologist assigned. These types of services are not contracted for by DSA.

12. QUESTION:

Please list all technical division personnel who have a scientific degree of Master or PhD?

Information Required by Senator Nelson
from Department of Defense

12. ANSWER:

The following Technical Division personnel have a scientific degree of Master:

LtCol Jordon D. Johnson, Jr., USAF, BSC	MS
LtCdr Paul B. Donnelly, MSC, USN	MS
Lt R. D. Tackitt, MSC, USN	MS
LtCol Douglas J. Silvernale, MSC, USA	MS
Mr. Leon Jozwiak	MS
Mr. William MacGowen	MS
Mr. Sidney Genn	MS
Mr. Paul Licht	MS
Mr. Robert Simon	MS
Mr. Glenn Kent	MS
Mr. Irving Meisel	MS

13. QUESTION:

For the 150 top drugs -- by dollar volume -- bought by DoD:

Which pharmaceutial companies supplies the information which was incorporated into each specification?

For each of these drugs, give the names of pharmaceutical companies who have been successful bidders on DPSC contracts for each product since original specification was first written. Please give stock numbers, and established and trade names of each product.

ANSWER: 150 TOP DRUGS

The "Remarks" column of the attached sheets has been annotated to show the names of other bidders who bid on the indicated item but have not received an award. In addition, the "Remarks" column includes information as to whether a New Drug approval, Antibiotic Certification (Form 6), or Bureau of Biologics (BoB) License is required by a firm as a prerequisite to marketing the item.

Information Required by Senator Nelson
from Department of Defense

13. ANSWER: (Cont'd)

The "Sources of Industry Information" column lists companies that furnished data. The industry information is always reviewed to determine its applicability and suitability. In addition, specification specialists develop significant product data with the assistance of quality assurance personnel, the Medical Laboratory, plant inspectors, and from literature.

A close working relationship exists between DPSC and the personnel of the FDA, United States Pharmacopeia, and the National Formulary. Further, every drug specification, purchase description and modification is forwarded to FDA, USP, NF, VA, and U.S. Public Health Service.

	(NDC)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
1	783-7218	Diazepam Tablets, NF, 5 mg, 500s	Valium Roche Laboratories	Roche Labs.	Roche Labs.	Patent, NDA
2	890-1856	Methyldopa Tablets, USP, 0.25 Gram, 100s	Aldomet Merck Sharp & Dohme	Merck Sharp & Dohme	Merck Sharp & Dohme	Patent, NDA
3	664-7116	Potassium Penicillin G for Injection, USP, 1,000,000 Units		Wyeth Labs E. R. Squibb & Sons Pfizer Labs. Eli Lilly & Co.	Pfizer Labs. E. R. Squibb & Sons Romar Labs.	Form 6
4	753-5042	Streptomycin Sulfate, USP, Equivalent to 1 Gram of Streptomycin Base		Pfizer Labs.	Pfizer Inc. Eli Lilly & Co.	E. R. Squibb & Sons Form 6
5	116-4500	Dextrose Injection, USP, 5%, 1000 cc, 6s			Travenol Labs. Baxter Labs. Cutter Labs.	
6	146-4425	Sulfisoxazole Tablets, USP, 0.5 Gram, 1000s	Gantrisin Roche Labs.	Roche Labs.	Roche Labs.	Warner-Chilcott Labs. Upjohn Labs. NDA
7	160-7410	Procaine Penicillin For Aqueous Injection, 1,500,000 Units			Pfizer Labs. E. R. Squibb & Sons Inc.	Form 6

	(NDA No.)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
8	181-7635	Ampicillin Capsules, USP, 0.25 Gram, 1000s	Polycillin Bristol Labs --- Beecham-Massengill Pharmaceuticals Totacillin --- Principen E. R. Squibb & Sons --- Penbritin Averst Labs. --- Omnipen Wveth Labs	Bristol Labs. Beecham-Massengill Pharmaceuticals E. R. Squibb & Sons Averst Labs.	Bristol Labs Wveth Labs Beecham Massengill	Averst Labs Upjohn Co. Form 6 Patent
9	165-6545	Cephalexin Monohydrate Capsules, Equivalent to 0.25 Gram of Cephalexin, 100s	Keflex Eli Lilly & Co.	Eli Lillv & Co.	Eli Lillv & Co.	Form 6
10	299-8179	Albumin, Normal Human Serum, USP, 25%, 100 cc			Metrix Div. of Armour Pharmaceutical Hyland Labs E.R. Squibb Cutter Labs Courtland Labs	BOB License
11	687-8047	Benzathine Penicillin G Suspension, Sterile, USP, 1,200,000 units in Aqueous Suspension, Cartridge-Needle Unit, 2 cc size, 20s	Bicillin Wveth Labs	Wveth Labs	Wveth Labs	Form 6
12	958-2364	Pronoxyphene Hydrochloride Capsules, USP, 65 mg, 500s	Darvon Pulvules Eli Lillv & Co.	Eli Lillv & Co.	Eli Lillv & Co. Smith Kline & French Labs.	NDA Rachelle Labs. Anabolic Labs. Nvlos Labs. Barr Labs. Lederle Labs. off patent in 1972

		PUBLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
13	961-5514	Nystatin, Gramicidin, Neomycin Sulfate, and Triamcinolone Acetonide Cream, Topical, 15 Grams	Mycolog Cream E. R. Squibb & Sons	E. R. Squibb & Sons	E. R. Squibb & Sons	Patent Form 6
14	890-1754	Plasma Protein Fraction, USP, Heat-Treated, 5% Solution, 250 cc	Plasmanate Cutter Labs	Cutter Labs Hyland, Div of Travenol Labs	Cutter Labs Hyland, Div of Travenol Labs	BOB License
15	014-1028	Chlorpheniramine Maleate, Isopropamide Iodide, and Phenylpropanolamine Hydrochloride Capsules, 500s	Ornade Spansules Smith Kline & French Labs	Smith Kline & French Labs	Smith Kline & French Labs	NDA Off patent in 1957
16	656-1612	Potassium Phenoxymethyl Penicillin Tablets, USP, 4000,000 Units, 100s	V-Cillin K Tablets Eli Lilly & Co. Pen-Vee K Tablets Wyeth Labs		Eli Lilly & Co. Abbott Laboratories Biocraft	Form 6
17	901-0043	Triamterene and Hydrochlorothiazide Capsules, 1000s	Dyazide Smith Kline & French Labs	Smith Kline & French Labs	Smith Kline & French Labs	NDA Patent
18	900-2146	Sodium Cephalothin, Sterile, USP, Equivalent to 1 Gram of Cephalothin	Keflin Eli Lilly & Co.	Eli Lilly & Co.	Eli Lilly & Co.	Form 6 Patent
19	059-9017	Chlordiazepoxide Hydrochloride Capsules, USP, 10 mg, 500s	Librium Roche Labs	Roche Labs	Roche Labs	Patent NDA
20	145-0429	Norgestrel and Ethinyl Estradiol Tablets, 63s	Ovral Wyeth Labs	Wyeth Labs	Wyeth Labs	NDA

	FSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
21	912-2404	Lincomycin Hydrochloride Capsules, USP, Equivalent to 0.50 Gram of Lincomycin, 100s	Lincocin The Upjohn Company	The Upjohn Co.	The Upjohn Co.	Patent Form 6
22	660-1676	Kanamycin Sulfate Injection, USP Equivalent to 0.333 Gram of Kanamycin per cc, 3 cc	Kantrex Bristol Labs	Bristol Labs	Bristol Labs	Patent Form 6
23	299-8615	Ringer's Injection, Lactated, USP, 1000 cc, 6s			Cutter Labs Baxter Labs McGaw Labs Travenol Labs	
24	662-9790	Erythromycin Tablets, 0.25 Gram, 100s	Ilotycin Eli Lilly & Company Erythrocin Abbott Labs	Eli Lilly & Co Abbott Labs	Eli Lilly & Co Abbott Labs	The Upjohn Co. Form 6 Off patent in 1972
25	782-6510	Griseofulvin Tablets, USP, 0.50 Gram, 500s	Grifulvin V Tablets McNeil Labs Fulvicin Schering Corp	McNeil Labs	McNeil Labs Schering Corp	Patent Form 6
26	181-7180	Gentamicin Sulfate Injection, Equivalent to 40 mg Gentamicin per cc, 2 cc	Garamycin Schering Corp	Schering Corp	Schering Corp	Form 6
27	142-9206	Tripolidine Hydrochloride and Pseudoephedrine Hydrochloride Tablets, 1000s	Actified Tablets Burroughs Wellcome & Co, Inc	Burroughs Wellcome & Co, Inc	Burroughs Wellcome & Co, Inc	Off-patent 1972 NDA
28	753-9609	Hydrocortisone Sodium Succinate for Injection, USP, Equivalent to 100 mg Hydrocortisone Base	Solu-Cortef Mix-O-Vial The Upjohn Company	The Upjohn Co.	The Upjohn Co.	Patent NDA

NO.	FSN (5505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
29	926-8996	SPIRONOLACTONE TABLETS, USP, 25mg, 500s	"ALDACTONE TABLETS" G. D. Searle & Co.	Searle	Searle	Patent, NDA
30	165-6519	MEASLES, MUMPS, and RUBELLA VIRUS VACINNE, LIVE, 10s	"MMR" Merck, Sharp, & Dohme	MSD	MSD	BoB license
31	117-6450	CHLOROQUINE PHOSPHATE TABLETS, USP, 0.5 Gram, 500s	"ARALEN PHOSPHATE" Winthrop Laboratories	Winthrop	Winthrop	Patent, NDA
32	998-4381	ALLOPURINOL TABLETS, USP, 100 mg, 100s	"ZYLOPRIM" Burroughs Wellcome & Co.	Burroughs Wellcome	Burroughs Wellcome	Patent, NDA
33	153-9738	ESTROGENS, CONJUGATED, TABLETS, USP, 1.25 mg, 500s	"PREMARIN" Ayerst Laboratories	Ayerst	Ayerst	NDA
34	926-9019	DEXBROMPHENIRAMINE MALEATE and PSEUDOEPHEDRINE SULFATE TABLETS, 100s	"DISOPHROL CHRONOTAB TABLETS" White Laboratories Inc. "DRIXORAL" Schering	White	Schering	Patent NDA
35	869-4178	SODIUM CEPHALOTHIN, STERILE, USP Equivalent to 4 Gram of CEPHALOTHIN	"KEFLIN" Eli Lilly & Co.	Lilly	Lilly	Patent, Form 6
36	782-2662	QUININE SULFATE TABLETS, USP, 0.324 Gram, 1000s			Vitarine Co. Strong Cobb Arner Panray	
37	965-2439	OXYGEN, USP, with Tube and Face Mask, 24 gal. (90 liters)	Life-O-Gen Life-O-Gen Co.	Union Carbide Corp (Linde) Life-O-Gen Oxequip Health Indust.	Life-O-Gen Co. Union Carbide Corp. (Linde)	
38	754-0086	DICYCLOMINE HYDROCHLORIDE, DOXYLAMINE SUCCINATE, and PYRIDOXINE HYDROCHLORIDE TABLETS, 100s	"BENDECTIN" Wm. S. Merrell	Wm. S. Merrell	Merrell-National Laboratories	NDA

NO.	(NDC)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
39	104-9000	Alcohol, USP, 5 gal. (18.92 liters)			U.S. Indus. Chem. Publicker Ind. Lac Chemicals Inc. Carbide and Carbon Chemicals Co. Div. of Union Carbide Enjay Chem. Co.	
40	071-6547	Triamcinolone Acetonide, Cream, USP, 0.5% 8oz. (227 Gram)	"Aristocort" Lederle Laboratories	Lederle	Lederle	NDA
41	854-2504	Halothane, USP, 125cc	"Fluothane" Ayerst Laboratories	Ayerst	Ayerst Halcarbon Ltd	Patent NDA
42	935-5836	Ethynodiol Diacetate with Mestranol Tablets, 63s	"Ovulen" G. D. Searle & Co.	Searle	Searle	NDA
43	890-1840	Metronidazole Tablets, USP, 0.25 Gram, 250s	"Flagyl" G. D. Searle & Co.	Searle	Searle	Patent NDA
44	764-3340	Multivitamin for Injection, 10cc	"Solu-B-Forte" Mix-O-Vial The Upjohn Co.	Upjohn	Upjohn	
45	159-4892	Clindamycin Hydrochloride Hydrate Capsules, Equivalent to 150 mg of Clindamycin, 100s	"Cleocin" The Upjohn Co.	Upjohn	Upjohn	Form 6

ID	NDC (4-3-2)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
46	146-2200	Sulfadiazine Tablets, USP, 0.5 Gram, 1000s			Lederle Labs Dorsey Labs Beecham-Massengill	NDA
47	116-5000	Dextrose and Sodium Chloride Injection, USP, 1000 cc, 6s			Travenol Labs Cutter Labs Abbott Labs McGaw Labs	
48	138-4610	Protein Hydrolysate Injection, USP, 1000 cc, 6s			McGaw Labs Travenol Labs Baxter Labs Don Baxter, Inc	
49	721-9383	Multivitamin Tablets, 100s			Strong Cobb Arner Chase Chem J. B. Roerig	
50	985-6535	Ampicillin for Oral Suspension, USP, 7.5 Gram	Penbritin Ayerst Laboratories Polycillin Bristol Laboratories Omnipen Wyeth Principen E. R. Squibb Amcill Parke-Davis & Co	Bristol Wyeth Ayerst	Bristol Wyeth Ayerst	Patent Form 6 Beecham-Massengill
51	062-3336	Furosemide Tablets, USP, 40 mg, 100s	Lasix Hoechst	Hoechst	Hoechst	Patent NDA
52	998-5872	Clofibrate Capsules, NF, 500 mg 100s	Atromid-S Ayerst	Ayerst	Ayerst	Patent NDA

	NDA (NDDG)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
53	890-1627	Dioctyl Calcium Sulfosuccinate Capsules, NF, 1000's	"Surfak Capsules" Hoechst	Lloyd Bros. Hoechst	Hoechst	PATENT
54	926-2154	Indomethacin Capsules, NF, 25 mg, 100s	"Indocin" Merck Sharp and Dohme	Merck Sharp and Dohme	Merck Sharp and Dohme	PATENT NDA
55	576-8842	Lidocaine Hydrochloride Injection, USP, 2%, with Epinephrine 1:100,000, 1.8 cc, 50's	"Xylocaine" Astra	Astra	Astra	NDA
56	074-4702	Diphenoxylate Hydrochloride and Atropine Sulfate Tablets, NF, 500's	"Lomotil" G. D. Searle & Co.	Searle	Searle	PATENT NDA
57	064-8755	Glyceryl Guaiacolate Syrup, NF, 100 mg per 5cc, 4 fl. oz. (118 cc)	"Robitussin Syrup" A. H. Robins	A. H. Robins	A. H. Robins G & W Laboratories Strassenburg Dorsey	Natcon
58	926-2241	Tolnaftate Solution, USP, 1 %, 10 cc	"Tinactin Solution" Schering	Schering	Schering	NDA PATENT
59	104-9723	Aspirin Tablets, USP, 75 mg, 36's	Children's Aspirin Various Firms		Plough	

	FSN (C...S)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
60	724-6331	Phenformin Hydrochloride Capsules, 50 mg, 1000s	"DBI-TD" Geigy "Meltrol-50" U.S.V.	USV Geigy	USV	Patented NDA Geigy
61	181-7774	Sodium Colistimethate, USP, Lyophilized, Equivalent to 0.15 Gram of Colistin Base	"Colymycin M" Warner Chilcott	Warner Chilcott	Warner Chilcott	Form 6 Patented
62	656-1344	Tetracycline Syrup, Equivalent to 25 mg of Tetracycline Hydrochloride per cc, 16 fl. oz. (473 cc)	"ACHROMYCIN-V Syrup" Lederle	Lederle Rachelle Roerig	Lederle Rachelle Roerig Reine Carlo Erba Pfizer	Form 6
63	559-5143	Calcium Gluceptate Injection, 5 cc, 25s		Eli Lilly Roussel	Vitarine Abbott Eli Lilly Pasadena Research Gotham	NDA
64	145-0309	Norethindrone and Mestranol Tablets, 63s	"Norinyl-1 plus 80" Syntex "Ortho-Novum 1/80" Ortho	Syntex Ortho	Syntex	NDA Ortho
65	935-4095	Brompheniramine Maleate, Phenylephrine Hydrochloride and Phenylpropanolamine Hydrochloride Elixir, 4 fl. oz. (118 cc)	"Dimetapp" A. H. Robins	A. H. Robins	A. H. Robins	NDA
66	914-3593	Povidone Iodine Solution, NF, 10%, 1/2 fl. oz., 15cc, 50s	"Betadine Solution" Purdue Frederick		Purdue Frederick	Off Patent in 1973

NO.	NDC (6-3-5)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
67	754-2436	Neomycin Sulfate, Hydrocortisone, and Polymyxin B Sulfate Suspension, Otic, 5 cc	Cortisporin Burroughs Wellcome	Burroughs Wellcome	Burroughs Wellcome	Patent Form 6
68	931-0680	Indomethacin Capsules, NF, 25 mg, 1000s	Indocin Merck-Sharp-Dohme	Merck-Sharp-Dohme	Merck-Sharp-Dohme	NDA Patent
69	853-4799	Imipramine Hydrochloride Tablets, USP, 25 mg, 100s	Tofranil Geigy Presamine USV	Geigy	Geigy USV	NDA Off patent in 1972
70	962-4375	Butalbital, Aspirin, Caffeine, and Phenacetin Tablets, 1000s	Fiorinal Sandoz	Sandoz	Sandoz	
71	935-1128	Plague Vaccine, USP, E Medium, 20 cc	Military Item	Cutter in cooperation with Walter Reed Army Institute of Research	Cutter	BoB License
72	074-4582	Quinine Dihydrochloride Injection NF, 0.3 Gram per cc, 2 cc, 12s			Mallinckrodt Chemical Works	
73	660-1601	Methocarbamol Tablets, NF, 0.5 Gram, 500s	Robaxin A. H. Robins	A. H. Robins	A. H. Robins	Off patent in 1973 NDA

	FSN (CSG)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
74	926-4768	Lincomycin Hydrochloride Injection, USP, Equivalent to 0.30 Gram of Lincomycin Base per cc, 10 cc	Lincocin Upjohn Co	Upjohn Co	Upjohn Co	Form 6 Patent
75	106-7395	Propranol Hydrochloride Tablets, 10 mg, 100s	Inderal Ayerst	Ayerst	Ayerst	Patent NDA
76	153-8651	Sodium Chloride Injection, USP, 1000 cc, 6s			Travenol Labs McGaw Labs Cutter Labs Abbott Labs Baxter Labs	
77	515-1584	Foot Powder, Fungicidal, 1 oz (28.35 Gram)	Desenex Foot Powder Maltbie Lab Division of Wallace-Tiernan, Inc	Wallace and Tiernan, Inc	Pharmacraff Seaboard Mfg Co	
78	985-7110	Fluocinolone Acetonide Cream, 0.025%, 15 Gram	Synalar Cream Syntex Labs	Syntex Labs	Syntex Labs	NDA
79	890-1907	Colistin Sulfate, Hydrocortisone Acetate, Neomycin Sulfate and Thonzonium Bromide Suspension, Otic, 5 cc	Coly-Mycin Otic Drops Warner Chilcott	Warner Chilcott	Warner Chilcott	Form 6 Patent
80	754-0374	Povidone-Iodine Solution, NF, 10%, 1 Gal (3.78 liters)	Betadine Solution Purdue Frederick	Tailby Nason Co Perdue-Frederick	Perdue-Frederick	NDA Off Patent in 1973

		ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
81	375-8955	Diazepam Injection, NF, 5 mg per cc, 2 cc, 10s	Valium Injection Roche Labs	Roche Labs	Roche Labs	NDA Patent
82	689-4177	Oxymetazoline Hydrochloride Solution, 0.05%, 15cc	AFRIN Spray Schering Corp.	Schering Corp.	Schering Corp.	NDA Patent
83	724-6358	Amitriptyline Hydrochloride Tablets,USP 25 mg, 100s	Elavil Merck Sharp & Dohme	Merck Sharp & Dohme	Marck Sharp & Dohme	NDA Patent
84	946-4700	Sodium Ampicillin, Sterile, USP, Equivalent to 0.50 Gram of Ampicillin	Polycillin-N Bristol Lab.	Bristol Lab	Bristol Lab	Ayerst Wyeth Beecham Massengill Form 6 Patent
85	994-7224	Detergent, Surgical, 7 1/2% Povidone-Iodine, 1 gal (3.78 liters)	Betadine Skin Cleanser Purdue-Fredericks	Tailby-Nason Physican's Products Co. Purdue-Fredericks	Purdue Fredericks	Off Patent in 1973 NDA
86	116-1750	Detergent, Surgical, Liquid, 1 Gal	PHISOHEX Winthrop Labs	Winthrop Labs	Winthrop Labs	Off Patent in 1959
87	299-9674	Isoniazid Tablets, USP, 100 mg, 100s	INH -Eli Lilly Niconyl- Parke Davis Nydrazid - Squibb		Mallinckrodt Parke Davis Panray Eli Lilly & Co. Strong Cobb Arner	NDA

NO.	FDC (CODE)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
88	299-8095	Isopropyl Alcohol, NF 5 gal.			George Senn & Co. Haskon Inc. Shell	
89	299-8671	Selenium Sulfide Lotion, NF 2.5%, 4 fl. oz. (118 cc)	Selsun Abbott Labs	Abbott Labs.	Abbott Labs.	NDA
90	163-6575	Rifampin Capsule 0.30 Gram, 100s	Rimactane-Ciba Rifadin-Dow Chem.	Ciba Pharm. Dow Chem. Co.	Ciba Pharm. Dow Chem. Firms receiving awards are Licensees and Liscensor is Grupo Lepetit, Spa, a subsidiary of Dow Chemical	PATENT Form 6
91	543-4048	Water for Injection, Sterile, USP, 5 cc, 25s			Lincoln Labs. Torrigian Lab. Vitarine Co.	
92	074-4692	Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules, 500's	Librax- Roche Labs.	Roche Labs.	Roche Labs.	PATENT NDA
93	616-9128	Nystatin Tablets, USP, Vaginal, 100,000 units, 15s	Mycostatin Vaginal Tablets, E. R. Squibb & Sons Nilstat Vaginal Tablets-USP Lederle Labs.	E. R. Squibb & Sons	Lederle Labs. E. R. Squibb & Sons	off Patent in 1972 Form 6
94	092-2659	Amitriptyline Hydrochloride Tablets, USP, 25 mg, 100's	Elavil, Merck Sharp & Dohme	Merck Sharp & Dohme	Merck Sharp & Dohme	PATENT NDA

NO.	FSN (65.5)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
95	889-7929	Hydrochlorthiazide tablets, USP, 50 mg, 1000's	Esedrex-Ciba Hydro-Diuril-Merck Sharp & Dohme Oretic-Abbott Lab.	Ciba Abbott Lab. Merck Sharp & Dohme	Abbott Lab. Ciba Pharm.	NDA
96	812-2579	Ethambutol Hydrochloride Tablets, 400 mg, 100s	Myambutol Tablets Lederle Labs.	Lederle Labs.	Lederle Labs.	Patent NDA
97	890-1534	Tuberculin, Old Dried, Tine Test (Rosenthal)	Tuberculin Tine Test (T-B Tine Test) Lederle Labs.	Lederle Labs.	Lederle Labs.	Patent BOB License
98	817-2279	Chlorpropamide Tablets, USP, 0.25 Gram 250s	Diabinese Tablets Pfizer Lab.	Pfizer Lab.	Pfizer Lab.	Patent NDA
99	558-1289	Aluminum Hydroxide Gel and Magnesium Trisilicate Tablets, 100s	Gelusel Tab Warner-Chilcott	Warner Chilcott	Warner Chilcott Labs. Chase Chemical Co.	
100	100-5245	Aspirin, Phenacetin, and Caffeine Tablets, NF, 1000	Empirin Compd. Burroughs Wellcome APC Tablets Other Firms	Strong Cobb Arner Norwich Pharmacal Co.	Whitehall Norwich Pharmacal Beecham-Massengill Upjohn Company E. R. Squibb	Strong Cobb Arner
101	890-1496	Prednisolone Sodium Phosphate Injection USP, Equivalent to 20 mg of Prednisolone Phosphate per cc, 5 cc	"Hydeltrasol" Merck Sharp & Dohme	Merck Sharp & Dohme	M.S.D.	Patent NDA

NDA	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
102 153-8750	Aspirin Tablets, USP, 0.324 Gm, 1000s			Norwich Strong Cobb Arner Parke-Davis E.R. Squibb	
103 770-8343	Ampicillin Capsules	"Polycillin" Bristol "Totacillin" Beecham-Massengill "Principen" E.R. Squibb "Penbritin" Ayerst "Omnipen" Wyeth	Bristol Laboratories Beecham-Massengill Pharm. E.R. Squibb & Sons Ayerst Laboratories	Ayerst Bristol Wyeth Beecham-Massengill E.R. Squibb	Ayerst Labs. Upjohn Co. Form 6 Patent
104 660-1798	Benzonatate Capsules, NF, 100 mg, 100s	"Tessalon Perles" Ciba Pharm.	Ciba Pharm.	Ciba Pharm.	Off-Patent 1972. NDA
105 080-0852	Potassium Phenoxymethyl Penicillin for Oral Soln (16,000,000 Units) (10 Gram)	Abbott "Compocillin-VK" Bristol "Betapen-VK" Eli Lilly & Co. V-Cillin K E.R. Squibb Veetids		Bristol Laboratories	Form 6 Pfizer Laboratories
106 926-8924	Ampicillin for Oral Suspension, USP, 3.75 Gm	"Penbritin" Ayerst "Polycillin" Bristol "Omnipen" Wyeth "Principen" E.R. Squibb "Amcill" Parke-Davis & Co.	Bristol Wyeth Ayerst	Ayerst Bristol	Patent Form 6 Wyeth Beecham-Massengill

	NDC (5-3-2)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
107	125-9922	Vitamin-Mineral Capsule, 100s	"Filibon F.A." Lederle Laboratories	Lederle Laboratories	Lederle Laboratories	
108	584-5997	Methenamine Mandelate Tablets, USP 0.5 Gm, 500s	"Mandelamine" Warner Chilcott	Warner Chilcott	Warner Chilcott	
109	059-2760	Sodium Oxacillin Capsules, USP, Equivalent to 0.5 Gram of Oxacillin in each capsule, 100s	"Prostaphlin" Bristol Laboratories	Bristol Laboratories	Bristol Laboratories	Patent Form 6 Beecham-Massengill
110	584-0398	Propantheline Bromide Tablets, USP, 15 mg, 1000s	"Pro-Banthine Bromide Tablets" G. D. Searle & Co.	Searle & Co.	Searle & Co.	NDA
111	050-4567	Psyllium Hydrophilic Mucilloid with Dextrose, 14 oz (397 Grams)	"Metamucil" G. D. Searle & Co.	G. D. Searle & Co.	G. D. Searle & Co. Burton-Parsons	
112	149-1720	Water for Injection, Sterile, USP, 1000 cc, 6s			Baxter Laboratories Don Baxter Inc. McGaw Travenol	
113	687-8205	Cetylpyridinium Chloride Lozenges, 400s	"Cepacol Throat Lozenges" Wm.S. Merrell	Wm. S. Merrell	Merrell- National Laboratories	NDA

		UNPUBLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
114	299-8617	Sodium Salicylate Tablets, USP, 0.324 Gram, 1000s			Strong Cobb Arner Eli Lilly Chase Chemical	
115	106-7309	Propranolol Hydrochloride Tablets, 40 mg, 100s	"Inderal" Ayerst	Ayerst	Ayerst	PATENT NDA
116	931-4329	Theophylline Ephedrine Sulfate and Hydroxyzine Hydrochloride Tablets	"Marax" J. B. Roerig	J. B. Roerig	J. B. Roerig	NDA
117	890-1551	Sodium Methicillin for Injection, USP, 1 Gram	"Staphcillin for Injection" Bristol Laboratories	Bristol	Bristol	PATENT Form 6
118	080-0975	Aluminum Hydroxide Gel, Magnesium Hydroxide and Simethicone Suspension, 5 fl oz., 48s	"Mylanta" Stuart	Stuart	Stuart	PATENT
119	880-3905	Plasma Protein Fraction, USP, Heat-Treated, 5%, 500cc	"Plasmanate" Cutter	Cutter Hyland Div. Travenol	Cutter Hyland Div. Travenol	BoB License
120	114-8935	Codeine Sulfate Tablets, NF, 32 mg, 100s			Premo Strong CobbArner Beecham Massengill Eli Lilly & Co. Norwich Wm S. Merrell Brewer & Co.	

	NDC (GCPC)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
121	764-5313	Chlorzoxazone and Acetaminophen Tablets, 500s	McNeil "Parafon Forte"	McNeil	McNeil	NDA Patent
122	985-7301	Acetaminophen Tablets, NF, 0.325 Gram, 1000s	"Tylenol" McNeil	McNeil Mead Johnson	McNeil Mead Johnson Dorsey	
123	685-5442	Dextrose in Lactated Ringer's Injection, 5%, 1000 cc, 6s			Travenol Cutter	
124	926-8985	Dextromethorphan Hydrobromide and Glyceryl Guaiacolate Syrup, 4 fl. oz., (118 cc)	"Robitussin-DM" A. H. Robins	Robins Dorsey	Robins G & W Pennwalt Reine	Natcon
125	926-9083	Atropine Injection, 2 mg			Rodana Research Corp.	Patent
126	782-6761	Triprolidine Hydrochloride and Pseudoephedrine Hydrochloride Syrup 4 fl. oz.	Actifed Syrup Burroughs Wellcome & Co.	Burroughs Wellcome and Co.	Burroughs Wellcome & Co.	off Patent in 1972 NDA
127	890-1355	Medroxyprogesterone Acetate Tablet, USP, 10 mg, 100s	Provera Tablets Upjohn Co.	Upjohn Co.	Upjohn Co.	Patent NDA

32-814 (Pt. 24) O - 74 - 7

	(NDC)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
128	584-2805	Hydralazine Hydrochloride Tablets, NF, 25 mg, 1000s	Apresoline Hydrochloride Tablets Ciba Pharm. Co.	Ciba Pharm. Co.	Ciba Pharm. Co.	NDA
129	982-9059	Tolbutamide Tablets, USP, 0.5 Gram, 200s	Orinase Tablets Upjohn Co.	Upjohn Co.	Upjohn Co.	PATENT NDA
130	937-1758	Ethinyl Estradiol Tablets & Diethesterone w/Ethinyl Estradiol Tablets, 63s	Oracon Mead Johnson Labs.	Mead Johnson	Mead Johnson	PATENT NDA
131	222-1357	Sodium Caloride Solution, USP, 0.9% 1500 cc, 6s		Cutter, Travenol McGaw Abbott	Travenol Lab. Abbott	McGaw Labs. Cutter Labs.
132	861-0867	Sodium Aminosalicylate Tablets, USP, 1.0 Gram, 1000s	Pasara Sodium Tablets Dorsey Parasal Sodium Panray Pamisyl Sodium Parke-Davis	Dorsey Lab	Dorsey Labs Strong Cobb Arner Panray Miles	NDA
133	890-2217	Sulfanilamide, Allantoin and Aminacrine Hydrochloride Cream, Vaginal, 4 oz (113.4 Gram)	AVC Vaginal Cream Merrell-National	Merrell-National	Merrell-National	NDA
134	074-2981	Ferrous Fumarate & Dioctyl Sodium Sulfosuccinate Capsules, 1000s	"Ferro Sequels Capsules" Lederle	Lederle	Lederle	

		PUBLISHED NAME	NAME NO. (S) & CO.	IMPACT OF INTRODUCTION	SUCCESSFUL BATTLES	REMARKS
135	299-8739	Chlortetracycline Hydrochloride Ophthalmic Ointment, 1%, 1/8 oz. 3.5 Gm, 12s	Aureomycin Ophthalmic Ointment, 1% Lederle Laboratories	Lederle	Lederle	Form 6 Patent
136	153-8278	Immune Serum Globulin, USP, Human, 10 cc			Hyland E. R. Squibb Lederle	BOB license
137	584-3277	Promethazine Hydrochloride Tablets, USP, 25 mg, 1000s	Phenergan Hydrochloride Tablets Wyeth Lab.	Wyeth	Wyeth	NDA Endo
138	963-5355	Dexamethasone Sodium Phosphate Injection, USP, Equivalent to 4 mg of Dexamethasone Phosphate per cc, 5 cc	Decadron Phosphate Merck Sharp & Dohme	Merck Sharp & Dohme	Merck Sharp & Dohme	NDA Patent
139	003-5112	Minocycline Hydrochloride Capsules, Equivalent to 100 mg of Minocycline, 50s	Minocin Lederle Labs.	Lederle	Lederle	Form 6 Patent
140	299-8013	Insulin, Isophane, Suspension, USP, U-80, 10 cc	Lilly NPH Iletin Squibb NPH Insulin	E. R. Squibb	Eli Lilly	NDA
141	890-1554	Flurandrenolide Cream, NF, 0.05%, 15 Grams	Cordran Cream Eli Lilly	Eli Lilly	Eli Lilly	Patent NDA

	[illegible]	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
142	080-0653	Erythromycin Ethylsuccinate for Oral Suspension, NF, Equivalent to 8 Grams of Erythromycin Base	Erythrocin Abbott Labs	Abbott	Abbott	Form 6
143	181-8387	Probenecid Tablets, USP, 0.5 Gram, 1000s	Benemid Merck, Sharp, and Dohme	Merck,Sharp,&Dohme	Merck, Sharp, & Dohme	NDA
144	584-0412	Estrogens, Conjugated, Tablets, USP, 0.625 mg, 1000s	Premarin Ayerst Labs.	Ayerst	Ayerst	NDA
145	159-6625	Bacitracin Ointment, USP, 500 Units per Gram, 1/2 oz (14.2 Grams) 12s			Day Baldwin Premo Pfizer Strong Cobb Arner Eli Lilly Abbott	Form 6
146	443-4559	Sodium Diatrizoate Injection, USP, 50%, 30 cc, 25s	Hypaque Sodium 50% Winthrop Labs.	Winthrop	Winthrop	NDA
147	299-8608	Oxtetracycline Hydrochloride and Polymyxin B Sulfate Ophthalmic Ointment 1/8 oz (3.5 Grams) 10s	"Terramycin Ophthalmic Ointment with Polymyxin B Sulfate" Pfizer	Pfizer	Pfizer	PATENT Form 6
148	130-1805	Nikethamide Injection, NF, 25%, 1-1/2 cc, 5s	"Coramine" Ciba		Premo Elkins-Sinn Natcon Vitarine Ciba Gotham Carlo Erba Brewer Torrigian Pharmich Gold Leaf	
149	130-1960	Nitrofurazone Ointment, NF, Water Soluble, 1:500, 1 lb. (453.6 Grams)	Furacin Soluble Dressing Eaton Labs.	Eaton	Eaton	PATENT NDA

	FSN (538(5)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
150	753-4766	Theophylline, Ephedrine Hydrochloride and Phenobarbital Tablets, NF, 1000s	Tedral Tablets Warner-Chilcott	Warner Chilcott	Eli Lilly Warner-Chilcott	

Information Required by Senator Nelson
from Department of Defense

14. QUESTION:

Number of drug contracts in Europe for the past year?
Number of DOD representatives in Europe that inspect drug facilities.

ANSWER:

During the past year DPSC did not have any contracts in Europe.

Surveys of overseas drug firms are conducted by a DPSC Liaison Officer.

15. QUESTION:

In the past several months Mr. Feinberg of the DPSC has publicized certain problems for which the Subcommittee is very anxious to secure additional information. His statement and our questions are as follows:

(a) "The rejection rate of DOD plant inspections is 45 percent and the rejection rate on pre-contract award sample inspections is 42 percent."

Would you please explain exactly how these figures were derived?

(b) "Based on my experience of drug plants, it is my firm conviction that the primary problem lies in the fact that many producers in the business today are in gross violation of FDA's good manufacturing practices regulations. Those same firms are manufacturing drugs on a daily basis."

Will you please supply: (1) the names of the firms; (2) the dates of the "gross violations" of FDA's good manufacturing practices regulations; (3) were these reported to the FDA and other government purchasing agencies, and if so, when and in what detail; (4) the exact description of the violation (not a general statement like "poor housekeeping," etc).

(c) "We have seen totally unacceptable housekeeping conditions involving dirt, filth, and rodents. We have reviewed production records that showed noncompliance with the companies' own standards. We have found instances where ingredients and finished products are not adequately tested."

As in the previous question, please supply the names of the companies involved; dates on which violations were found; were these reported to the FDA and other government agencies, and if so, when and how; and the exact description of the violation.

Information Required by Senator Nelson
from Department of Defense

15. QUESTION: (Cont'd)

(d) With respect to problems of digoxin tablets -- "This was no surprise to the drug specialists in DPSC because we know of many other examples demonstrating that compliance with laboratory standards is not necessarily indicative of clinical effectiveness."

When did the DPSC drug specialists first learn about the problem with some digoxin tablets on the market?

Was the FDA informed of this problem by your organization and if so, when and how?

Which of your drug specialists first became acquainted with the problem?

Please name the "many other examples" mentioned. Was the FDA informed? When and how? Give name and title of drug specialists who discovered these problems?

(e) "We develop definitive product specifications which often exceed official or commercial standards."

Please name each product for which such specifications have been developed; the significance for each product of these extra requirements; and the medical purpose served by these extra requirements.

ANSWER:

(a) The 45 percent rejection rate in plant inspections refers to our FY 1973 responses to the contracting officer regarding award or no award recommendations resulting from pre-award surveys of manufacturers of drugs and devices. There were 216 such responses where an award/no award recommendation was made as a result of a pre-award survey. Of those, 97 or 44.9% recommended no award.

The 42 percent rejection rate on pre-award samples refers to our FY 1973 responses to the contracting officer regarding award or no award recommendations resulting from the evaluation of pre-award samples from manufacturers of drugs and devices. There were 320 where an award/no award recommendation was made as a result of evaluation of a pre-award sample. Of those, 136 or 42.5% recommended no award.

Information Required by Senator Nelson
from Department of Defense

15. ANSWER: (Cont'd)

(b) and (c) Upon completion of a plant inspection, an exit interview is generally conducted with the company representatives at which time the findings are discussed. A summary of those findings is then forwarded to the company as a matter of record. Copies of the findings are mailed to FDA (Mr. Raymond Hamilton, Division of Case Guidance), Veterans' Administration, and U. S. Public Health Service.

The attached compilation depicts examples and dates of quality control and housekeeping deficiencies requested in 15 (b) and (c).

	INSPECTION DATE	REPORT TO FDA DATE	DESCRIPTION OF VIOLATION
Inland Alkaloid Co. St. Louis, MO	December 1971	January 1972	No qualified professional person in charge of production and no full-time qualified quality control manager. Dust and refuse was found on the floor and in the work areas. Paint had flaked from the ceiling at many locations in the plant.
Tablicaps, Inc. Franklinville, NJ	December 1971	January 1972	White tablets of a product identified as Lot 30550 "CPM with AC" was placed on trays in a wooden rack prior to coating. Heavy pink dust was observed on the racks and on the accompanying batch record papers laying on a tray in the rack. This condition indicates possibility of cross contamination. The drying oven was found to contain red Bristophen granulation and a yellow Bristophen granulation in trays in the same oven. This condition could lead to cross-contamination of two products. The different colors represent different dosage strengths of the same product.
Poly Research Inc. Plainview,L.I.,NY	January 1972	January 1972	The company's staffing consisted of two full time employees (President and Vice President) plus two part time employees (high school students). Neither of the two full time employees had experience relating to pharmaceutical preparations. The President's background was in the printing field and the Vice President was a graduate chemist with experience only in analytical laboratories. Washroom was not clean; no receptacle for used towels, and only a loose, slightly soiled roll of towels was available for drying the hands.

[illegible]	INSPECTION DATE	MAILED TO FDA, HA, PHS	DESCRIPTION OF VIOLATION
White Cross Pharmacal Company Detroit, Mich.	February 1972	February 1972	The firm has no full time Quality Control Director. A pharmacist who owns a retail drugstore would be called in. This pharmacist was not in the plant at the time of the survey. The firm used Urea, Manufactured by Merck & Company, Lot 51432, in their formulation of the Vaginal Cream. This lot of material is 21 years old. The United States Pharmacopeia XIV was then in effect. Tests in the melting range and lack of assay requirements differ from the requirements of the current United States Pharmacopeia XVIII. The firm has no program of retesting material in stock. No Master-Formula or Batch-Production Record was available for the bid item, Sulfacetamide, Sulfabenzamide, Sulfathiozolic and Urea Vaginal Cream. The firm had an inadequate lot control numbering system. Finished material (Hydrocortisone Cream and Sulfathiazole Cream) had no lot numbers. A bag of "Sulfathiazole", lot ST53338, which is a component in the bid item, Vaginal Cream, was found in the same container with a bag of "Salicylic Acid".
Bolar Pharmaceutical Corp.	February 1972	February 1972	There was a lack of efficient exhaust system in their tablet compression area. At time of visit, the firm was compressing Vitamin B 12, Lot 012909. The entire area was heavily laden with the pink powder. Hardly a wall, equipment or container did not have a heavy layer of pink powder on it. Walls, floors and overhead pipes in the quarantine location (where hold material is sampled) were dusty and dirty. The firm's policy is to assign only one lot number to incoming raw materials, no matter how many different lots of the same item they received at the same time. An example was: Bolar's Ascorbic Acid, lot 5037 was composed of supplier's lots F2925, F2975, and F2907.

FIRM'S NAME	INSPECTION DATE	MAILED TO FDA, VA, PHS	DESCRIPTION OF VIOLATION
General Packaging Serv. Waldwick, NJ	February 1972	March 1972	The storage area is dirty. Layers of dust, powder rest on surfaces of containers and packaging material. These surfaces are not cleaned prior to transfer into the production area. Handling is such that the dust, dirt, powder on the containers and packaging material are discharged into the atmosphere of the drug processing area. Contamination of various products with foreign matter may occur. A second storage area for material requiring air conditioning temperature is also dirty. Cartons and containers and shelving are covered with layers of dust and dirt. No room exists for orderly placement of material. Tablets in cellophane strip packages and bottles of Sine-aid tablets were scattered over the floor. One drum of Tonel laxative tablets, lot 051124, was also identified as Coricidin tablets.
Biocraft Labs.Inc. East Patterson, NJ	May 1972	May 1972	Quarantine material found available for use in the production area.
Linden Labs. Inc. Los Angeles, CA	May 1972	May 1972	A bird and flying insects were noted in the areas for quarantine, sampling and storage. The Howe scale #8142 used in the weighing area was heavily encrusted with residue from previous weighings. There were various colored materials on the equipment.
R.S.A. Corp. Ardsley, NY	September 1972	September 1972	Improper release of products. Analytical records for approved Diiodohydroxyquin Lot 1-1971, (which is the same item used in the manufacture of the bid tablets), reported a "Loss on Drying" USP Test, of 4.8%. This should never have been approved. The tolerance specified in the U.S.P. is "Not more than 0.5%". In addition, the required USP "Identification Test" was never performed. Improper testing of raw material. Diiodohydroxyquin, Lot 1-1971 "Residue on Ignition" test was run at 500°C, whereas the USP specified 800°C.

FIRM NAME City & State	INSPECTION DATE	MAILED TO FDA, VA, PHS	DESCRIPTION OF VIOLATION
Ketchum Labs Amityville, NY	October 1972	October 1972	The overhead duct in the area used for sampling of raw materials was heavily laden with dust. In this area, raw material containers are opened for sampling and thus, dust could enter raw material. Ceiling tiles were loose and separated from the ceiling in the Granulation storage area. No documented procedures were available for housekeeping and maintenance methods for cleaning production equipment.
Universal Oil Products East Rutherford, NJ	October 1972	October 1972	Reactors, vessels, and crystallizers are dirty. Outside surfaces and associated piping are rusty and covered with a black oily substance. Tank and piping asbestos insulation are in disrepair. These conditions represent a potential source of contamination. Scoops, hoppers, shovels, trays, dippers used in the handling of Procaine Hydrochloride crystals are not cleaned promptly after use. These utensils are dirty and encrusted with product and are potential sources of contamination.

FIRM NAME AND ADDRESS	INSPECTION DATE	MAILED TO FDA, HQ, HHS	DESCRIPTION OF VIOLATION
Packaging Corporation of America Vernon, CA	October 1972	November 1972	Toilets open directly to the manufacturing area.
Lypho-Med, Inc. Chicago, IL	November 1972	November 1972	Failure to perform complete monograph testing of propylparaben, lot RLM68, and methylparaben, lot RLM155 in accordance with the company's written test requirements. Loss on drying for each raw material was not done as required.
Zenith Laboratories Northvale, NJ	February 1973	February 1973	Failure to maintain building free of insects. A live cockroach was noted in the raw material storage area. The general appearance of the "Quarantine Area" reflects a lack of adequate janitorial service. It was heavily laden with dust and evidence of spilled raw material. It is not orderly and not arranged to facilitate cleaning and handling of containers.
Reine Pharm. Corp Roosevelt L.I., NY	March 1973	March 1973	The Technical Quality Control Director is not a full time employee and may be absent, due to family commitments at home, as noted during the survey visit. There is no designated assistant to assume duties of the Quality Control Director in the temporary absence of the Technical Quality Control Director. The plant was in poor state of repair. Observations included a cracked wooden floor in the receiving department and leakage from ceiling in the liquid fill area. Pools of water in the filling room were noted that could be tracked from one room to another. The floor drain appeared clogged with water from the leaking roof with water up to level of the drain cover.

[illegible]	INSPECTION DATE	ISSUED TO DATE WAS DISC	DESCRIPTION OF VIOLATION
Hygeia Products Inc. New York, NY	March 1973	April 1973	There are no written quality control procedures. The firm assigns a single lot number to multiple batches and this results in a lack of traceability to source material and manufacturing data for the specific batches. The platform scale used to weigh ingredients was inaccurate. The zero reading was plus 5 lbs. The section of the scale holding the weight indicator was shaky. There is no hot running water or individual towels in the ladies washroom and there is no hot running water in the men's washroom. The platform scale used to weigh ingredients is heavily crusted.
Allergan America Hormigueros, P.R.	April 1973	April 1973	A sterile 40 liter glass jug previously cleaned and sterilized and awaiting use as a surge vessel in a sterile filtration was found with an oily film and visible oil droplets on the inside surface of the bottle. The oily area was larger than the size of a half dollar. Use of the jug would have contaminated the product with foreign material and compromised the purity of the final product.
Zenith Laboratories Northvale, NJ	June 1973	June 1973	The general appearance of the "Quarantine area" reflects a lack of adequate general janitorial service. It was heavenly laden with dust and dirt. It is not orderly and not arranged to facilitate cleaning and handling of material. Failure to maintain building free of insects. Flies were noted in the production and other plant areas. Prior labeling was not effaced. A metal drum still bore the label as "Ascorbic Acid" on the container while it was also labeled Starch, lot 11239.

[illegible]	INSPECTION DATE	MAILED TO FDA, VA. PHS	DESCRIPTION OF VIOLATION
Abbott Pharmaceuticals Inc. Barceloneta, P.R.	June 1973	July 1973	Excessive use of masking tape on capsule filling machines provides a potential for contamination of product. Equipment was not routinely inspected and cleaned before each use. A capsule machine in room 506 showed evidence of dust and powdery residues when claimed to be clean and ready for use and start up.
Bay Laboratories Inc. Skokie, IL	August 1973	September 1973	The Quality Control Director has never worked in a pharmaceutical manufacturing plant. His only experience has been in retail pharmacy stores. On his own admission he does not have the necessary experience related to drug manufacturing operations.
Abbott Laboratories Ltd. Queensborough, Kent, England	August 1973	September 1973	The operator batch production records for bulk Trimethadione does not reflect the total yield of material obtained in each batch process. The records for blended commercial lots of Trimethadione did not include the quantity and batch number of all production batches entering into the final blend lots. There was no operator record covering the milling/blending step for Trimethadione to show such information as component batches, and input weights, times, equipment and operator.

FIRM NAME AND STREET ADDRESS	INSPECTION DATE	MAILED TO FDA, VA, PHS	DESCRIPTION OF VIOLATION
Kentuckiana Pharmaceuticals Inc. Louisville, KY	September 1973	October 1973	No written operating or inspection procedures. Insecticide, Sodium Fluoride, is packaged in the center of a large room used to store chemicals used in formulations. Metal scoops in ready-for-use racks had residue material from previous batches. Stainless steel tanks had residue of previously manufactured liquid material. Two of the tanks had odoriferous mold growth in the liquid.
Solar Laboratories Brooklyn, NY	December 1973	December 1973	Master Formula for the proposed production batch of Lanolated Mineral Oil not available. Control of labels and labeling not established. Written procedures not available for production, quality control, laboratory, calibration, maintenance and sanitation.
Mallinckrodt Chemical Works St. Louis, MO	November 1973	December 1973	The low velocity exhaust system in hood area permits residue to fall on the work area in the hood. The hood exhaust system and balances in the hood area contained residue of previous operation.
Pfizer Pharmaceuticals Barceloneta, PR	December 1973	December 1973	Cobwebs and dust was noted in the synthesis plant on a large number of drums of raw material. A fly was noted in the area where Meclizine Hydrochloride Powder was being transferred, after centrifuging, into plastic bags. The three different shifts in the plant use differing Systems of lot identification for the same product. As a result the integrity of the lot numbering system could not be satisfactorily explained by the company.

32-814 (Pt. 24) O - 74 - 8

15. **ANSWER:** (Cont'd)

(e) EXPLANATORY NOTES FOR ADDITIONAL REQUIREMENTS

ADDITIONAL REQUIREMENT	EXPLANATION AND SIGNIFICANCE
Color Limits	In the procurement of injectables and other preparations, the procuring agency experienced instances wherein the products offered varied in color (darker than usually encountered) within the lots, from lot to lot, and from manufacturer to manufacturer. This was objectionable to the medical personnel administering the injections or dispensing the preparations, because the discolored or tinted liquids were suspected of being degraded, and therefore not suitable for issue and use. Without standards for color limits, a "colorless" requirement could not be enforced contractually. It became necessary to develop color limit standards in order to uniformly procure material of adequate purity so that the contents are suitable not only at the time of procurement but after exposure through the military supply channels. Color development can be progressive in nature, and thus it is the desire to start with a product which has less color at the outset and therefore, represents a purer material with less possibility of degradation at time of use.

ADDITIONAL REQUIREMENT	EXPLANATION AND SIGNIFICANCE
Classification of Defects	Classification of Defects is a list of deficiencies which can be tolerated to a limited extent. These physical defects are detected upon examination of the product. For contractual purposes it is necessary to delineate the physical characteristics, designate a sampling plan, and determine the amount of defective characteristics that are permitted within the sampled quantity. It should be noted that such test characteristics as strength and purity are not designated within the Classification of Defects because compliance with those requirements is fully mandatory. Without a Classification of Defects and an Acceptable Quality Level, a procurement agency could not contractually limit such defects as excessively chipped tablets, excessive powder in a tablet container, broken tablets, cracked capsules, etc. The Classification of Defects, therefore, defines the general quality of the item in terms of physical characteristics, which subsequently may have a bearing on the dosage administration to the patient.
Solubility Time Limit	With the advent of Parenterals for Injection in which powdered or freeze-dried material is solubilized prior to use, it became necessary to assure that the contents would readily and completely solubilize upon addition of diluents prior to use. This requirement establishes the rate of solubility and presents a basis for examining for the presence of particulate matter. Compliance with such requirements renders the product more rapidly available for use and precludes the injection of particulated or undissolved material for which there are no official standards.

ADDITIONAL REQUIREMENT	EXPLANATION AND SIGNIFICANCE
Hardness Limits	Tablet hardness is a function of the pharmaceutical manufacturing process and is an appropriate tool to measure uniformity and consistency in products. It may have a bearing on breakage or crumbling of the tablets in shipment as well as uniformity from lot to lot and within a lot. Therefore tablet hardness represents another important control factor in assuring uniform and constant dosage for the patient.
Accelerated Aging Test	In the large volume procurement of medical materiel, which may undergo lengthy and adverse transportation and storage, it is desirable to determine in advance whether a product that may be offered will remain stable for the required period of time. In addition, drug products generally have a deterioration rate which may vary with the product, the formulation, and the method of manufacture. In those instances where proof of stability is necessary because of a predetermined long shelf life or because deterioration has been experienced, it is necessary to establish standards prior to contracting. This serves to preclude the potential for administering/dispensing deteriorated medicaments. Compliance with this requirement contributes to longer shelf life and reduces the possibility of having deteriorated stock on hand that must be destroyed.
Maximum Unrefrigerated Shipping Times for Items Requiring Refrigerated Storage	Drug products which require refrigeration are sensitive to unrefrigerated conditions such as room temperature or elevated temperature. There are no established requirements which would limit the unrefrigerated shipping time from manufacturer to depots and

ADDITIONAL REQUIREMENT	EXPLANATION AND SIGNIFICANCE
	to the ultimate user. In order to prevent or retard deterioration or decomposition, it is necessary to designate how long a refrigerated product may be out of refrigeration. This reduces the potential for administration of substandard medication.
Leakage Tests for Ampuls	There was a time when the procuring agency experienced leakage of flame-sealed ampuls. In order to preclude the procurement of material with such defects, it is required that all flame-sealed ampuls be subjected to a leakage test. Ampuls which are not totally sealed are subject to contamination which would be detrimental to a patient.
Taste/Palatability Panel	The procuring agency experienced instances wherein a product could not be tolerated by patients because of objectionable taste. DPSC experienced a drug recall because of such circumstances. Accordingly, when appropriate for the particular item, samples are requested from bidders and are evaluated by a panel for acceptance of taste and palatability. This helps to preclude the problem of patients refusing to take medicine because of particularly objectionable taste.

Thioridazine Hydrochloride Tablets USP, 10 mg, 1000's Thioridazene Hydrochloride Tablets, USP, 50 mg, 1000's Thioridazene Hydrochloride Tablets, USP, 100 mg, 1000's Thioridazene Hydrochloride Tablets, USP, 25 mg, 1000s	Disintegration	Allow less time to assure the tablets will disintegrate faster & thus release the active ingredient sooner.
	Limits for foreign substances (arsenic and heavy metals)	To assure that impurities are detected that may arise from production procedures or from changes in sources of materials or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Additional Assay	A more specific assay in as much as it is being compared to a reference standard. See Explanatory Notes.
	Classification of defects	
Isoproterenol Hydrochloride Inhalation, USP, 1:200 Solution, 10 cc	Color limits	See Explanatory Notes.
	Accelerated Aging Test (Stability Test)	See Explanatory Notes.
	Additional assay	This additional assay method was necessary since the fluorometric procedure is more specific for the isoproterenol molecule in that a trihydroxyindole derivative is formed with intact isoproterenol.
Potassium Permanganate Tablets for Solution, USP, 0.30 Gram, 100s	Solubility Time Limit (Tablets)	To assure that the tablets will dissolve within a reasonable time so that the solution can be used by the patient for external use. See Explanatory Notes.
	Classification of Defects	
Nitroglycerin Tablets, USP, 0.6 mg, 100s Nitroglycerin Tablets, USP, 0.3 mg, 100s	Solubility Time Limit (Tablets)	Specify a tighter time limit of 30 seconds in lieu of 2 minutes. Complaints on regular U.S.P. tablets were received including one from the physician to the Congress of the United States.
	Accelerated Aging Tests	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.

Glyceryl Guaiacolate Syrup, NF, 100 mg per 5cc, 4 fl. oz. and 1 gal.	Taste/Palatability Test	See Explanatory Notes.
	Accelerated Aging Test	See Explanatory Notes.
	Color value, Specific Gravity, Refractive Index.	There is no official requirement defining the vehicle for this syrup in the N.F. monograph. These requirements tend to define the vehicle and yet permit competitive formulations.
Benztropine Mesylate Tablets, USP, 2 mg, 100s	Hardness limits (for tablets)	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Hydrochlorothiazide Tablets, USP, 50 mg., 1000s	Classification of Defects	See Explanatory Notes.
Propylhexedrine Inhalant, NF, 0.25 Gram	Assay limits	The lower assay limit is tighter than that in the N.F. since this type of item is made for inhalation and to readily release its active ingredient by volatilization. This assures that at least 100 percent of label claim is present at time of delivery.
Meperidine Hydrochloride Injection, USP, 50 mg per cc, 30cc	Color limits	See Explanatory Notes
	Classification of Defects	See Explanatory Notes
Aminophylline Anesthetic Suppositories 0.5 Gram, 12s	Melting time for Suppositories	To assure that the suppositories are made with a base which will melt within a specified time frame to release its medicament. No such requirement exists in the compendia.
	Leakage Test (for packaging)	To assure that this product will not leak in its packaging.

Idoxuridine Ophthalmic Ointment, USP, 0.5%, 4 Grams	Particle size of active ingredient in ointment (not over 50 microns)	This requirement is not covered by the USP monograph. This requirement was added to control the particle size of the active ingredient in the ointment which is instilled into the eyes.
	Leakage test	To assure that the tubes of ophthalmic ointment do not leak.
	NOTE: For ophthalmic ointments this Center tried for sterile ointments in early 1960's and again in 1971. In the interim the Center did have baterial limits with no pseudomonas organisms to be present. In 1973 the USP, NF and FDA took action for sterility for ophthalmic ointments.	
Alcohol, USP, 5 gal (18.92 liters)	Color Limits	See Explanatory Notes.
	Classification of Defects.	See Explanatory Notes.
Zinc Bacitracin, Neomycin Sulfate, and Polymyxin B Sulfate Ophthalmic Ointment, 1/8 oz.	Particle size of active ingredients in ointment	This requirement was added to control the particle size of the active ingredients in the ointment which is instilled into the eyes.
	Leakage Test	To assure that the tubes of ophthalmic ointment do not leak.
	Melting Range	To assure that the ophthalmic ointment with a base which will melt upon application to the eyes.
	Classification of Defects	See Explanatory Notes.

	ADDITIONAL REQUIREMENT	SPECIFIC USE
Lidocaine Hydrochloride Injection, USP, 1-1/2%, with Epinephrine 1:200,000, 30 cc, 5s	Color limits	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Corticotropin Injection, USP, 40 USP Units	Color limits	See Explanatory Notes.
	Solubility time limit	See Explanatory Notes.
	Content Uniformity	The U.S.P. monograph does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and thus proper and uniform dosage.
	Classification of defects	See Explanatory Notes.
Hyaluronidase For Injection, NF,25s	Color limits	See Explanatory Notes.
	Solubility time limit	See Explanatory Notes.
	Content uniformity	The N.F. Monograph does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and thus proper and uniform dosage.
	Classification of Defects	See Explanatory Notes.
Methylergonovine Maleate Injection, USP, 0.2 mg, 1cc, 12s	Color limits	See Explanatory Notes.
	Leakage test for ampuls	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.

Lidocaine Hydrochloride Injection USP, 0.5%, 50 cc	Color Limits	See Explanatory Notes.
Lidocaine Hydrochloride Injection USP, 1%, 50 cc	pH Limits	A tighter pH range is specified in order to assure greater stability over the shelf-life of the item
Lidocaine Hydrochloride Injection USP, 2%, 20 cc	Classification of Defects	See Explanatory Notes.
Tripelennamine Hydrochloride Tablets, USP, 50 mg, 1000s	Classification of Defects	See Explanatory Notes.
Ephedrine Sulfate Tablets, USP 0.2 mg, 100s	Classification of Defects	See Explanatory Notes.
Sodium Phenobarbital Injection, USP, 0.162 Gm per cc, 2 cc, 5s	Color Limits	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.

Information Required by Senator Nelson
from Department of Defense

15. ANSWER: (Cont'd)

(d) RE: Digoxin Tablets

Learned of problem - 1965.

Information to FDA - No record. This was before the Intra-Governmental Professional Advisory Council on Drugs and Devices (IPADD) was fully operational.

Drug Specialist - Cannot determine who became acquainted with problem first. The subject arose as a result of field complaints.

RE: Other examples

The other examples refer to information obtained through published literature, and complaint reports received by DPSC.

Such publications as The Bio-availability of Drug Products by the American Pharmaceutical Association and the Pharmacokinetics discuss equivalence and inequivalence of drug products.

Such drug products as Diphenylhydantoin Sodium Capsules, Nitrofurantoin Tablets, Prednisone Tablets, Nitroglycerin Tablets, Cortisone Tablets, and Thyroid Tablets were the subject of field complaints dealing with effectiveness. All field complaints are routinely forwarded to FDA as agreed upon via IPADD. The dates of complaint submittals are shown as follows:

ITEM INEFFECTIVE	FDA ADVISED
Diphenylhydantoin Sodium Capsules	4 December 1963
	12 December 1963
	15 April 1964
	27 January 1966
	2 May 1966
Nitrofurantoin Tablets	22 May 1961
	16 June 1961
	5 March 1962
	11 April 1962
	25 November 1969 (2 reports)
	23 December 1969
	2 January 1970
	17 February 1970
	15 May 1970
	12 July 1971

Information Required by Senator Nelson
from Department of Defense

15. ANSWER: (Cont'd)

ITEM INEFFECTIVE	FDA ADVISED
Predisone Tablets	16 March 1970 12 December 1970 12 July 1971
Nitroglycerin Tablets	12 July 1971
Cortisone Acetate Tablets	12 July 1971 16 November 1973
Thyroid Tablets	16 February 1961 14 March 1961 6 July 1961 8 September 1961 16 October 1961

The drug specialists who first became acquainted with the problems are those who saw the field complaints first. Our records do not identify the personnel in that manner.

Information Required by Senator Nelson
from Department of Defense

16. QUESTION:

(a) Please state deviations from FDA's good manufacturing practices regulations which the DOD considers significant, and which are not considered significant by the FDA?
Please identify where there is a difference of opinion.

(b) Who in DPSC makes the determination whether the raw observations are significant?

(c) What criteria does DPSC use?

(d) Does DPSC relate the violation to a particular product? In other words, does the violation, for example, contribute to the contamination of the product?

ANSWER:

(a) The FDA Papers of April 1967 in an article "Good Manufacturing Practice" states the Food and Drug Administration is convinced that most, if not all, of the problems of drug quality can be solved by compliance with the minimum requirements of the Current Good Manufacturing Practice regulations. The article also states, "Analysis of the fiscal year 1966 recalls shows that 351, or 78 percent, were for reasons which would be related to a failure to observe GMP regulations." The FDA Handbook of Total Drug Quality of July 1971 states in an article: Case Studies of Drug Recalls, "We found that 75-80 percent of the errors contributing to drug recalls were due to deficiencies and failures to meet the requirements of the Current Good Manufacturing Practice regulations." The FDA Compilation of Case Studies of Drug Recalls of March 1973, lists case after case with the applicable GMP sections which relates to the apparent cause(s) of the recall.

All the GMP's are considered significant in order to manufacture quality drug products. The problem is that the FDA GMP's provide only general guidelines. This is recognized by FDA as in the Federal Register of January 15, 1971, it was stated, "In the Federal Register of August 22, 1969 (34 F. F. 13553) a notice was published proposing a revision of Section 133.1 - 133.14 to clarify, strengthen, and make more specific the good manufacturing practice regulations for drugs."

The DPSC Standards for the Manufacture and Packaging of Drugs, Pharmaceuticals and Biologicals were published in 1968. It was necessary to set these practices down in more detail and with a higher degree of specificity. This is absolutely necessary to accomplish the mission of DPSC -- to deal with our suppliers and potential suppliers in a contractual, not a regulatory capacity. A prime obligation of this relationship is that DPSC must deal with all on an equal basis and before this equality can be established it is essential that all suppliers and potential

Information Required by Senator Nelson
from Department of Defense

16. ANSWER: (Cont'd)

suppliers fully understand the requirements that must be met. The DPSC Drug Standards with their definitiveness are very essential for the continued support of quality procurement. It has been announced that the following proposed revisions in GMP's will be made in 1974:

a. Add a section on Sanitation.

b. Personnel responsible for Quality Control shall not also be responsible for production.

c. Requirement that all production and control procedures be reduced to writing.

d. Provision for the establishment of definitive records of all tests and assays.

e. A written record shall reflect which pieces of equipment within each operation are or were in operation at any point in time.

f. Establish a requirement for the formal training of employees.

g. Each container sampled shall be suitably identified.

h. Require reserve samples of inactive ingredients shall be retained.

i. Qualifications of consultants.

(b) A brief explanation of the scope and effectiveness of the pre-award survey is as follows:

The Armed Services Procurement Regulation (ASPR) requires that the contracting officer shall make a determination of responsibility or non-responsibility of the prospective contractor. If the information available to the purchasing office is not sufficient to enable the contracting officer to make a determination regarding a prospective contractor, a pre-award survey is conducted by the Contract Administration Office.

Information Required by Senator Nelson
from Department of Defense

16. ANSWER: (Cont'd)

A Pre-Award Survey required in-depth knowledge of various technical areas in order to derive the necessary professional judgments regarding the bidder's capability to perform in accordance with the terms and conditions of proposed contract. The Pre-Award Survey involves expertise in such areas as finance, development and production operations, production engineering, specialized engineering, quality control, accounting, industrial management, industrial property management and disposal, commodity specialist and purchasing activity representatives. In addition, assistance frequently may be required from legal, small business and industrial labor relations specialist. Consideration is given to utilization of available DCAS experts and likewise to those technicians and specialists available from purchasing activities. Each team member contributes his specialized knowledge and professional judgment under and with the overall guidance of the team coordinator and Pre-Award Survey Monitor. The monitor, in turn, is responsible for submitting the integrated results of the survey to the chairman of the Pre-Award Survey Board for approval and transmittal to the purchasing office. The survey report and recommendations are then forwarded to DPSC where the report is reviewed and evaluated by personnel in the Quality Assurance Branch. A summary of technical findings, which required approval by the Chief of the Branch, is prepared together with a recommendation to the contracting officer.

(c) DPSC utilizes the DPSC Drug Standards; Federal Standards on Tablets, Capsules and Parenteral Preparations; Military Inspection System Specification, and any other specific specifications contained in the procurement solicitations.

(d) Inspection is done in the plant for the procurement item to determine compliance of plant and product to requirements. Violations may contribute to the contamination of the product.

CONTENTS

ENCLOSURE 1

TAB A

QUESTIONNAIRE

INFORMATION REQUIRED BY SENATOR NELSON FROM DEPARTMENT OF DEFENSE (DCAS INPUT)

2. QUESTION:

What percent of pre-award surveys are done by DPSC? By DSA?

ANSWER: (Revision to answer contained in first increment)

All pre-award surveys are done by Defense Contract Administration Services. Defense Personnel Support Center may elect to participate. In Fiscal Year 1973 Defense Contract Administration Services conducted 397 pre-award surveys on medical material. Of these 235 were on drugs. Defense Personnel Support Center participated in a total of 156 pre-award surveys. Of these participations, 101 were on drug pre-award surveys. During Fiscal Year 1973, Defense Contract Administration Services devoted 5 man-years to medical pre-award surveys. Of this figure, 3.4 man-years were devoted to drug pre-award surveys.

4. QUESTION:

How many man-years were devoted in FYs 1969, 1971 and 1973 to the inspection of drugs by DPSC? By DSA?

ANSWER: By DSA. (DCAS)

Fiscal Year 1969 -- Approximately 30 ✓
Fiscal Year 1971 -- Approximately 30 ✓
Fiscal Year 1973 -- Approximately 30 ✓

5. QUESTION:

What percentage of man-years of inspection time was devoted in the same years to:

Pre-award surveys?
In-process inspection?
Acceptance of product inspection?
Other?

ANSWER:

DCAS	Fiscal Year 1973	Fiscal Year 1971	Fiscal Year 1969
Pre-Award Surveys	Approx. 11%	Approx. 14%	Approx. 20%
In-Process Inspection	Approx. 19%	Approx. 18%	Approx. 18%
Acceptance of Product Inspection	Approx. 39%	Approx. 42%	Approx. 40%
Other	Approx. 31%	Approx. 26%	Approx. 22%

7. QUESTION:

For Fiscal Year 1973 please give the number of people in:

DSA -- Overhead assigned to DPSC Medical Material
DCAS -- Medical material support for drugs and other medical material
DPSC -- Medical Directorate
Supply Operations
Technical Operations
Laboratory
Overhead
Procurement Directorate
Medical Division
Drugs
Other

ANSWER:

DCAS -- Medical material support for drugs and other medical material:

Drugs -- 303
Other -- 267

It should be emphasized that the above figures represent full, part-time and/or backup personnel. Those on part-time or backup assignments have other non-drug or non-medical duties such as medical devices, chemicals and petroleum. Consequently, man-years give more objective measurement of manpower, as was done in the answer to question 4 covering drug procurements for Fiscal Years 1969, 1971, and 1973. A similar measurement in man-years would be helpful in assessing the other non-drug medical procurement manpower data. For Fiscal Year 1973, the Defense Contract Administration Services manpower effort (full, part-time and backup) in support of drug procurement is broken down by organizational units approximately as follows: Quality Assurance -- 71 percent, Production -- 12 percent, Contract Administration -- 15 percent and 2 percent for other support.

9. QUESTION:

Please give total DoD annual budget involved in inspection of drugs for Fiscal Years 1969, 1971 and 1973.

ANSWER:

Defense Contract Administration Costs -- Drugs

Fiscal Year	Quality	Production	Contract Administration	Other	Total
1969	$443,304	$121,756	$80,698	$9993	$655,751
1971	$404,593	$103,076	$96,373	$4393	$608,435
1973	$547,090	$ 87,859	$89,853	$5750	$730,552

TAB B

NON-PROCUREMENT QUALITY ASSURANCE TASKS PERFORMED BY DRUG QUALITY ASSURANCE REPRESENTATIVES (DCAS)

Quality assurance representatives support other contract administration elements and the Defense Personnel Support Center in the following areas upon request or as the occasion demands:

a. Damage, Abuse, Destruction of Government Furnished Material. Unauthorized damage, abuse, or destruction of Government-owned material is reported to the property administrator.

b. Strikes and Walkouts. Occurrences are reported to Industrial Labor Relations.

c. Buy American Act. Unauthorized purchases of raw materials from foreign sources are reported to Defense Personnel Support Center.

d. Physical Security. Unsecure storage and handling of narcotics and dangerous drugs are reported to the contractor and the Drug Enforcement Administration of the Department of Justice.

e. Accidents. The Office of Specialized Safety and Flight Operations is advised of accidents resulting in injury to Government employees or jeopardy to delivery schedules.

f. Termination Settlements. Costs are validated in support of the termination contracting officer.

g. Carrier Damage Complaints. Complaints are investigated in support of the Office of Transportation.

h. Production Support. Problems that may influence delivery schedules are reported to the industrial specialist.

PREAWARD SURVEYS
(DCAS)

In the process of awarding a contract for goods or services, it is the policy of the United States Government to evaluate business organizations submitting bids as to their competence, capability and responsibility to perform on the contract. The purpose of this policy is to assure timely delivery of quality products at fair and reasonable prices. The evaluation is called a "preaward survey."

Another preaward action, separate and distinct from the one described above, is performed by Department of Defense Contracts Compliance Offices. This is known as a preaward review and is performed to determine if the contractor is in compliance with Executive Orders and Department of Labor regulations regarding equal employment opportunity. Preaward reviews performed by Contracts Compliance Offices are separate and distinct from preaward surveys. The two should not be confused.

For the Department of Defense and other selected Government agencies, the majority of preaward surveys are made by nationwide offices of the Defense Contract Administration Services (DCAS) according to guidelines outlined in the Armed Services Procurement Regulations. As the situation may require, other DoD or non-DoD specialists may participate in the surveys also.

A survey is conducted at the request of a buying agency. It is a team effort by military and civilian personnel who are specialists in fields such as accounting, production, contract management, business administration, property management, quality assurance, engineering, transportation, packaging, industrial labor relations, industrial security, legal counsel, and industrial readiness. They investigate the prospective contractor's technical capability, production capability, purchasing and subcontracting methods, accounting methods, quality control system, transportation and packaging facilities, plant safety, labor resources, performance record, and other factors which may be specifically requested by the buying agency. The findings are reported to the purchasing agency who makes a determination of the contractor's responsibility, as well as the decision to award the contract.

The enclosed pamphlet describes preaward surveys in detail.

1 Encl
Preaward Survey Information
for Prospective Government
Contractors, January 1973

TAB C

QUESTIONNAIRE

INFORMATION REQUIRED BY SENATOR NELSON FROM DEPARTMENT OF DEFENSE (DPSC INPUT)

4. QUESTION:

How many man-years were devoted in FYs 1969 and 1971 to the inspection of drugs by DPSC? By DSA?

ANSWER:

Approximately 5.5 man-years of the technical personnel assigned to the Quality Assurance Branch DPSC were devoted to the inspection of drugs in FYs 69 and 71.

5. QUESTION:

What percentage of man-years of inspection time was devoted in the same years to:

Pre-award surveys?
In-process inspection?
Acceptance of product inspection?
Other?
In-store (Depot) surveillance?

ANSWER:

	FY 69	FY 71
Domestic Pre-Award Surveys		
Preparation/on site DPSC Participation and Report Preparation	19%	19%
Requesting, Evaluation, and Report Preparation where DPSC did not participate	32%	32%
Foreign Surveys	19%	19%
In-Process Inspection	-	-
Other		
Pre-Award Samples	10%	8%
Misc (Supervision, Review of Protocol, Special Inspection Requests, Contract Review, etc.)	15%	17%
In-Store (Depot) Surveillance (Quality Systems Management Visit only)	5%	5%
	100%	100%

6. QUESTION:

For FYs 1969, 1971 and 1973 how many man-years of laboratory work went into support of the inspection process? Please break down the total laboratory man-years into:

DPSC laboratory
Contract laboratories
Other (specify)

ANSWER:

Laboratory work in support of the inspection process for drugs and non-drugs ** (covering pre-award samples, contractual samples, pre-acceptance samples and samples submitted by the QAR for verification) is as follows:

	FY 69		FY 71		FY 73	
DPSC Laboratory	12 man-years (4.4 man-years devoted to drugs)		7 man-years (1.8 man-years devoted to drugs)		9 man-years (2.3 man-years devoted to drugs)**	
	Samples*	Cost	Samples*	Cost	Samples*	Cost
Contract Laboratories	14	$845.00	9	$380.00	8	$845.00
Other Laboratories	413	$7,720.18	464	$8,032.59	213	$4,819.55
Walter Reed	373	$6,585.74	390	$6,327.86	144	$3,101.00
U.S. Army Medical Research Lab, Ft. Knox	40	$1,134.44	74	$1,704.73	69	$1,718.55

* Man-year data not available.
**Added for clarification.

9. QUESTION:

Please give total DoD annual budget involved in inspection of drugs for Fiscal 1969, 1971, 1973.

ANSWER:

Estimated DPSC Budget for Inspection of Drugs

FY 69	$165,000 - See 9a for details.
FY 71	$157,000 - See 9b for details.
FY 73	$187,000 - See 9c for details.

9.a. FY 69

Lab - Technical and Clerical

# Persons	X Annual Salary @ GS-9	+ Related (8+1/2%)	
4.4	X $9320.00	X 1.085	$44,827.86

ATQ - Quality Assurance Branch Technical

# Persons	X Annual Salary @ GS-12	+ Related (8+1/2%)	
5.5	X $13,389.00	X 1.085	79,898.86

ATQ - Quality Assurance Branch Clerical

# Persons	X Annual Salary @ GS-3	+ Related (8+1/2%)	
1	X $4360.00	X 1.085	4,730.60

DPSC Overhead

# Persons	X Annual Salary @ GS-7	+ Related (8+1/2%)	
2	X $7639.00	X 1.085	16,576.63

TDY

Foreign & Domestic		
$3650.00	$6900.00	10,550.00

Outside Lab Testing

Walter Reed & Ft. Knox & Commercial		
$6585.74	& $1134.44 & $845.00	8,565.18

$ 165.149.13

9.b. FY 71

Lab - Technical and Clerical

# Persons	X Annual Salary @ GS-10	+ Related (8+1/2%)	
1.8	X $10,252	X 1.085	$20,022.16

ATQ - Quality Assurance Branch Technical

# Persons	X Annual Salary @ GS-12	+ Related (8+1/2%)	
5.5	X $15,040	X1.085	89,805.45

ATQ - Quality Assurance Branch Clerical

# Persons	X Annual Salary @ GS-3	+ Related (8+1/2%)	
1	X $5524	X 1.085	5.993/54

DPSC Overhead

# Persons	X Annual Salary @ GS-7	+ Related (8+1/2%)	
2	X $8582	X 1.085	18,622.94

TDY

Foreign	&	Domestic	
$7490	&	$7300	14,390.00

Outside Lab Testing

Walter Reed	&	Ft. Knox	&	Commercial	
$6327.86	&	1704.73	&	380.00	8,412.59

$157,246.68

9.c. FY 73

Lab - Technical and Clerical

# Persons	X Annual Salary @ GS-10	+ Related (8+1/2%)	
2.3	$12,775	X 1.085	$31,880.01

ATQ - Quality Assurance Branch Technical

# Persons	X Annual Salary @ GS-12	+ Related (8+1/2%)	
6	X $16,682	X 1.085	108,599.82

ATQ - Quality Assurance Branch Clerical

# Persons	X Annual Salary @ GS-3	+ Related (8+1/2%)	
1	X $6128	X 1.085	6,648.88

DPSC Overhead

# Persons	X Annual Salary @ GS-7	+ Related (8+1/2%)	
2	X $9520	X 1.085	20,658.40

TDY

Foreign	&	Domestic	
$6150	&	$7030	13,180.00

Outside Lab Testing

Walter Reed	&	Ft. Knox	&	Commercial	
$3101.00	&	1718.55	&	845.00	5,664.55

$186,631.86

13. QUESTION:

For the 150 top drugs -- by dollar volume -- bought by DoD:

Which pharmaceutical companies supplied the information which was incorporated into each specification?

For each of these drugs, give the names of pharmaceutical companies who have been successful bidders on DPSC contracts for each product since original specification was first written. Please give stock numbers, and established and trade names of each product.

ANSWER:

The list of 150 top drug items forwarded with original submittal was based upon demands from customers. This was the only listing that was available within the prescribed time frame.

We have now developed a list of top dollars purchased (drugs) and find that 27 products should be added to the list, and correspondingly 27 items should be deleted from the list.

Attachment (a) is the list of 27 items that should be added. It should be noted that the numerical sequence is stated for each item. The numerical sequence of the original list (attachment (b)) is modified accordingly and forwarded herewith.

NO.	FSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
54	721-9232	Diiodohydroxyquin Tablets, USP, 0.65 Gram, 60's	Diodoquin G. D. Searle & Co.	G. D. Searle & Co.	G. D. Searle & Co. Strong, Cobb, Arner Panray	
57	104-8069	Methylprednisolone Sodium Succinate for Injection, NF, Equivalent to 1 Gram of Methylprednisolone	Solu-Medrol 1000 mg Upjohn Company	Upjohn Company	Upjohn Company	Patent NDA
62	105-9500	Aminophylline Injection, USP, 25 mg per cc, 10 cc, 25's	Aminophylline IV 250 mg, 10 ml G. D. Searle & Co.		Gotham Vitarine Elkins-Sinn Natcon	
65	985-7224	Test Kit, Syphilis Detection, Brewer Type, 100 Tests	Brewer Diagnostic Kit-RPR Card Test Hynson, Wescott and Dunning, Inc.	Hynson, Westcott and Dunning Inc.	Hynson, Westcott and Dunning.	
69	299-8610	Chlorpheniramine Maleate Tablets, USP, 4 mg, 1000's	Chlor-Trimeton Tablets Schering Corp	Schering Corp.	Anabolic Inc. Dow Nutrilite Nysco Beecham-Massengill Panray Schering Corp.	NDA
84	890-2172	Potassium Penicillin G, Sterile, USP, 20,000,000 Units	Penicillin G Potassium Ampoules, Sterile, USP No. 537, 20,000,000 Units 100 ml. size Eli Lilly & Co.	Eli Lilly & Co.	Pfizer Eli Lilly Premo	Form 6
97	299-8175	Sodium Sulfacetamide Ophthalmic Ointment, Modified 30%, 1/8 oz., 12's		Schering Corp. Strong Cobb Arner	Schering Corp. Strong Cobb Arner	NDA

NO.	FSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
101	680-7352	Promethazine Hydrochloride Injection, USP, 25 mg per cc, 25's	Phenergan Injection Wyeth Labs.	Wyeth Labs.	Wyeth Labs.	NDA
107	530-6470	Prednisone Tablets, USP, 5 mg, 1000s	Meticorten Schering Deltra Merck, Sharp & Dohme Deltasone Upjohn Co.	Schering Merck, Sharp & Dohme Upjohn Co.	Schering Premo Upjohn Co. Lemmon Halsey Strong Cobb Arner Success Chase	NDA
108	900-0354	Sodium Oxacillin for Injection, USP, Equivalent to 1.0 Gram of Oxacillin	Prostaphlin Bristol Labs.	Bristol Labs.	Bristol Labs.	Form 6
112	890-1373	Simethicone Tablets, 40 mg, 500's	Mylicon Tablets Stuart	Stuart	Stuart Reed & Carnrick	Patent
118	914-5297	Hemorrhoidal Suppositories with Hydrocortisone Acetate, 12's	Anusol-HC Warner Chilcott Labs.	Warner Chilcott Labs.	Warner Chilcott Labs.	
120	226-1203	Test Strips and Color Chart Urinary Glucose and Protein, 100's	Uristix Ames Co.	Ames Co.	Ames Co.	
122	181-7895	Phenylbutazone Tablets, USP, 100 mg, 1000's	"Butazolidin" Geigy Azolid U. S. Vitamin Pharm. Corp.	Geigy U. S. Vitamin Pharm. Corp.	U. S. Vitamin Pharm. Corp. Geigy	NDA
124	064-3940	Triamcinolone Acetonide Cream, USP, Topical, 0.1%, 5 lb. (2.27 kg)	Aristocort Cream Lederle Labs. Kenalog E. R. Squibb & Sons	Lederle Labs. E. R. Squibb & Sons	Lederle Labs. E. R. Squibb & Sons	NDA

NO.	FSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
125	105-8900	Aluminum Hydroxide Gel, USP, 1 pt. (473 cc)	Amphojel Suspension Wyeth Laboratories	Wyeth Labs.	Wyeth Labs.	
129	080-0617	Test Kit, Pregnancy Determination, 25 Tests	Pregnosticon Accuspheres Organon Inc.	Organon Inc.	Organon Inc.	B O B
131	159-5011	Test Kit, Syphilis Detection, Brewer Type, 500 Tests	Brewer Diagnostic Kit-RPR Card Test Hynson, Westcott, and Dunning, Inc.	Hynson, Westcott, and Dunning, Inc.	Hynson, Westcott and Dunning, Inc.	
133	854-2242	Guanethidine Sulfate Tablets, USP, 10 mg, 100's	Ismelin Ciba Pharmaceutical Co.	Ciba Pharm. Co.	Ciba Pharm. Co.	Patent NDA
134	784-4977	Sodium Iothalamate Injection, USP, 66.8%	Conray 400 Mallinckrodt Chemical Works	Mallinckrodt Chem. Wks.	Mallinckrodt Chem. Wks.	
135	559-8456	Sodium Chloride Injection, USP, 5 cc, 25's			Natcon Lincoln Labs. Vitarine Abbott Torigian	
136	890-1657	Kaolin and Pectin Mixture, Dehydrated, 47 Grams		Upjohn Co.	Upjohn Co.	
138	253-8480	Hydrogen Peroxide Solution, USP, 1 lb., (453.6 Grams)			Peroxide & Specialties Co. Dewey Products Co. Certified Labs.	Amole

	NDA NUMBER	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
139	584-3179	Methylphenidate Hydrochloride Tablets, USP, 10 mg, 1000's	"Ritalin" Ciba Pharm.	Ciba Pharm.	Ciba Pharm.	NDA
141	142-9203	Mumps Virus Vaccine, Live, Attenuated, Jeryl Lynn, (B Level) Strain Lyophilized Dried, Equivalent to 0.5 cc, Single Doses	"Lyovac Mumpsvax" Merck, Sharp & Dohme	Merck, Sharp & Dohme	Merck, Sharp & Dohme	Patent B O B
148	107-0922	Betamethasone Valerate Cream, NF, Equivalent to 0.1% of Betamethasone, 45 Grams	"Valisone" Schering Corp.	Schering Corp.	Schering Corp.	NDA
149	138-7400	Quinidine Sulfate Tablets, USP, 0.2 Gram, 100's			Norwich Eli Lilly Premo Wm. S. Merrell Parke Davis Davies Rose Hoyt Strong Cobb Arner Vitarine	

JAN 26 1974

	FSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
1	2 783-7218	Diazepam Tablets, NF, 5 mg, 500s	Valium Roche Laboratories	Roche Labs.	Roche Labs.	Patent, NDA
2	1 890-1856	Methyldopa Tablets, USP, 0.25 Gram, 100s	Aldomet Merck Sharp & Dohme	Merck Sharp & Dohme	Merck Sharp & Dohme	Patent, NDA
3	6 664-7116	Potassium Penicillin G for Injection, USP, 1,000,000 Units		Wyeth Labs E. R. Squibb & Sons Pfizer Labs. Eli Lilly & Co.	Pfizer Labs. E. R. Squibb & Sons Romar Labs.	Form 6
4	753-5042	Streptomycin Sulfate, USP, Equivalent to 1 Gram of Streptomycin Base		Pfizer Labs.	Pfizer Inc. Eli Lilly & Co.	E. R. Squibb & Sons Form 6
5	28 116-4600	Dextrose Injection, USP, 5%, 1000 cc, 6s			Travenol Labs. Baxter Labs. Cutter Labs.	
6	29 146-4425	Sulfisoxazole Tablets, USP, 0.5 Gram, 1000s	Gantrisin Roche Labs.	Roche Labs.	Roche Labs.	Warner-Chilcott Labs. Upjohn Labs. NDA
7	3 160-7410	Procaine Penicillin For Aqueous Injection, 1,500,000 Units			Pfizer Labs. E. R. Squibb & Sons Inc.	Form 6

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 10057

JAN 26 1972

NO.	FSN (3525)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
8 10	181-7635	Ampicillin Capsules, USP, 0.25 Gram, 1000s	Polycillin Bristol Labs Beecham-Massengill Pharmaceuticals Totacillin Principen E. R. Squibb & Sons Penbritin Ayerst Labs. Omnipen Wyeth Labs	Bristol Labs. Beecham-Massengill Pharmaceuticals E. R. Squibb & Sons Ayerst Labs.	Bristol Labs Wyeth Labs Beecham Massengill	Averst Labs Upjohn Co. Form 6 Patent
9 5	165-6545	Cephalexin Monohydrate Capsules, Equivalent to 0.25 Gram of Cephalexin, 100s	Keflex Eli Lilly & Co.	Eli Lilly & Co.	Eli Lilly & Co.	Form 6
10 50	299-8179	Albumin, Normal Human Serum, USP, 25%, 100 cc			Metrix Div. of Armour Pharmaceutical Hyland Labs E.R. Squibb Cutter Labs Courtland Labs	BOB License
11 58	687-8047	Benzathine Penicillin G Suspension, Sterile, USP, 1,200,000 units in Aqueous Suspension, Cartridge-Needle Unit, 2 cc size, 20s	Bicillin Wyeth Labs	Wyeth Labs	Wyeth Labs	Form 6
12 12	958-2364	Propoxyphene Hydrochloride Capsules, USP, 65 mg, 500s	Darvon Pulvules Eli Lilly & Co.	Eli Lilly & Co.	Eli Lilly & Co. Smith Kline & French Labs.	NDA Rachelle Labs. Anabolic Labs. Nylos Labs. Barr Labs. Lederle Labs. off patent in 1972

	NDC (5-3-2)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
13	11 961-5504	Nystatin, Gramicidin, Neomycin Sulfate, and Triamcinolone Acetonide Cream, Topical, 15 Grams	Mycolog Cream E. R. Squibb & Sons	E. R. Squibb & Sons	E. R. Squibb & Sons	Patent Form 6
14	17 890-1764	Plasma Protein Fraction, USP, Heat-Treated, 5% Solution, 250 cc	Plasmanate Cutter Labs	Cutter Labs Hyland, Div of Travenol Labs	Cutter Labs Hyland, Div of Travenol Labs	BOB License
15	9 014-1028	Chlorpheniramine Maleate, Iscpropamide Iodide, and Phenylpropanolamine Hydrochloride Capsules, 500s	Ornade Spansules Smith Kline & French Labs	Smith Kline & French Labs	Smith Kline & French Labs	NDA Off patent in 1957
16	27656-1612	Potassium Phenoxymethyl Penicillin Tablets, USP, 4000,000 Units, 100s	V-Cillin K Tablets Eli Lilly & Co. Pen-Vee K Tablets Wyeth Labs		Eli Lilly & Co. Abbott Laboratories Biocraft	Form 6
17	7 901-0043	Triamterene and Hydrochlorothiazide Capsules, 1000s	Dyazide Smith Kline & French Labs	Smith Kline & French Labs	Smith Kline & French Labs	NDA Patent
18	22900-2146	Sodium Cephalothin, Sterile, USP, Equivalent to 1 Gram of Cephalothin	Keflin Eli Lilly & Co.	Eli Lilly & Co.	Eli Lilly & Co.	Form 6 Patent
19	20059-9017	Chlordiazepoxide Hydrochloride Capsules, USP, 10 mg, 500s	Librium Roche Labs	Roche Labs	Roche Labs	Patent NDA
20	19145-0429	Norgestrel and Ethinyl Estradiol Tablets, 63s	Ovral Wyeth Labs	Wyeth Labs	Wyeth Labs	NDA

JAN 26 1974

	FSN (CSCD)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
21 123	912-2404	Lincomycin Hydrochloride Capsules, USP, Equivalent to 0.50 Gram of Lincomycin, 100s	Lincocin The Upjohn Company	The Upjohn Co.	The Upjohn Co.	Patent Form 6
22 8	660-1676	Kanamycin Sulfate Injection, USP Equivalent to 0.333 Gram of Kanamycin per cc, 3 cc	Kantrex Bristol Labs	Bristol Labs	Bristol Labs	Patent Form 6
23 63	299-8615	Ringer's Injection, Lactated, USP, 1000 cc, 6s			Cutter Labs Baxter Labs McGaw Labs Travenol Labs	
24 13	662-9790	Erythromycin Tablets, 0.25 Gram, 100s	Ilotycin Eli Lilly & Company Erythrocin Abbott Labs	Eli Lilly & Co Abbott Labs	Eli Lilly & Co Abbott Labs	The Upjohn Co. Form 6 Off patent in 197
25 26	782-6510	Griseofulvin Tablets, USP, 0.50 Gram, 500s	Grifulvin V Tablets McNeil Labs Fulvicin Schering Corp	McNeil Labs	McNeil Labs Schering Corp	Patent Form 6
26 14	181-7180	Gentamicin Sulfate Injection, Equivalent to 40 mg Gentamicin per cc, 2 cc	Garamycin Schering Corp	Schering Corp	Schering Corp	Form 6
27 16	142-9206	Tripolidine Hydrochloride and Pseudoephedrine Hydrochloride Tablets, 1000s	Actified Tablets Burroughs Wellcome & Co, Inc	Burroughs Wellcome & Co, Inc	Burroughs Wellcome & Co, Inc	Off-patent 1972 NDA
28 38	753-9609	Hydrocortisone Sodium Succinate for Injection, USP, Equivalent to 100 mg Hydrocortisone Base	Solu-Cortef Mix-O-Vial The Upjohn Company	The Upjohn Co.	The Upjohn Co.	Patent NDA

JAN 2 6 1974

	FSN (7505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
29 25	926-8996	SPIRONOLACTONE TABLETS, USP, 25mg, 500s	"ALDACTONE TABLETS" G. D. Searle & Co.	Searle	Searle	Patent, NDA
30 15	165-6519	MEASLES, MUMPS, and RUBELLA VIRUS VACINNE, LIVE, 10s	"MMR" Merck, Sharp, & Dohme	MSD	MSD	BoB license
31 64	117-6450	CHLOROQUINE PHOSPHATE TABLETS, USP, 0.5 Gram, 500s	"ARALEN PHOSPHATE" Winthrop Laboratories	Winthrop	Winthrop	Patent, NDA
32 51	998-4381	ALLOPURINOL TABLETS, USP, 100 mg, 100s	"ZYLOPRIM" Burroughs Wellcome & Co.	Burroughs Wellcome	Burroughs Wellcome	Patent, NDA
33 126	153-9738	ESTROGENS, CONJUGATED, TABLETS, USP, 1.25 mg, 500s	"PREMARIN" Ayerst Laboratories	Ayerst	Ayerst	NDA
34 32	926-9019	DEXBROMPHENIRAMINE MALEATE and PSEUDOEPHEDRINE SULFATE TABLETS, 100s	"DISOPHROL CHRONOTAB TABLETS" White Laboratories Inc. "DRIXORAL" Schering	White	Schering	Patent NDA
35 23	869-4178	SODIUM CEPHALOTHIN, STERILE, USP Equivalent to 4 Gram of CEPHALOTHIN	"KEFLIN" Eli Lilly & Co.	Lilly	Lilly	Patent, Form 6
36 4	782-2662	QUININE SULFATE TABLETS, USP, 0.324 Gram, 1000s			Vitarine Co. Strong Cobb Arner Panray	
37 43	965-2439	OXYGEN, USP, with Tube and Face Mask, 24 gal. (90 liters)	Life-O-Gen Life-O-Gen Co.	Union Carbide Corp. (Linde) Life-O-Gen Oxequip Health Indust.	Life-O-Gen Co. Union Carbide Corp. (Linde)	
38 37	754-0086	DICYCLOMINE HYDROCHLORIDE, DOXYLAMINE SUCCINATE, and PYRIDOXINE HYDROCHLORIDE TABLETS, 100s	"BENDECTIN" Wm. S. Merrell	Wm. S. Merrell	Merrell-National Laboratories	NDA

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 10061

JAN 2 0 1974

	PSN (DSCS)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
39 96	104-9000	Alcohol, USP, 5 gal. (18.92 liters)			U.S. Indus. Chem. Publicker Ind. Lac Chemicals Inc. Carbide and Carbon Chemicals Co. Div. of Union Carbide Enjay Chem. Co.	
40 77	071-6547	Triamcinolone Acetonide, Cream, USP, 0.5% 8oz. (227 Gram)	"Aristocort" Lederle Laboratories	Lederle	Lederle	NDA
41 128	854-2504	Halothane, USP, 125cc	"Fluothane" Ayerst Laboratories	Ayerst	Ayerst Halcarbon Ltd	Patent NDA
42 43	935-5836	Ethynodiol Diacetate with Mestranol Tablets, 63s	"Ovulen" G. D. Searle & Co.	Searle	Searle	NDA
43 30	890-1840	Metronidazole Tablets, USP, 0.25 Gram, 250s	"Flagyl" G. D. Searle & Co.	Searle	Searle	Patent NDA
44 31	764-3340	Multivitamin for Injection, 10cc	"Solu-B-Forte" Mix-O-Vial The Upjohn Co.	Upjohn	Upjohn	
45 21	159-4892	Clindamycin Hydrochloride Hydrate Capsules, Equivalent to 150 mg of Clindamycin, 100s	"Cleocin" The Upjohn Co.	Upjohn	Upjohn	Form 6

JAN 2 6 1974

	FSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
46	146-2200	Sulfadiazine Tablets, USP, 0.5 Gram, 1000s			Lederle Labs Dorsey Labs Beecham-Massengill	NDA
47	116-5000	Dextrose and Sodium Chloride Injection, USP, 1000 cc, 6s			Travenol Labs Cutter Labs Abbott Labs McGaw Labs	
48	138-4610	Protein Hydrolysate Injection, USP, 1000 cc, 6s			McGaw Labs Travenol Labs Baxter Labs Don Baxter, Inc	
49	721-9383	Multivitamin Tablets, 100s			Strong Cobb Arner Chase Chem J. B. Roerig	
50 47	935-6535	Ampicillin for Oral Suspension, USP, 7.5 Gram	Penbritin Ayerst Laboratories Polycillin Bristol Laboratories Omnipen Wyeth Principen E. R. Squibb Amcill Parke-Davis & Co	Bristol Wyeth Ayerst	Bristol Wyeth Ayerst	Patent Form 6 Beecham-Massengil
51 42	062-3336	Furosemide Tablets, USP, 40 mg, 100s	Lasix Hoechst	Hoechst	Hoechst	Patent NDA
52 55	998-5872	Clofibrate Capsules, NF, 500 mg 100s	Atromid-S Ayerst	Ayerst	Ayerst	Patent NDA

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 10063

ITEM NO.	NDC NO.	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
53	890-1627	Dioctyl Calcium Sulfosuccinate Capsules, NF, 1000's	"Surfak Capsules" Hoechst	Lloyd Bros. Hoechst	Hoechst	PATENT
54	926-2154	Indomethacin Capsules, NF, 25 mg, 100s	"Indocin" Merck Sharp and Dohme	Merck Sharp and Dohme	Merck Sharp and Dohme	PATENT NDA
55	576-8342	Lidocaine Hydrochloride Injection, USP, 2%, with Epinephrine 1:100,000, 1.8 cc, 50's	"Xylocaine" Astra	Astra	Astra	NDA
56	074-4702	Diphenoxylate Hydrochloride and Atropine Sulfate Tablets, NF, 500's	"Lomotil" G. D. Searle & Co.	Searle	Searle	PATENT NDA
57	064-8765	Glyceryl Guaiacolate Syrup, NF, 100 mg per 5cc, 4 fl. oz. (118 cc)	"Robitussin Syrup" A. H. Robins	A. H. Robins	A. H. Robins G & W Laboratories Strassenburg Dorsey	Natcon
58	926-2241	Tolnaftate Solution, USP, 1 %, 10 cc	"Tinactin Solution" Schering	Schering	Schering	NDA PATENT
59	104-9723	Aspirin Tablets, USP, 75 mg, 36's	Children's Aspirin Various Firms		Plough	

JAN 26 1974

NDC (065-)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
30 105 724-6331	Phenformin Hydrochloride Capsules, 50 mg, 1000s	"DBI-TD" Geigy "Meltrol-50" U.S.V.	USV Geigy	USV.	Patented NDA Geigy
31 142 181-7774	Sodium Colistimethate, USP, Lyophilized, Equivalent to 0.15 Gram of Colistin Base	"Colymycin M" Warner Chilcott	Warner Chilcott	Warner Chilcott	Form 6 Patented
32 73 656-1344	Tetracycline Syrup, Equivalent to 25 mg of Tetracycline Hydrochloride per cc, 16 fl. oz. (473 cc)	"ACHROMYCIN-V Syrup" Lederle	Lederle Rachelle Roerig	Lederle Rachelle Roerig Reine Carlo Erba Pfizer	Form 6
33 35 559-5143	Calcium Gluceptate Injection, 5 cc, 25s		Eli Lilly Roussel	Vitarine Abbott Eli Lilly Pasadena Research Gotham	NDA
34 140 145-0309	Norethindrone and Mestranol Tablets, 63s	"Norinyl-1 plus 80" Syntex "Ortho-Novum 1/80" Ortho	Syntex Ortho	Syntex	NDA Ortho
35 82 935-4095	Brompheniramine Maleate, Phenylephrine Hydrochloride and Phenylpropanolamine Hydrochloride Elixir, 4 fl. oz. (118 cc)	"Dimetapp" A. H. Robins	A. H. Robins	A. H. Robins	NDA
36 HK 914-3593	Povidone Iodine Solution, NF, 10%, 1/2 fl. oz., 15cc, 50s	"Betadine Solution" Purdue Frederick		Purdue Frederick	Off Patent in 1973

JAN 2 6 1974

	NSN (6505)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
67 89	754-2436	Neomycin Sulfate, Hydrocortisone, and Polymyxin B Sulfate Suspension, Otic, 5 cc	Cortisporin Burroughs Wellcome	Burroughs Wellcome	Burroughs Wellcome	Patent Form 6
68 75	931-0680	Indomethacin Capsules, NF, 25 mg, 1000s	Indocin Merck-Sharp-Dohme	Merck-Sharp-Dohme	Merck-Sharp-Dohme	NDA Patent
69 83	853-4799	Imipramine Hydrochloride Tablets, USP, 25 mg, 100s	Tofranil Geigy Presamine USV	Geigy	Geigy USV	NDA Off patent in 1972
70	962-4375	Butalbital, Aspirin, Caffeine, and Phenacetin Tablets, 1000s	Fiorinal Sandoz	Sandoz	Sandoz	
71	935-1128	Plague Vaccine, USP, E Medium, 20 cc	Military Item	Cutter in cooperation with Walter Reed Army Institute of Research	Cutter	BoB License
72 94	074-4582	Quinine Dihydrochloride Injection NF, 0.3 Gram per cc, 2 cc, 12s			Mallinckrodt Chemical Works	
73	660-1601	Methocarbamol Tablets, NF, 0.5 Gram, 500s	Robaxin A. H. Robins	A. H. Robins	A. H. Robins	Off patent in 1973 NDA

JAN 26 1972

	NDC (DRUG)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
4	18 926-4768	Lincomycin Hydrochloride Injection, USP, Equivalent to 0.30 Gram of Lincomycin Base per cc, 10 cc	Lincocin Upjohn Co	Upjohn Co	Upjohn Co	Form 6 Patent
5	74 106-7395	Propranol Hydrochloride Tablets, 10 mg, 100s	Inderal Ayerst	Ayerst	Ayerst	Patent NDA
6	41 153-8651	Sodium Chloride Injection, USP, 1000 cc, 6s			Travenol Labs McGaw Labs Cutter Labs Abbott Labs Baxter Labs	
7	127 515-1584	Foot Powder, Fungicidal, 1 oz (28.35 Gram)	Desenex Foot Powder Maltbie Lab Division of Wallace-Tiernan, Inc	Wallace and Tiernan, Inc	Pharmacraff Seaboard Mfg Co	
8	110 985-7110	Fluocinolone Acetonide Cream, 0.025%, 15 Gram	Synalar Cream Syntex Labs	Syntex Labs	Syntex Labs	NDA
9	890-1907	Colistin Sulfate, Hydrocortisone Acetate, Neomycin Sulfate and Thonzonium Bromide Suspension, Otic, 5 cc	Coly-Mycin Otic Drops Warner Chilcott	Warner Chilcott	Warner Chilcott	Form 6 Patent
30	88 754-0374	Povidone-Iodine Solution, NF, 10%, 1 Gal (3.78 liters)	Betadine Solution Purdue Frederick	Tailby Nason Co Perdue-Frederick	Perdue-Frederick	NDA Off Patent in 1973

JAN 2 6 1974

		ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
31 61	375-8955	Diazepam Injection, NF, 5 mg per cc, 2 cc, 10s	Valium Injection Roche Labs	Roche Labs	Roche Labs	NDA Patent
32 59	689-4177	Oxymetazoline Hydrochloride Solution, 0.05%, 15cc	AFRIN Spray Schering Corp.	Schering Corp.	Schering Corp.	NDA Patent
33	724-6358	Amitriptyline Hydrochloride Tablets,USP 25 mg, 100s	Elavil Merck Sharp & Dohme	Merck Sharp & Dohme	Marck Sharp & Dohme	NDA
34 &	946-4700	Sodium Ampicillin, Sterile, USP, Equivalent to 0.50 Gram of Ampicillin	Polycillin-N Bristol Lab.	Bristol Lab	Bristol Lab	Ayerst Wyeth Beecham Massengill Form 6 Patent
35 44	994-7224	Detergent, Surgical, 7 1/2% Povidone-Iodine, 1 gal (3.78 liters)	Betadine Skin Cleanser Purdue-Fredericks	Tailby-Nason Physican's Products Co. Purdue-Fredericks	Purdue Fredericks	Off Patent in 1973 NDA
36	116-1750	Detergent, Surgical, Liquid, 1 Gal	PHISOHEX Winthrop Labs	Winthrop Labs	Winthrop Labs	Off Patent in 1959
37 30	299-9674	Isoniazid Tablets, USP, 100 mg, 100s	INH -Eli Lilly Niconyl- Parke Davis Nydrazid - Squibb		Mallinckrodt Parke Davis Panray Eli Lilly & Co. Strong Cobb Arner	NDA

JAN 2 6 1974

NSN (NDC)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
88 299-8095 56	Isopropyl Alcohol, NF 5 gal.			George Senn & Co. Haskon Inc. Shell	
89 299-8671 27	Selenium Sulfide Lotion, NF 2.5%, 4 fl. oz. (118 cc)	Selsun Abbott Labs	Abbott Labs.	Abbott Labs.	NDA
90 165-6575 79	Rifampin Capsule 0.30 Gram, 100s	Rimactane-Ciba Rifadin-Dow Chem.	Ciba Pharm. Dow Chem. Co.	Ciba Pharm. Dow Chem. Firms receiving awards are Licensees and Liscensor is Grupo Lepetit, Spa, a subsidiary of Dow Chemical	PATENT Form 6
91 543-4048 24	Water for Injection, Sterile, USP, 5 cc, 25s			Lincoln Labs. Torrigian Lab. Vitarine Co.	
92 074-4692 104	Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules, 500's	Librax- Roche Labs.	Roche Labs.	Roche Labs.	PATENT NDA
93 616-9128	Nystatin Tablets, USP, Vaginal, 100,000 units, 15s	Mycostatin Vaginal Tablets, E. R. Squibb & Sons Nilstal Vaginal Tablets-USP Lederle Labs.	E. R. Squibb & Sons	Lederle Labs. E. R. Squibb & Sons	off Patent in 1972 Form 6
94 082-2659 103	Amitriptyline Hydrochloride Tablets, USP, 25 mg, 100's	Elavil, Merck Sharp & Dohme	Merck Sharp & Dohme	Merck Sharp & Dohme	PATENT NDA

JAN 26 '67

No.	FSN (6505-)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
95 99	889-7929	Hydrochlorthiazide tablets, USP, 50 mg, 1000's	Esedrex-Ciba Hydro-Diuril-Merck Sharp & Dohme Oretic-Abbott Lab.	Ciba Abbott Lab. Merck Sharp & Dohme	Abbott Lab. Ciba Pharm.	NDA
96 115	812-2579	Ethambutol Hydrochloride Tablets, 400 mg, 100s	Myambutol Tablets Lederle Labs.	Lederle Labs.	Lederle Labs.	Patent NDA
97 76	890-1534	Tuberculin, Old Dried, Tine Test (Rosenthal)	Tuberculin Tine Test (T-B Tine Test) Lederle Labs.	Lederle Labs.	Lederle Labs.	Patent BOB License
98 53	817-2279	Chlorpropamide Tablets, USP, 0.25 Gram 250s	Diabinese Tablets Pfizer Lab.	Pfizer Lab.	Pfizer Lab.	Patent NDA
99 132	558-1289	Aluminum Hydroxide Gel and Magnesium Trisilicate Tablets, 100s	Gelusel Tab Warner-Chilcott	Warner Chilcott	Warner Chilcott Labs. Chase Chemical Co.	
100	100-6245	Aspirin, Phenacetin, and Caffeine Tablets, NF, 1000	Empirin Compd. Burroughs Wellcome APC Tablets Other Firms	Strong Cobb Arner Norwich Pharmacal Co.	Whitehall Norwich Pharmacal Beecham-Massengill Upjohn Company E. R. Squibb	Strong Cobb Arner
101 90	890-1496	Prednisolone Sodium Phosphate Injection USP, Equivalent to 20 mg of Prednisolone Phosphate per cc, 5 cc	"Hydeltrasol" Merck Sharp & Dohme	Merck Sharp & Dohme	M.S.D.	Patent NDA

JAN 26 1974

	NDC (5-3-2)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
102	153-8750 52	Aspirin Tablets, USP, 0.324 Gm, 1000s			Norwich Strong Cobb Arner Parke-Davis E.R. Squibb	
103	770-8343	Ampicillin Capsules	"Polycillin" Bristol "Totacillin" Beecham-Massengill "Principen" E.R. Squibb "Penbritin" Ayerst "Omnipen" Wyeth	Bristol Laboratories Beecham-Massengill Pharm. E.R. Squibb & Sons Ayerst Laboratories	Ayerst Bristol Wyeth [illegible] E.R. Squibb	Ayerst Labs. Upjohn Co. Form 6 [illegible]
104	660-1798	Benzonatate Capsules, NF, 100 mg, 100s	"Tessalon Perles" Ciba Pharm.	Ciba Pharm.	Ciba Pharm.	Off-Patent 1972. NDA
105	080-0852	Potassium Phenoxymethyl Penicillin for Oral Soln (16,000,000 Units) (10 Gram)	Abbott "Compocillin-VK" Bristol "Betapen-VK" Eli Lilly & Co. V-Cillin K E.R. Squibb Veetids		Bristol Laboratories	Form 6 Pfizer Laboratories
106	926-8924 130	Ampicillin for Oral Suspension, USP, 3.75 Gm	"Penbritin" Ayerst "Polycillin" Bristol "Omnipen" Wyeth "Principen" E.R. Squibb "Amcill" Parke-Davis & Co.	Bristol Wyeth Ayerst	Ayerst Bristol	Patent Form 6 Wyeth Beecham-Massengill

JAN 2 0 197

ITEM (P. O.)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
107 125-9922 150	Vitamin-Mineral Capsule, 100s	"Filibon F.A." Lederle Laboratories	Lederle Laboratories	Lederle Laboratories	
108 584-5997	Methenamine Mandelate Tablets, USP 0.5 Gm, 500s	"Mandelamine" Warner Chilcott	Warner Chilcott	Warner Chilcott	
109 059-2760 85	Sodium Oxacillin Capsules, USP, Equivalent to 0.5 Gram of Oxacillin in each capsule, 100s	"Prostaphlin" Bristol Laboratories	Bristol Laboratories	Bristol Laboratories	Patent Form 6 Beecham-Massengill
110 584-0398 119	Propantheline Bromide Tablets, USP, 15 mg, 1000s	"Pro-Banthine Bromide Tablets" G. D. Searle & Co.	Searle & Co.	Searle & Co.	NDA
111 050-4567 116	Psyllium Hydrophilic Mucilloid with Dextrose, 14 oz (397 Grams)	"Metamucil" G. D. Searle & Co.	G. D. Searle & Co.	G. D. Searle & Co. Burton-Parsons	
112 149-1720	Water for Injection, Sterile, USP, 1000 cc, 6s			Baxter Laboratories Don Baxter Inc. McGaw Travenol	
113 687-8205 92	Cetylpyridinium Chloride Lozenges, 400s	"Cepacol Throat Lozenges" Wm.S. Merrell	Wm. S. Merrell	Merrell- National Laboratories	NDA

	NDC	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
114 95	299-8617	Sodium Salicylate Tablets, USP, 0.324 Gram, 1000s			Strong Cobb Arner Eli Lilly Chase Chemical	
115 81	106-7399	Propranolol Hydrochloride Tablets, 40 mg, 100s	"Inderal" Ayerst	Ayerst	Ayerst	PATENT NDA
116 111	931-4329	Theophylline Ephedrine Sulfate and Hydroxyzine Hydrochloride Tablets	"Marax" J. B. Roerig	J. B. Roerig	J. B. Roerig	NDA
117 100	890-1561	Sodium Methicillin for Injection, USP, 1 Gram	"Staphcillin for Injection Bristol Laboratories	Bristol	Bristol	PATENT Form 6
118 41	080-0975	Aluminum Hydroxide Gel, Magnesium Hydroxide and Simethicone Suspension, 5 fl oz., 48s	"Mylanta" Stuart	Stuart	Stuart	PATENT
119	880-3905	Plasma Protein Fraction, USP, Heat-Treated, 5%, 500cc	"Plasmanate" Cutter	Cutter Hyland Div. Travenol	Cutter Hyland Div. Travenol	BoB License
120 60	114-8985	Codeine Sulfate Tablets, NF, 32 mg, 100s			Premo Strong CobbArner Beecham Massengill Eli Lilly & Co. Norwich Wm S. Merrell Brewer & Co.	

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY 10073

JAN 2 0 197

	VPN (NSN)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
21 145	764-3313	Chlorzoxazone and Acetaminophen Tablets, 500s	McNeil "Parafon Forte"	McNeil	McNeil	NDA Patent
22	985-7301	Acetaminophen Tablets, NF, 0.325 Gram, 1000s	"Tylenol" McNeil	McNeil Mead Johnson	McNeil Mead Johnson Dorsey	
23 102	685-5442	Dextrose in Lactated Ringer's Injection, 5%, 1000 cc, 6s			Travenol Cutter	
24 114	926-8985	Dextromethorphan Hydrobromide and Glyceryl Guaiacolate Syrup, 4 fl. oz., (118 cc)	"Robitussin-DM" A. H. Robins	Robins Dorsey	Robins G & W Pennwalt Reine	Natcon
25 68	926-9083	Atropine Injection, 2 mg			Rodana Research Corp.	Patent
26 70	782-6761	Triprolidine Hydrochloride and Pseudoephedrine Hydrochloride Syrup 4 fl. oz.	Actifed Syrup Burroughs Wellcome & Co.	Burroughs Wellcome and Co.	Burroughs Wellcome & Co.	off Patent in 1972 NDA
27 131	890-1355	Medroxyprogesterone Acetate Tablet, USP, 10 mg, 100s	Provera Tablets Upjohn Co.	Upjohn Co.	Upjohn Co.	Patent NDA

ITEM (CHAR)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
128 584-2895 117	Hydralazine Hydrochloride Tablets, NF, 25 mg, 1000s	Apresoline Hydrochloride Tablets Ciba Pharm. Co.	Ciba Pharm. Co.	Ciba Pharm. Co.	NDA
129 982-9069 109	Tolbutamide Tablets, USP, 0.5 Gram, 200s	Orinase Tablets Upjohn Co.	Upjohn Co.	Upjohn Co.	PATENT NDA
130 937-1758 143	Ethinyl Estradiol Tablets & Diethesterone w/Ethinyl Estradiol Tablets, 63s	Oracon Mead Johnson Labs.	Mead Johnson	Mead Johnson	PATENT NDA
131 222-1357 78	Sodium Caloride Solution, USP, 0.9% 1500 cc, 6s		Cutter, Travenol McGaw Abbott	Travenol Lab. Abbott	McGaw Labs. Cutter Labs.
132 861-0867 34	Sodium Aminosalicylate Tablets, USP, 1.0 Gram, 1000s	Pasara Sodium Tablets Dorsey Parasal Sodium Panray Pamisyl Sodium Parke-Davis	Dorsey Lab	Dorsey Labs Strong Cobb Arner Panray Miles	NDA
133 890-2217	Sulfanilamide, Allantoin and Aminacrine Hydrochloride Cream, Vaginal, 4 oz (113.4 Gram)	AVC Vaginal Cream Merrell-National	Merrell-National	Merrell-National	NDA
134 074-2981 146	Ferrous Fumarate & Dioctyl Sodium Sulfosuccinate Capsules, 1000s	"Ferro Sequels Capsules" Lederle	Lederle	Lederle	

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	NDC (5-3-2)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
135 40	299-8739	Chlortetracycline Hydrochloride Ophthalmic Ointment, 1%, 1/8 oz. 3.5 Gm, 12s	Aureomycin Ophthalmic Ointment, 1% Lederle Laboratories	Lederle	Lederle	Form 6 Patent
136	153-8278	Immune Serum Globulin, USP, Human, 10 cc			Hyland E. R. Squibb Lederle	BOB license
137	584-3277	Promethazine Hydrochloride Tablets, USP, 25 mg, 1000s	Phenergan Hydrochloride Tablets Wyeth Lab.	Wyeth	Wyeth	NDA Endo
138 46	963-5355	Dexamethasone Sodium Phosphate Injection, USP, Equivalent to 4 mg of Dexamethasone Phosphate per cc, 5 cc	Decadron Phosphate Merck Sharp & Dohme	Merck Sharp & Dohme	Merck Sharp & Dohme	NDA Patent
139 137	003-5112	Minocycline Hydrochloride Capsules, Equivalent to 100 mg of Minocycline, 50s	Minocin Lederle Labs.	Lederle	Lederle	Form 6 Patent
140 99	299-8013	Insulin, Isophane, Suspension, USP, M-SC, 10 cc	Lilly NPH Iletin Squibb NPH Insulin	E. R. Squibb	Eli Lilly	NDA
141 106	590-1554	Flurandrenolide Cream, NF, 0.05%, 15 Grams	Cordran Cream Eli Lilly	Eli Lilly	Eli Lilly	Patent NDA

NDA (NDS)	ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
142 080-0653 66	Erythromycin Ethylsuccinate for Oral Suspension, NF, Equivalent to 8 Grams of Erythromycin Base	Erythrocin Abbott Labs	Abbott	Abbott	Form 6
143 181-8387 144	Probenecid Tablets, USP, 0.5 Gram, 1000s	Benemid Merck, Sharp, and Dohme	Merck,Sharp,&Dohme	Merck, Sharp, & Dohme	NDA
144 584-0412 113	Estrogens, Conjugated, Tablets, USP, 0.625 mg, 1000s	Premarin Ayerst Labs.	Ayerst	Ayerst	NDA
145 159-6625	Bacitracin Ointment, USP, 500 Units per Gram, 1/2 oz (14.2 Grams) 12s			Day Baldwin Premo Pfizer Strong Cobb Arner Eli Lilly Abbott	Form 6
146 443-4559	Sodium Diatrizoate Injection, USP, 50%, 30 cc, 25s	Hypaque Sodium 50% Winthrop Labs.	Winthrop	Winthrop	NDA
147 299-8508	Oxtetracycline Hydrochloride and Polymyxin B Sulfate Ophthalmic Ointment 1/8 oz (3.5 Grams) 10s	"Terramycin Ophthalmic Ointment with Polymyxin B Sulfate" Pfizer	Pfizer	Pfizer	PATENT Form 6
148 130-1805	Nikethamide Injection, NF, 25%, 1 1/2 cc, 5s	"Coramine" Ciba		Premo Elkins-Sinn Natcon Vitarine Ciba Gotham Carlo Erba Brewer Torrigian Pharmich Cold Leaf	
149 130-1960	Nitrofurazone Ointment, NF, Water Soluble, 1:500, 1 lb. (453.6 Grams)	Furacin Soluble Dressing Eaton Labs.	Eaton	Eaton	PATENT NDA

ESTABLISHED NAME	TRADE NAME(S) & CO.	SOURCES OF INDUSTRY INFO.	SUCCESSFUL BIDDERS	REMARKS
Theophylline, Ephedrine Hydrochloride and Phenobarbital Tablets, NF, 1000s	Tedral Tablets Warner-Chilcott	Warner Chilcott	Eli Lilly Warner-Chilcott	

15. QUESTION:

In the past several months Mr. Feinberg of the DPSC has publicized certain problems for which the Subcommittee is very anxious to secure additional information. His statement and our questions are as follows:

(e) "We develop definitive product specifications which often exceed official or commercial standards."

Please name each product for which such specifications have been developed; the significance for each product of these extra requirements; and the medical purpose served by these extra requirements.

ANSWER:

There are approximately 1200 drug items in FSC 6505 managed by DPSC. About 800 items are monographed in the USP or NF; the balance is not covered by official standards.

In preparing specifications for USP and NF items, the compendial standards are the focal point for the technical data. Additional standards are added in those instances where the need exists. Included are general requirements that exceed the standards of the USP and NF, such as Classification of Defects which are necessary for quality and contractual pruposes, limit on unrefrigerated shipping time for refrigerated items, and leakage testing for flame-sealed ampuls. Standards for individual items are added when problem areas are anticipated or complaint background develops. Such additional data may be obtained or developed from literature, industry, DMMB, DPSC staff, or DCAS Quality Assurance Representatives.

For those items that are not covered by the USP/NF, specification data are requested from those firms listed by the DMMB as the commercial reference. The Chemists/Pharmacists carefully review the submitted specifications, taking into account published information found in the literature, journals, handbooks, as well as their background and experience with similar items. There are times when a firm's submitted data do not contain sufficient requirements to insure a quality product. Other times, the methods are not entirely satisfactory.

The DPSC specifications are coordinated in house before a specification review board which consists of members of the Technical Services Branch, the Office of Counsel, the DPSC Medical Laboratory, and the Quality Assurance Branch.

Additional requirements for USP and NF items follow.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Cinnamon Oil, USP, 1 oz (28.35 Gm)	Free from sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
Riboflavin Tablets, USP, 1 mg, 100s	Classification of Defects	See Explanatory Notes.
Chloral Betaine Tablets, NF, 0.50 Gram, 30s	Hardness Limits	See Explanatory Notes.
	Moisture Limits	To assure the stability of the product, in that excessive moisture may cause deterioration.
	Additional test requirement for the active ingredient (Melting Range) Classification of Defects	Additional test to assure the purity of active ingredient. Not in NF monograph. See Explanatory Notes.
Diazepam Tablets, NF, 5 mg, 500s Diazepan Tablets, NF, 2 mg, 500s Diazepam Tablets, NF, 5 mg, 100s	Classification of Defects	See Explanatory Notes.
Acetohexamide Tablets	Classification of Defects	See Explanatory Notes.
Acetyl Sulfisoxazole Oral Suspension, NF, Pediatric, 1 pt	Color	To assure that the proper appearance of the product is obtained since complaints have been received on this product due to discoloration. Complaint history.
Aluminum Hydroxide Gel, Dried, Tablets, USP, 0.324 Gm, 100s	Classification of Defects Acid consuming capacity	See Explanatory Notes. To assure that the tablets do neutralize excess gastric acidity
Desipramine Hydrochloride Tablets, NF, 50 mg, 1000s	Classification of Defects Hardness Limits	See Explanatory Notes. See Explanatory Notes.

[illegible]	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Digoxin Injection, USP, 0.25 mg/cc, 2 cc, 12s	Classification of Defects Leakage Tests for Ampuls Color Limits	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes.
Dichlorotetrafluoethane, NF, 8 oz (227 Grem)	Classification of Defects Initial boiling and end boiling point. Specific gravity	See Explanatory Notes. The NF monograph only requires an approximate temperature. To define the purity of the item which is used as a local anesthetic on the skin. The NF monograph has no official requirement. This requirement is an additional measurement of purity of active ingredient.
Dextroamphetamine Sulfate Tablets, USP 5 mg, 100s	Classification of Defects	See Explanatory Notes.
Diphenhydramine Hydrochloride Elixir, USP, 1 gal	Free from sediment	To assure that proper filtration of the Elixir was utilized in accordance with good manufacturing practices.
Diphenhydramine Hydrochloride Capsules, USP, 50 mg, 100s Diphenhydramine Hydrochloride Capsules, USP, 50 mg, 1000s	Classification of Defects	See Explanatory Notes.
Diiodohydroxyquin Tablets, USP, 0.65 Grem, 60s	Classification of Defects	See Explanatory Notes.
Digoxin Tablets, USP, 0.25 mg, 100s	Classification of Defects	See Explanatory Notes.
Dimenhydrinate Tablets, USP, 50 mg, 100s	Classification of Defects	See Explanatory Notes.

NAME	ADDITIONAL REQUIREMENT	SIGNIFICANCE
Sodium Secobarbital Capsules, USP, 100 mg, 100s Sodium Secobarbital Capsules, USP, 100 mg, 500s	Classification of Defects	See Explanatory Notes.
Amitriptyline Hydrochloride Tablets, USP, 10 mg, 100s Amitriptyline Hydrochloride Tablets, USP, 25 mg, 100s	Accelerated Aging	See Explanatory Notes.
Amitriptyline Hydrochloride Tablets, USP, 25 mg, 1000s	Classification of Defects	See Explanatory Notes.
Insulin, Protamine Zinc, Suspension, USP, U-40, 10 cc Insulin Injection, USP, U-40, 10cc Insulin Injection, USP, U-80, 10cc Insulin, Isophane, Suspension, USP, U-80, 10 cc Insulin, Isophane Suspension, USP, U-40, 10 cc Insulin, Zinc Suspension, USP, U-40, 10 cc Insulin, Zinc Suspension, USP, U-80, 10 cc	Maximum unrefrigerated shipping times for items requiring refrigerated storage Classification of Defects	See Explanatory Notes. See Explanatory Notes.
Aminophylline Tablets, 0.2 Gram, USP, 100s	Tablets shall be white. Tablets shall be free of ammoniacal odor.	Aminophylline is composed of theophylline and ethylene diamine held together by weak chemical bonds. The ethylene diamine component is responsible for the ammonia-like odor produced and this odor will be more prevelant after decomposition of the aminophylline. This type of chemical decomposition may be due to age of material, conditions of storage, the quality of the active ingredient, the method of manufacture of the product or a combination of any of these factors.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Quinidine Sulfate Tablets, USP, 0.2 Gm, 100s	Classification of Defects	See Explanatory Notes.
Castor Oil, USP, 1 qt	Free from sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
Cyanocobalamin Injection, USP, 1000 micrograms per cc, 10 cc	Classification of Defects pH Limits	See Explanatory Notes. To assure greater stability over the shelf life of the item. Not included in USP monograph.
Corticotropin Injection, Repository, USP, 40 units per cc, 5 cc	Classification of Defects Maximum unrefrigerated shipping times for items requiring refrigerated storage.	See Explanatory Notes. See Explanatory Notes.
Colchicine Tablets, USP, 0.65 mg, 100s	Classification of Defects	See Explanatory Notes.
Cephalexin Monohydrate for Oral Suspension	Weight Variation	CFR does not specifically require compliance with weight variation for this item. Our requirement assures uniform weight variation within limits and thus proper and uniform dosage.
Diazepam Injection, NF, 5 mg per cc, 2 cc, 10s	Classification of Defects Leakage Test for Ampuls	See Explanatory Notes. See Explanatory Notes.
Cephalexin Monohydrate Capsules, Equivalent to 0.25 Gram of Cephalexin, 100s	Classification of Defects	See Explanatory Notes.
Cascara Tablets, NF, 0.25 Gm, 100s	Classification of Defects	See Explanatory Notes.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Chlorpromazine Hydrochloride Injection, USP, 25 mg per cc, 2 cc, 6s	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Limits for foreign substances (color, pH, unchlorinated compound for active ingredient and 4-Chlorophenothiazine for intermediate)	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Amyl Nitrite Inhalant, NF, Ampuls, 0.33 cc, 12s	Preservatives	To assure greater stability over the shelf life of the item.
	Classification of Defects	See Explanatory Notes.
Cod Liver Oil, NF, 1 pt (473 cc)	Higher minimum limits for vitamins A and D	More potent Cod Liver Oil so that the quantity of oil taken per dose may be reduced.
Dehydrocholic Acid Tablets, NF, 0.25 Gram, 100s	Classification of Defects	See Explanatory Notes.
Prochlorperazine Edisylate Injection, USP, Equivalent to 5 mg of Prochlorperazine per cc, 2 cc, 100s	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Limits for foreign substances (color, pH, unchlorinated compound for active ingredient and 4-Chlorophenothiazine for intermediate)	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Cyproheptadine Hydrochloride Tablets, NF, 4 mg, 100s	Classification of Defects	See Explanatory Notes.
	Hardness	See Explanatory Notes.
	Free and combined Hydrochloric Acid	Quantitative assay for the chloride as well as for the limit of the impurity free hydrochloric acid.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Aminophylline Injection, USP, 25 mg per cc, 10 cc	Color Limits Leakage Tests for Ampuls Classification of Defects	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes.
Benzalkonium Chloride Solution, USP, 10%, 4 fl oz (118 cc)	Benzalkonium Chloride, USP, is not available to manufacture this monographed item. Therefore Defense MEdical Purchase Description delineates tests and requirements for a Benzalkonium Chloride concentrate for use in manufacture of 10% solution. The USP monograph for the solution requires limited tests since it is assumed USP Benzalkonium Chloride will be used.	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices
Acetazolamide Tablets, USP, 250 mg, 100s	Classification of Defects	See Explanatory Notes.
Cortisone Acetate Suspension, Sterile, USP, 25 mg per cc, 20 cc	Classification of Defects Shall be isotonic	See Explanatory Notes. To assure less irritation upon instillation into the eye.
Collodion, Flexible, USP, 1 fl oz (29.5 cc)	Classification of Defects	See Explanatory Notes.
Atropine Sulfate Ophthalmic Solution, USP, 1%, 15 cc	Tighter pH Isotonic Rabbit Eye Irritation Test	A tighter pH range is specified in order to afford greater stability over the shelf life of the item. To assure less irritation upon instillation into the eye. To reduce the potential for irritation to the eye.
Chlorpropamide Tablets, USP, 0.25 Gram, 250s	Classification of Defects	See Explanatory Notes.
Clofibrate Capsules, NF, 500 mg, 100s	Classification of Defects	See Explanatory Notes.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Aspirin, Phenacetin and Caffeine Tablets, NF	Moisture Content	To assure the stability of the product, in that excessive moisture may cause deterioration.
	Classification of Defects	See Explanatory Notes.
Aspirin Tablets, USP, 0.324 Gram, 100s	Accelerated Aging Test	See Explanatory Notes.
	Hardness	See Explanatory Notes.
Aspirin Tablets, USP, 0.324 Gram, 1000s	Moisture Content	To assure the stability of the product, in that excessive moisture may cause deterioration.
	Classification of Defects	See Explanatory Notes.
Calcium Lactate Tablets, NF, 0.65 Gram, 100s	Classification of Defects	See Explanatory Notes.
Chlorthalidone Tablets, USP, 100 mg, 100s	Classification of Defects	See Explanatory Notes.
	Hardness limit	See Explanatory Notes.
Chlorpromazine Hydrochloride Tablets, USP, 25 mg, 1000s Chlorpromazine Hydrochloride Tablets, USP, 50 mg, 1000s Chlorpromazine Hydrochloride Tablets, USP, 100 mg, 1000s	Classification of Defects	See Explanatory Notes.
	Limits for foreign substances (Color, pH, unchlorinated compound for active ingredient and 4-Chlorophenothiazine for intermediate)	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Chlorotrianisene Capsules, NF, 72 mg, 48s	Classification of Defects	See Explanatory Notes.
Caffeine and Sodium Benzoate Injection, USP, 0.25 Gram per cc, 2 cc, 12s	Color Limits	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Phenylephrine Hydrochloride Injection, USP, 1%, 1 cc, 25s	Color Limits	See Explanatory Notes.
	Leakage Tests for Ampuls.	See Explanatory Notes.
	Shall be isotonic	To prevent hemolysis of red blood cells at the site of the injection.
	Classification of Defects	See Explanatory Notes.
Aspirin Tablets, USP, 0.324 Gram, 12s	Hardness	See Explanatory Notes.
	Moisture	To assure the stability of the product, in that excessive moisture may cause deterioration.
	Classification of Defects	See Explanatory Notes.
Allopurinol Tablets, USP, 100 mg 100s	Classification of Defects	See Explanatory Notes.
Aspirin Tablets, USP, 0.324 Gram, 1000s, (Enteric Coated)	More Stringent Limits of Impurities (Non-aspirin salicylates)	To provide tighter limits in order to assure the best production procedures and controls are utilized consistent with good manufacturing practices. Complaint history.
	Classification of Defects	See Explanatory Notes.
Benzonatate Capsules, NF, 100 mg, 100s	Classification of Defects	See Explanatory Notes.
	Identity	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Albumin, Normal Human Serum, USP, 25%, 100 cc	Maximum unrefrigerated shipping time	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Ascorbic Acid Tablets, USP, 50 mg, 100s	Classification of Defects	See Explanatory Notes.
Ascorbic Acid Tablets, USP, 0.50 Gm, 100s		

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Chlorpheniramine Maleate Tablets, USP, 4 mg, 1000s	Classification of Defects	See Explanatory Notes.
Atropine Sulfate Injection, USP, 2 mg per cc, 25cc	pH Limits	A tighter pH range is specified in order to assure greater stability over the shelf life of the item.
	Tighter Assay Limits	To assure a tighter manufacturing control since this item contains 2 mg of Atropine Sulfate per cc.
	Color Limits	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Atropine Sulfate Injection, USP, 0.4 mg (1/150 gr) per cc, 20 cc	Color Limits	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Bethanechol Chloride Tablets, USP, 10 mg, 100s	Classification of Defects	See Explanatory Notes.
	Hardness Limits	See Explanatory Notes.
	Moisture Content	To assure the stability of the product, in that excessive moisture may cause deterioration.
	Limits for foreign substances (Heavy Metals), pH and clarity of solution for active ingredient	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Aspirin Tablets, USP, 75 mg, 36s	Palatability	See Explanatory Notes.
	Hardness	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Ammonia Spirit, Aromatic, NF, 1/4 pt	Removal torque for closure on immediate containers	To assure that the active ingredient is not readily lost from the containers.
Chloroquine Hydrochloride Injection, USP	Classification of Defects	See Explanatory Notes.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Epinephrine Suspension, Sterile, USP, 1:500, 1 cc, 12s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
Epinephrine Injection, USP, 1:1000, 1 cc, 25s	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
	Clarity of Solution	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Leakage Tests for Ampuls	See Explanatory Notes.
Ergotamine Tartrate and Caffeine Tablets, NF, 100s	Classification of Defects	See Explanatory Notes.
	Tighter Assay Limits	To provide tighter limits in order to assure the best production procedures and controls are utilized consistent with good manufacturing practices.
	Limit for Alkaloid Isomer	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Tighter Disintegration	To allow less time to assure the tablets are disintegrated faster and thus release the active ingredient sooner.
	Accelerated Aging Test	See Explanatory Notes.
	One-Year Storage Test	To assure that tablets conform to all the requirements for one year after the date of delivery to the Government.
	Dissolution Test	To assure the proper release of the active ingredient. Complaint history.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Histamine Phosphate Injection, USP, 1 mg, 1 cc, 6s	Classification of Defects Leakage Test for Ampuls Color Limits	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes.
Flurandrenolide Cream, NF, 0.05%, 225 Grams Flurandrenolide Cream, NF, 0.05%, 15 Grams Flurandrenolide Cream, NF, 0.025%, 60 Grams	Classification of Defects Leakage Test	See Explanatory Notes. To assure that the containers of cream do not leak.
Dioctyl Calcium Sulfosuccinate Capsules, NF, 0.24 Gram, 100s Dioctyl Calcium Sulfosuccinate Capsules, NF, 0.24 Gram, 1000s Dioctyl Calcium Sulfosuccinate Capsules, NF, 0.24 Gram, 5000s	Classification of Defects Leakage Test	See Explanatory Notes. To assure that the liquid fill does not leak.
Dioctyl Sodium Sulfosuccinate Capsules, USP, 100 mg, 1000s	Classification of Defects Limits for foreign substance (arsenic) in the active ingredient	See Explanatory Notes. To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Doxapram Hydrochloride Injection, NF, 20 mg per cc, 20 cc	Classification of Defects	See Explanatory Notes.
Digoxin Elixir, USP, 0.05 mg/cc, 60 cc	Free from sediment	To assure the best production procedures and controls are utilized consistent with good manufacturing practices.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Erythromycin Tablets, 0.25 Gram,100s	Classification of Defects	See Explanatory Notes.
Diphenylhydantoin Tablets, USP, 50 mg, 100s	Classification of Defects	See Explanatory Notes.
	Tighter Assay Limits	To assure a tighter manufacturing control.
	Tighter Assay and Melting Range for Active Ingredient	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Cortisone Acetate Tablets, USP, 25 mg, 40s	Classification of Defects	See Explanatory Notes.
Ethchlorvynol Capsules, NF, 500 mg, 100s	Classification of Defects	See Explanatory Notes.
Emetine Hydrochloride Injection, USP, 65 mg, 1 cc, 6s	Classification of Defects	See Explanatory Notes.
	Leakage Tests for Ampuls	See Explanatory Notes.
Ethyl Chloride, NF, 100 Grams	Free from Sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
Formaldehyde Solution, USP, 1 qt (946 cc)	Free from Sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
	APHA Color	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Assay Requirement for Methanol	To assure proper quantity of this stabilizer to prevent polymerization.

32-814 (Pt. 24) O - 74 - 12

	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Eugenol, USP, 1 oz (28.35 Grams)	free from sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
Ergotamine Tartrate Tablets, USP, 1 Gr, 100s	Classification of Defects	See Explanatory Notes.
Erythromycin Ethylsuccinate for Oral Suspension, NF, Equivalent to 8 Grams of Erythromycin Base	Weight Variation	The NF monograph does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and thus proper and uniform dosage. See Explanatory Notes.
	Taste/Palatability Test	
Erythromycin Lactobionate for Injection, USP, Equivalent to 1 Gram of Erythromycin, 5s	Weight Variation	The USP monograph does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and thus proper and uniform dosage. See Explanatory Notes.
	Solubility Time Limit	See Explanatory Notes.
	Classification of Defects	
Ether, USP, 1/4 lb	More Stringent Limits of Impurities (Non-Volatile Residue) (Foreign Odor) (Substances Darkened by Sulfuric Acid)	To provide tighter limits in order to assure the best production procedures and controls are utilized consistent with good manufacturing practices.
	Peroxides	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Color	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Stability	To assure that the product is stable over the shelf life of the item. Complaint history.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Digitoxin Tablets, USP, 0.0 mg, 100s	Classification of Defects	See Explanatory Notes.
	Color	The color pink for this dosage is important to differentiate it from another dosage size.
Haloperidol Tablets, NF, 2 mg, 1000s	Classification of Defects	See Explanatory Notes.
	Hardness	See Explanatory Notes.
	Thin Layer Chromatography for Active Ingredient	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Glycopyrrolate Tablets, NF, 1 mg, 100s	Classification of Defects	See Explanatory Notes.
	Hardness	See Explanatory Notes.
Fluocinonolide Ointment, NF, 0.05%, 15 Gram	Classification of Defects	See Explanatory Notes.
	Leakage Test	To assure that the tubes of ointment do not leak.
Oleovitamin A and D Capsules, NF, 100s	Upper assay limits	To preclude possibility of use of superpotent material.
	Classification of Defects	See Explanatory Notes
Gamma Benzene Hexachloride Cream, USP, 1%, 60 Grams	Leakage Test	To assure that the tubes of cream do not leak.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Fluorouracil Injection, USP, 50 mg per cc, 10 cc, 10s	Classification of Defects Shall contain not more than 0.3 mg free fluoride per ml	See Explanatory Notes. To provide tighter limits in order to assure the best production procedures and controls are utilized consistent with good manufacturing practices.
	Injection shall be colorless to faint yellow Pyrogen Test Leakage Test for Ampuls	See Explanatory Notes. To assure that pyrogens are not present. See Explanatory Notes.
Lactic Acid, USP	Free from Sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
Iophendylate Injection, USP, 3 cc, 3s	Classification of Defects Leakage Test for Ampuls	See Explanatory Notes. See Explanatory Notes.
Hydrocortisone Tablets, USP, 20 mg, 100s	Classification of Defects	See Explanatory Notes.
Griseofulvin Tablets, USP, 0.50 Gm, 500s	Classification of Defects	See Explanatory Notes.
Iodized Oil, NF, 20 cc	Classification of Defects	See Explanatory Notes.
Iron Dextran Injection, USP, 10 cc	Classification of Defects	See Explanatory Notes.
Iodochlorhydroxyquin, USP, 1/4 lb (113.4 Gm)	Color and Clarity of Solutions	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Kaolin Mixture with Pectin, NF, 1 gal (3.78 liters)		
	Kaolin Seive Size	Aids in maintaining suspension and ease of resuspension.
Lidocaine Ointment, USP, 5%, 35 Gram	Color Limits	See Explanatory Notes.
	pH Limits	To assure greater stability over the shelf life of the item. Not included in USP monograph.
	Classification of Defects	See Explanatory Notes.
	Leakage Test	To assure that the tubes of ointment do not leak.
Bacitracin Ointment, USP, 500 Units per Gram, 1/2 oz (14.2 Grams) 12s	Upper Assay Limit	To preclude possibility of use of super-potent material. No upper assay limit given in regulations.
	Leakage Test	To assure that tubes of ointment do not leak.
Furosemide Tablets, USP, 40 mg, 100s	Disintegration	To allow less time to assure the tablets are disintegrated faster and thus release the active ingredient sooner.
	Classification of Defects	See Explanatory Notes.
	Hardness Limits	See Explanatory Notes.
	Color of solution, limits for chloride and sulfate, and Percent of Furosemide breakdown for active ingredient	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.

ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Ethinyl Estradiol Tablets, USP Ethinyl Estradiol and Dimethisterone Tablets, NF, #5	Classification of Defects Color of Tablets	See Explanatory Notes. In order to differentiate tablets taken in beginning of cycle with those to be taken toward end of dosage cycle.
Folic Acid Tablets, USP, 1 mg, 1000s Folic Acid Tablets, USP, 0.25 mg, 1000s	Classification of Defects	See Explanatory Notes.
Meclizine Hydrochloride Tablets, USP, Chewable, 25 mg, 100s	Classification of Defects Palatability Loss on Drying Accelerated Aging Test (Stability)	See Explanatory Notes. See Explanatory Notes. To assure the stability of the product, in that excessive moisture may cause deterioration. See Explanatory Notes.
Hydralazine Hydrochloride Tablets, NF, 25 mg, 1000s	Weight Variation Classification of Defects	As an added check to assure proper manufacture of this tablet which consists of a core which is then coated with dry ingredients and compressed. See Explanatory Notes.
Dioctyl Sodium Sulfosuccinate Solution, NF, 1%, 30 cc	Limits for Foreign Substances (Arsenic) for Active Ingredient	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.

NAME	ADDITIONAL REQUIREMENT	SIGNIFICANCE
Betamethasone Valerate Cream, NF, Equivalent to 0.1% of Betamethasone, 45 Grams	pH	A pH range is not given in NF, thus a pH range is specified to assure greater stability over the shelf life of the item.
Betamethasone Valerate Cream, NF, Equivalent to 0.1% of Betamethasone, 15 Grams	Microbial Limits	Bacteria limits to control the amount of viable microorganisms and to prohibit those organisms that should not be present in the product. This assures that undesirable contamination is not present in the product.
	Leakage Test	To assure that the tubes of cream do not leak.
Bisacodyl Suppositories, NF, 10 mg, 50s	Weight of Suppository	To assure uniformity in weights of suppositories. Not included in NF monograph.
	Drip point and melting time for suppositories	To assure that the suppositories are made with a base which will melt within a specified time frame to release its medicament. No such requirement exists in the compendia.
	pH limits	To assure greater stability over the shelf life of the item. Not included in NF monograph.
Guanethidine Sulfate Tablets, USP, 25 mg, 100s	Hardness Limits	See Explanatory Notes.
Guanethidine Sulfate Tablets, USP, 10 mg, 100s	Limit for Foreign Substance and Melting Range for Active Ingredient	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Guanethidine Sulfate Tablets, USP, 25 mg, 1000s		
Primaquine Phosphate Tablets, USP, 26.3 mg, 130s	Classification of Defects	See Explanatory Notes.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Diphenhydramine Hydrochloride Injection, USP, 50 mg per cc, 10 cc	Color Limits	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
Diphenhydramine Hydrochloride Injection, USP, 10 mg per cc, 10 cc		
Magnesium Sulfate Injection, USP, 50%, 2 cc, 12s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
Belladonna Tincture, USP, 1 pt (473 cc)	Free from sediment	To assure the best production procedures and controls are utilized consistent with good manufacturing practice.
Procaine Hydrochloride, Sterile, USP, 100 mg, 10s	Leakage Test for Ampuls	See Explanatory Notes.
	Classification of Defects	See Explanatory Notes.
	Solubility Time Limit	See Explanatory Notes.
	Autoclave Test	To assure the suitability of the product to withstand autoclaving.
Ephedrine Sulfate Injection, USP, 25 mg, 1 cc, 12s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Color Limits	See Explanatory Notes.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Iopanoic Acid Tablets, USP, 0.5 Gram, 25s	Classification of Defects	See Explanatory Notes.
Methysergide Maleate Tablets, NF, 2 mg; 500s	Classification of Defects	See Explanatory Notes.
Globulin, Immune Serum, USP, (Human), 10 cc	Classification of Defects	See Explanatory Notes.
	Maximum unrefrigerated shipping times for items requiring refrigerated storage	See Explanatory Notes.
	No albumin or fibrinogen shall be permitted in the finished product.	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Derived from Venous Blood Only	To avoid unwanted blood specific substances which are present in placental blood.
	Clear and Free of Turbidity, Sediment, and Particulate Matter	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Dextrose and Sodium Chloride Injection, USP, 5% Dextrose in 0.9% Solution of Sodium Chloride, 1000 cc, 6s	Classification of Defects	See Explanatory Notes.
Sodium Chloride Injection, USP, 5 cc, 25s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Color Limits	See Explanatory Notes.

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Globulin, Tetanus, Immune, USP, 250 Units	Classification of Defects	See Explanatory Notes.
	Maximum Unrefrigerated Shipping Time for Items Requiring Refrigerated Storage	See Explanatory Notes.
	Venous Blood Origin	To avoid unwanted blood specific substances which are present in placental blood.
	Shall be clear and free from Turbidity, Sediment, and Particulate Matter	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Shall not Contain Albumin or Fibrinogen	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Sodium Chloride Injection, USP, 1000 cc, 6s Sodium Chloride Injection, USP, 100 cc, 12s Sodium Chloride Injection, USP, 250 cc, 12s	Classification of Defects	See Explanatory Notes.
Water for Injection, Sterile, USP, 5 cc, 25s	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
Water for Injection, Sterile, USP, 1000 cc, 6s Water for Injection, Sterile, USP 5 cc	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
Sodium Chloride Solution, USP, 0.9%, 1000 cc, 6s	Color Limits	See Explanatory Notes.
	Sterility and Pyrogenicity	To assure proper requirements for a solution used as irrigating fluid.
Protein Hydrolysate Injection, USP, 1000 cc, 6s	Classification of Defects	See Explanatory Notes.

	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Dextrose Injection, USP, 50%, 50 cc, 6s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes
	Color Limits	See Explanatory Notes.
Dextrose Injection, USP, 5%, 1000 cc, 6s	Classification of Defects	See Explanatory Notes.
Dextrose Injection, USP, 10%, 1000 cc, 6s		
Dextrose Injection, USP, 5%, 250 cc, 12s		
Methocarbamol Injection, NF, 100 mg per cc, 10 cc, 5s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
Hydrocortisone Acetate Suspension, Sterile, USP, 25 mg per cc, 5 cc	Isotonic	To prevent hemolysis of red blood cells at site of injection.
	Classification of Defects	See Explanatory Notes.
Methoxyflurane, NF, 125 cc	Assay Limits for Stabilizer (if used)	To assay the proper quantity of stabilizer.
	Color Limits	See Explanatory Notes.
	Moisture	To assure the stability of the product.
Meglumine Diatrizoate Injection, USP, 30%, 300 cc, 10s	Classification of Defects	See Explanatory Notes.
Methylergonovine Maleate Tablets, USP, 0.2 mg, 100s	Hardness	See Explanatory Notes.
Meperidine Hydrochloride Injection, USP, 50 mg per cc, 30 cc	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
Methyl Salicylate, USP, 1 pt (473 cc)	Free of Sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
	APHA Color	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Methocarbamol Tablets, NF, 0.5 Gram, 500s	Classification of Defects	See Explanatory Notes.
Dextrose Injection, USP, 10%, 3 cc, 10s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
	Autoclave Test	To assure the suitability of the product to withstand autoclaving.
Metaraminol Bitartrate Injection, USP, Equivalent to 10 mg of Metaraminol per cc, 10 cc	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
Procaine Hydrochloride Injection, USP, 1%, 2 cc, 12s	Color Limits	See Explanatory Notes.
	Isotonic	To prevent hemolysis of red blood cells at the site of injection.
	Leakage Test for Ampuls	See Explanatory Notes.
Furaxolidone and Nifuroxime Suppositories, NF, Vaginal, 24s	Melting Time for Suppositories	To assure that the suppositories are made with a base which will melt within a specified time frame to release its medicament. No such requirement exists in the compendia.
	Leakage Test	To assure the suppositories do not leak from container.
Prednisone Tablets, USP, 5 mg, 1000s	Classification of Defects	See Explanatory Notes.
Methyltestosterone Tablets, NF, 10 mg, 100s	Classification of Defects	See Explanatory Notes.
Methypryion Capsules, NF, 0.3 Gram, 500s	Classification of Defects	See Explanatory Notes.
Ephedrine Sulfate Capsules, USP, 25 mg, 500s	Classification of Defects	See Explanatory Notes.

	ADDITIONAL REQUIREMENTS	STIPULATION
Iodochlorhydroxyquin and Hydrocortisone Cream, NF, with 1% Micronized Hydrocortisone, 1 oz (28.35 Grams)	Microbial Limit	To control the amount of viable microorganisms and to prohibit those organisms that should not be present in the product. This assures that undesirable contamination is not present in the product. See Explanatory Notes.
	Accelerated Aging (Stability)	
Antipyrine and Benzocaine Solution, NF, 15 cc	Classification of Defects Moisture Limit (NMT 0.2% moisture at time of delivery to the Government)	See Explanatory Notes. To assure the stability of the product, in that excessive moisture may cause deterioration.
Hydroxyzine Hydrochloride Syrup, NF, 2 mg per cc, 1 pt (473 cc)	Tighter Assay Limits Taste/Palatability Panel	To assure a tighter manufacturing control. See Explanatory Notes.
Hydroxyzine Hydrochloride Injection, NF, 50 mg per cc, 10 cc	Classification of Defects pH Limits	See Explanatory Notes. A tighter pH range is specified in order to assure greater stability over the shelf life of the item.
	Color Limits	See Explantory Notes.
Lactose, USP, 1 lb (453.6 Gm)	Particle Size Limits for the Powder	To assure better incorporation of the lactose when mixed with other ingredients.
Lemon Oil, USP, 1 fl oz (29.5 cc)	Free from Sediment	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Nikethamide Injection, NF, 25%, 1-1/2 cc, 5s	Classification of Defects Color Limits Leakage Test for Ampuls	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes.

Isoxsuprine Hydrochloride Injection, USP, 0.2%, 4 cc, 10s	Classification of Defects	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
	Isotonic	To prevent hemolysis of red blood cells at the site of the injection.
	Color Limits	See Explanatory Notes.
Neostigmine Methylsulfate Injection, USP, 1:1000, 10 cc	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
Neostigmine Methylsulfate Injection, USP, 1:2000, 1 cc, 12s	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
	Leakage Test for Ampuls	See Explanatory Notes.
Niacinamide Tablets, USP, 50 mg, 100s	Classification of Defects	See Explanatory Notes.
Hydroxyzine Hydrochloride Tablets, NF, 10 mg, 500s Hydroxyzine Hydrochloride Tablets, NF, 25 mg, 500s	Classification of Defects	See Explanatory Notes.
	Hardness Limits	See Explanatory Notes
Hydroxyzine Pamoate Capsules, NF, Equivalent to 50 mg Hydroxyzine Hydrochloride, 500s	Classification of Defects	See Explanatory Notes.
	Moisture Limit	To assure the stability of the product, in that excessive moisture may cause deterioration.
Niacin Tablets, NF, 50 mg, 1000s	Classification of Defects	See Explanatory Notes.
Nonivamide Hydrochloride and Levodesoxyephedrine Injection, NF, 2%, 1.5 cc, 50s	Classification of Defects	See Explanatory Notes.
	Color Limits	See Explanatory Notes.
Lincomycin Hydrochloride Capsules, USP, Equivalent to 0.50 Gram of Lincomycin Base, 100s	Weight Variation	CFR does not specifically require compliance with weight variation for this item. Our requirement assures uniform weight within limits and thus proper and uniform dosage.
	Classification of Defects	See Explanatory Notes.

	ALLEGED DEFICIENCIES	SPECIFICATIONS
Imipramine Hydrochloride Tablets, USP, 25 mg, 100s	Classification of Defects	See Explanatory Notes.
Mineral Oil, USP, 1 qt (946 cc) Mineral Oil, USP, 1 gal (3.78 liters)	Shall be free from visible water, particulate matter & sediment.	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Shall be tested by and shall comply with the method & specifications of the Journal of the Association of Official Analytical Chemists.	To detect and limit potential carcinogenic polynuclear hydrocarbons.
Phytonadione Injection, USP, 1 mg, 0.5 cc, 25s	Classification of Defects	See Explanatory Notes.
Phytonadione Injection, USP, 10 mg, 1 cc, 6s	IR Identification of Raw Material	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Leakage Test for Ampuls	See Explanatory Notes
Phenylbutazone Tablets, USP, 100 mg, 100's	Classification of Defects	See Explanatory Notes
Phenylbutazone Tablets, USP, 100 mg, 1000s	Accelerated Aging Test	See Explanatory Notes

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Streptomycin Sulfate, USP, Equivalent to 1 Gram of Streptomycin Base	Classification of Defects Solubility Time limit Weight Variation	See Explanatory Notes See Explanatory Notes The USP and Code of Federal Regulations do not specifically require compliance with weight variation limits. Our requirement assures a uniform quantity within limits, and thus, proper and uniform dosage.
Terpin Hydrate and Codeine Elixir, NF, 4 fl. oz.	Free from sediment	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Classification of Defects	See Explanatory Notes
Potassium Penicillin G, Sterile, USP, 20,000,000 Units	Classification of Defects Color limits Weight Variation	See Explanatory Notes See Explanatory Notes The USP monograph and CFR does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and the proper and uniform dosage.
	Solubility Time Limit	See Explanatory Notes
Sodium Methicillin for Injection, USP, 1 Gram	Classification of Defects Solubility Time Limit Weight Variation	See Explanatory Notes See Explanatory Notes The USP monograph and CFR does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and the proper and uniform dosage.

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Methylprednisolone Sodium Succinate for Injection, NF, Equivalent to 1 Gram of Methylprednisolone	Classification of Defects Color limits Solubility Time Limit Content uniformity	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes. The NF Monograph does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and thus proper and uniform dosage.
Methylprednisolone Sodium Succinate for Injection, NF, Equivalent to 40 mg of Methylprednisolone Methylprednisolone Sodium Succinate for Injection, NF, Equivalent to 125 mg of Methylprednisolone	Classification of Defects Color limits Solubility Time Limit Content uniformity	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes. The NF Monograph does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and thus proper and uniform dosage.
Sodium Bicarbonate Injection, USP, 75 mg per cc, 50 cc, 6s	Classification Defects Leakage Test for ampuls Color limits	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes.
Potassium Penicillin G for Injection, USP, 1,600,000 Units Potassium Penicillin G for Injection, USP, 5,600,000 Units	Classification of Defects Solubility Time Limit Color limits Weight Variation	See Explanatory Notes. See Explanatory Notes. See Explanatory Notes. The USP monograph and CFR does not specifically require compliance with content uniformity for this item. Our requirement assures uniform quantity within limits and proper and uniform dosage.

Retain for future reference

OCTOBER 1973 issue of CALIFORNIA PHARMACIST

SOME MANUFACTURERS DISCLOSE SOURCES OF SUPPLY

The last issue of the *California Pharmacist* (September, 1973, page 5) reported the implementation of regulations which require pharmaceutical manufacturers to disclose the name and place of business of the manufacturer who produces the finished dosage form of their products. The regulation, effective July 28, 1973, provides that manufacturers must either include the names of the mixer of the final ingredients and the encapsulator or tabulator in the product's labeling and advertising material; or provide this information in response to the written or oral request of any physician, pharmacist, or their professional associations.

In an effort to supply information to the profession, the California Pharmaceutical Association requested the identity of the manufacturer who mixed the final ingredients and encapsulated or tableted the finished dosage forms of products manufacturered or distributed by over fifty different companies. The results of these requests, mailed on the 15th and 16th of August, are compiled in the following table. At the time of publication, over one month past the date of writing to the manufacturers, many firms have not complied with the Association's request for information.

Under the provisions of these regulations (Section 10386 of Title 17 of the California Administrative Code), failure to respond to requests for the identity of the manufacturer of the finished dosage form shall result in the products of the firm failing to respond being deemed misbranded. Those companies who have not responded to the Association's requests are being sent a final notice which will preceed the institution of legal proceedings against non-complying firms.

Pharmacists who have not been provided information as to the identity of the manufacturer of any prescription drug as provided for in California law, should notify the CPhA offices so that appropriate action may be taken.

The following list indicates the replies received at this office as of October 1, 1973. "Acknowledged request" indicates that the distributor has advised CPhA of the receipt of the request but has not supplied the name of the manufacturer of the final dosage form prior to press time.

DISTRIBUTOR	MANUFACTURER[1]	DATE REPLIED
AMPICILLIN TRIHYDRATE 250 mg Capsules		
American Pharmaceutical Co.	**No Reply**	
American Quinine Products	Zenith Labs., Inc. (Northvale, NJ)	8-29-73
B. F. Ascher & Co., Inc.	International Labs., Inc.[2] (Mayaguez, Puerto Rico)	9-07-73
Ayerst Laboratories	Beecham-Massengill Pharm.[3] (Piscataway, NJ)	9-05-73
Beecham-Massengill Pharm.	Beecham, Inc.	9-27-73
Bristol Laboratories, Div. of Bristol-Myers Co.	Bristol Labs. (E. Syracuse, NY)	8-29-73
Coastal Pharmaceutical Co.	**No Reply**	
Columbia Medical Company	Biocraft Labs. (E. Paterson, NJ)	9-05-73
Consolidated Midland Corp.	Reid Provident [4] or Zenith Labs., Inc.	8-21-73
ICN Pharmaceuticals, Inc. Strong Cobb Arner	**No Reply**	
Parke, Davis & Company	Replied[13]	9-19-73
Purepac Pharmaceutical Co.	**No Reply**	
Rachelle Laboratories, Inc.	International Labs.[5] (Atlanta, GA)	8-24-73
Sherry Pharm. Co., Inc.	**No Reply**	
Smith Kline & French, Labs.	**No Reply**	
E. R. Squibb & Sons, Inc.	E. R. Squibb & Sons, Inc.	8-31-73
Stayner Corporation	International Labs. (Atlanta, GA)	8-20-73
Towne, Paulsen & Co., Inc.	International Labs. (Atlanta, GA)	8-27-73
	John D. Copanos & Co., Inc. (Baltimore, MD)	
	Biocraft Labs. (E. Paterson, NJ)	
West-ward, Inc.	**No Reply**	
Wotins Pharmacal Corp.	Biocraft Labs.	9-06-73

DISTRIBUTOR	MANUFACTURER[1]	DATE REPLIED
AMPICILLIN ANHYDROUS		
Wyeth Laboratories	Wyeth Labs. (Philadelphia, PA)	8-24-73
BROPHENIRAMINE MALEATE —Elixir (Dimetane)		
A. H. Robins Company	A. H. Robins Company (Richmond, VA)	8-27-73
—Sustained Release Tablets (Dimetane Extentabs)		
A. H. Robins Company	ICN Pharmaceuticals Strong Cobb Arner (Cincinnati, OH)	8-27-73
—Sustained Release Tablets with phenylephrine and phenylpropanolamine (Dimetapp Extentabs)		
A. H. Robins Company	ICN Pharmaceuticals Strong Cobb Arner (Cincinnati, OH)	8-27-73
DEXAMETHASONE 0.75 mg Tablets		
CIBA Pharmaceutical Co.	**No Reply**	
Consolidated Midland Corp.	Danbury Pharmacal[4] or Cord Laboratories	8-21-73
Merck Sharp & Dohme Div. of Merck & Co., Inc.	acknowledged request	8-20-73
Organon, Inc.	Organon, Inc.	8-23-73
Schering Corp.	Schering Corp.	9-18-73
Sherry Pharm. Co., Inc.	**No Reply**	
USV Pharmaceutical Corp.	USV Pharmaceutical Corp.	8-31-73
Zenith Laboratories, Inc.	Zenith Labs., Inc. (Northvale, NJ)[6]	8-20-73

(Continued on page 8)

(Continued from page 7)

DISTRIBUTOR	MANUFACTURER[1]	DATE REPLIED
DONNATAL Tablets		
A. H. Robins Company	A. H. Robins Company (Richmond, VA)	8-27-73
ERYTHROMYCIN BASE 250 mg Tablets		
Eli Lilly & Company	Eli Lilly & Company (Indianapolis, IN)	8-30-73
The Upjohn Company	The Upjohn Company	8-30-73
ERYTHROMYCIN STEARATE 250 mg Tablets		
Abbott Laboratories	Abbott Labs.[6]	8-24-73
American Quinine Products	Zenith Labs., Inc. (Northvale, NJ)	8-29-73
Bristol Laboratories, Div. of Bristor-Myers Company	Bristol Laboratories (E. Syracuse, NY)	8-29-73
Columbia Medical Company	Zenith Labs., Inc. (Northvale, NJ)	9-05-73
Mallinckrodt Pharmaceuticals	**No Reply**	
Parke, Davis & Company	Replied[13]	9-19-73
Sherry Pharm. Co., Inc.	**No Reply**	
Smith Kline & French Labs.	**No Reply**	
Towne, Paulsen & Co., Inc.	Mylan Pharmaceuticals (Morgantown, WV)	8-29-73
West-ward, Inc.	**No Reply**	
Wyeth Laboratories	Mylan Pharmaceuticals[7] (Morgantown, WV)	8-24-73
Zenith Laboratories, Inc.	Zenith Labs., Inc.[6] (Northvale, NJ)	8-20-73
FENFLURAMINE 20 mg Tablets		
A. H. Robins Company	A. H. Robins Company (Richmond, VA)	8-27-73
GLYCERYL GUAIACOLATE Syrup		
A. H. Robins Company	A. H. Robins Company (Richmond, VA)	8-27-73
HEPARIN SODIUM 1000 Units/cc Injection		
Abbott Laboratories	Abbott Laboratories[6]	8-24-73
Century Pharmaceuticals, Inc.	Medwick Laboratories, Inc. (Chicago, IL)	8-29-73
Consolidated Midland Corp.	Elkins-Sinn or Medical Chemicals[4]	8-27-73
Eli Lilly & Company	Eli Lilly & Company (Indianapolis, IN)	8-30-73
Medwick Laboratories, Inc.	**No Reply**	
Organon, Inc.	Organon, Inc.	8-27-73
Parke, Davis & Company	Replied[13]	9-19-73
Robinson Laboratories, Inc	**No Reply**	
Towne, Paulsen & Co., Inc.	Medwick Laboratories, Inc. (Melrose Park, IL)	8-27-73
The Upjohn Company	The Upjohn Company	8-30-73
Wyeth Laboratories	Wyeth Laboratories (Philadelphia, PA)	8-24-73
HYDROCHLOROTHIAZIDE 50 mg Tablets		
Geigy Pharmaceuticals Div. of Ciba-Geigy Corp.	**No Reply**	
Merck Sharp & Dohme Div. of Merck & Co., Inc.	acknowledged request	8-20-73
Wolins Pharmacal Corp.	Zenith Labs., Inc.	9-06-73
L-DOPA 250 mg Capsules		
Eaton Laboratories, Div. Morton-Norwich Products, Inc.	Eaton Laboratories, Inc. (Norwich, NY)	8-23-73
Roche Laboratories, Div. Hoffmann-LaRoche, Inc.	Roche Laboratories (Nutley, NJ)	8-21-73
MEPROBAMATE 200 & 400 mg Tablets		
American Pharmaceutical Co.	**No Reply**	
American Quinine Products	Zenith Labs., Inc. (Northvale, NJ)	8-29-73
Barr Laboratories, Inc.	Barr Labs., Inc. (Northvale, NJ)	8-20-73
Columbia Medical Co.	Zenith Labs., Inc.	9-05-73
ICN Pharmaceuticals, Inc. Strong Cobb Arner	**No Reply**	
Kirkman Laboratories[8]	**No Reply**	
McKesson Laboratories, Div. Foremost-McKesson, Inc.	**No Reply**	
Parke, Davis & Company	Replied[13]	9-19-73
Purepac Pharmaceutical Co.	**No Reply**	
Richlyn Laboratories, Inc.[8]	Richlyn Labs., Inc. (Philadelphia, PA)	9-05-73
Sherry Pharm. Co., Inc.	**No Reply**	
Stanlabs, Inc.	**No Reply**	
Smith Kline & French Labs.	**No Reply**	
Stayner Corp.	Zenith Labs., Inc. (Northvale, NJ)	8-20-73
Towne, Paulsen & Co., Inc.	Towne, Paulsen & Co., Inc. (Monrovia, CA)	8-27-73
Wallace Pharmaceuticals Div. of Carter-Wallace, Inc.	Carter-Wallace, Inc. (Cranbury, NJ)	8-20-73
Wolins Pharmacal Corp.[8]	Heather Drug Co., Inc.	9-06-73
Wyeth Laboratories	Wyeth Labs. (Philadelphia, PA)	8-24-73
Zenith Laboratories, Inc.	Zenith Labs., Inc.[6] (Northvale, NJ)	8-20-73
PENICILLIN V POTASSIUM 250 mg Tablets		
ICN Pharmaceuticals, Inc. Strong Cobb Arner	**No Reply**	
Lederle Laboratories, Div. of American Cyanamid Company	Lederle Laboratories	8-24-73
Eli Lilly & Company	Eli Lilly & Company[8] (Indianapolis, IN)	8-21-73
A. H. Robins Company	Biocraft Laboratories (E. Paterson, NJ)	8-27-73
Robinson Laboratory, Inc.	**No Reply**	
Sherry Pharm. Co., Inc.	**No Reply**	
E. R. Squibb & Sons, Inc.	E. R. Squibb & Sons, Inc.	8-29-73
Towne, Paulsen & Co., Inc.	Mylan Pharmaceuticals Inc. (Morgantown, WV) John D. Copanos & Co., Inc. (Baltimore, MD)	8-27-73
West-ward, Inc.	**No Reply**	
McKesson Laboratories, Div. Foremost-McKesson, Inc.	**No Reply**	
Pfizer Laboratories, Div. Pfizer, Inc.	**No Reply**	
Purepac Pharmaceutical Co.	**No Reply**	
PREDNISONE 5 mg Tablets		
American Pharmaceutical Co.	**No Reply**	
Barr Laboratories, Inc.	Barr Labs., Inc. (Northvale, NJ)	8-20-73
Columbia Medical Co.	Blue Cross Products (Brooklyn, NY)	9-05-73
First Texas Pharm., Inc.	First Texas Pharm., Inc. (Dallas, TX)	8-23-73
ICN Pharmaceuticals, Inc. Strong Cobb Arner	**No Reply**	
Kirkman Laboratories	**No Reply**	
McKesson Laboratories, Div. Foremost-McKesson, Inc.	**No Reply**	

ITEM	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Isopropyl Alcohol, NF, 54 gal (204.4 liters) Isopropyl Alcohol, NF, 5 gal (18.92 liters) Isopropyl Alcohol, NF, 1 qt (946 cc) Isopropyl Alcohol, NF, 1 qt (946 cc)	APHA Color	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
Poliovirus Vaccine, Live, Oral, USP, Types 1, 2, and 3, 10 doses Poliovirus Vaccine, Live, Oral, USP, Types 1, 2 and 3, 100 doses	Classification of Defects	See Explanatory Notes
Prednisolone Sodium Phosphate Injection, USP, Equivalent to 20 mg of Prednisolone Phosphate per cc, 5 cc	Classification of Defects Color limits	See Explanatory Notes See Explanatory Notes
Mannitol Injection, USP, 15%, 150 cc, 6s	Classification of Defects	See Explanatory Notes
Histoplasmin, USP, 0.01 cc	Maximum unrefrigerated shipping times for items requiring refrigerated storage. Dye	See Explanatory Notes This is a skin test and the dye shows the placement of the material.
Protamine Sulfate Injection, USP, 10 mg per cc, 5cc, 6s	Classification of Defects Color limits Leakage Test for Ampuls Max Unrefrigerated Shipping times for items requiring refrigerated storage.	See Explanatory Notes See Explanatory Notes See Explanatory Notes See Explanatory Notes

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Sodium Oxacillin For Injection, USP, Equivalent to 1.0 Gram of Oxacillin Sodium Oxacillin For Injection, USP, Equivalent to 0.5 Gram of Oxacillin	Classification of Defects Solubility Time Limit Color Limits Weight Variation	See Explanatory Notes See Explanatory Notes See Explanatory Notes The USP monograph & CFR do not specifically require compliance with content uniformity for this item. Our requirements assure uniform quantity within limits & thus proper uniform dosage.
Lidocaine Hydrochloride Jelly, USP, USP, 2%, 30cc	Classification of Defects Viscosity Leakage Test	See Explanatory Notes The USP monograph does not require compliance with viscosity, yet this characteristic is necessary for the proper consistency to allow for the spreading & application of the jelly. To assure the containers of jelly do not leak.
Sodium Warfarin Tablets, USP, 5 mg, 100s Sodium Warfarin Tablets, USP, 2 mg, 100s	Shall be Endo Laboratories "Coumadin"	Professional requirement.
Stannous Fluoride, NF, 120 Gram	Limits for foreign substances (Iron, Nickel, Copper, Lead, and Arsenic)	To assure that impurities are detected that may arise from production procedures or from changes in sources of materials, or in the production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.

dispensed in the United States. The pharmacist's interest stems primarily from the fact that the pharmacist knows how important the medication is to the patient and the pharmacist has to look the patient or a member of his family in the eye. The pharmacist has no vested economic self-interest in the price the manufacturer charges for his drug products because the pharmaceutical service system provides that the pharmacist be reimbursed what the pharmacist pays for the drug product. On the other hand, the pharmacist does have an obvious professional objective in providing patients with effective and safe medication at reasonable prices.

No subject investigated by your subcommittee in the almost 7 years of your extensive work is, from the pharmacist and patient point of view, more important than the hearings you are now holding. More than two billion prescriptions are being dispensed annually—more than five million daily—and the patients who take these prescriptions have a right to expect their government to resolve the question of how much confidence can be placed in the medicines their pharmacists dispense.

APhA as the national professional society for all pharmacists has no ax to grind for anybody, but the patient and his pharmacist. The pharmacist does not care whether a drug product is made and marketed by a large firm or a small firm, as long as the pharmacist can be assured of the product's safety and efficacy. APhA knows that high quality prescription drugs can be and are fabricated by manufacturers of all sizes.

APhA also knows that the hallmark of quality is not derived by giving a product a euphonious brand name. And we have watched with interest the development of so-called "branded generics" by such fine firms as Lilly, Lederle, SKF and Upjohn.

Simply stated, the situation in our country today is that one agency of the Federal Government says that you can depend on the quality of the Nation's drug supply, and another agency of the same Government would like you to believe otherwise. Regardless of how this controversy is resolved, APhA is sick and tired of having the finest drug supply in the world under a constant cloud of suspicion. It was bad enough when only the pharmacist was the target of this propaganda, but now prescribers and patients are asking the pharmacist for assurance.

APhA believes the country can ill afford further delay in putting the issue to rest.

Thank you, Mr. Chairman. I will be glad to answer questions now or after Dr. Feldmann submits his testimony.

Senator NELSON. Well, when you refer to "another agency of the same government," you are referring to the Defense Department?

Dr. APPLE. Mr. Chairman, I am saying that HEW—the Food and Drug Administration—says the drug supply is good, and the Department of Defense has been casting clouds over the Nation's drug supply for the last several years with statements made by some of their spokesmen.

Senator NELSON. Well, the same thing is true, is it not, of the Pharmaceutical Manufacturers Association in respect to generics?

In other words, they repeatedly said, sometimes subtly, more frequently not so subtly, that you can only trust the big brand name companies, of which most all of them are members of the PMA, is that not so?

Dr. APPLE. I would certainly have to agree that that is the thrust of their propaganda.

Senator NELSON. I thought it was interesting. You say that the APhA "also knows that the hallmark of quality is not derived by giving a drug product a euphonious trade name, and we have watched with interest the development of so-called 'branded generics' by such fine firms as Lilly, Lederle, SKF and Upjohn."

I found interesting a recent report from the FDC reports—frequently called the Pink Sheet—of July 16, 1973, which states that:

> Squibb, Pfizer and Wyeth have recently joined SKF, Robins and Parke-Davis as purchasers of antibiotics and other generic dosage forms from Mylan a private formula manufacturer in Morgantown, West Virginia. Mylan's private formula sales to major drug manufacturers jumped to $4,800,000 in fiscal year 1973 ending March 31 from $2,200.000 a year earlier.
>
> Emerging as Mylan's top major pharmaceutical marketing customer in fiscal year 1973, Squibb purchased $1.3 million erythromycin in the first year it bought anything from the Morgantown private formula manufacturer. Mylan is sole supplier for Squibbs' erythromycin. introduced in 1972.
>
> A Squibb spokesman said the company decided to use Mylan rather than processing erythromycin itself because of the "difficult technology involved." Mylan is one of the few companies capable of making the product, the Squibb spokesman said.

Well, I think that is rather interesting, since their own association keeps attacking the generics as not being of the same quality as the trade name products. And here you have Squibb saying that this little company which hardly anybody has heard of has the difficult technology to master this, and I think we ought to lay to rest this propaganda campaign that the Pharmaceutical Manufacturers Association and the DOD have been carrying on.

Dr. APPLE. Mr. Chairman, if I could comment on that. We tried to lay that issue to rest. Our association has a policy encouraging legislation that would reveal the actual identity of the fabricator of the dosage form on the label, as well as the identity of the distributor. That legislation has been enacted in the State of California and more recently in the State of Kentucky.

There is an effort by the Pharmaceutical Manufacturers Association now in California to have that legislation amended, and I regret to say that it has already passed one House of the California legislature.

For the record, I can give you the information that California was able to gather under prevailing regulations of this so-called "Crown Statute." And I would particularly like to call to your attention an editorial which appeared in the November 1973 California Pharmacist, in which the editor asked, "It is difficult to understand why the drug industry is fearful of having the pharmacist and physician know who really makes their drug products. PMA consistently maligns small manufacturers by suggesting their products may not be of adequate quality. Yet, they are attempting to deny the pharmacist the informa-

NAME	ADDITIONAL REQUIREMENTS	SIGNIFICANCE
Phenazopyridine Hydrochloride Tablets, NF, 0.1 Gram, 1000s Phenazopyridine Hydrochloride Tablets, NF, 0.1 Gram, 50s	Classification of Defects Additional identity test	See Explanatory Notes. To further assure that the active ingredient is present in the tablets.
Norethindrone Acetate and Ethinyl Estradiol Tablets, NF, 63s	Classification of Defects	See Explanatory Notes.
Idoxuridine Ophthalmic Solution, USP, 0.1%, 15cc	Maximum unrefrigerated shipping times for items requiring refrigerated storage.	See Explanatory Notes.
Nalidixic Acid Tablets, NF, 0.50 Gram, 1000s	Classification of Defects Moisture	See Explanatory Notes. To assure the stability of the product, in the excessive moisture may cause deterioration.
Propylene Glycol, USP, 1 lb (453.6 Gram)	APHA Color	To assure that impurities are detected that may arise from production procedures, or from changes in sources of materials, or in the processing of the item. The presence of these impurities is inconsistent with good manufacturing practices.
	Free from sediment	To assure best production procedures and controls are utilized consistent with good manufacturing practices.
Ringer's Injection, Lactated, USP, 1000 cc, 6s	Classification of Defects	See Explanatory Notes.
Quinine Dihydrochloride Injection, NF, 0.3 Gm per cc, 2 cc, 12s	Classification of Defects Leakage Test for Ampuls	See Explanatory Notes. See Explanatory Notes.
Smallpox Vaccine, USP, Freeze Dried, Jet Gun, 100 Doses Smallpox Vaccine, USP, Freeze Dried, Jet Gun, 25 Doses Smallpox Vaccine, USP, Freeze Dried, Jet Gun, 100 Doses	Classification of Defects Maximum unrefrigerated Shipping Times for Items Requiring Refrigerated Storage	See Explanatory Notes. See Explanatory Notes.