effectiveness as defined by Feldman(21). The largest amount a patient in this study could receive during the flexible dosage period was 300 mgs./day, the upper limit of Feldman's range. That 150 mgs./day was not optimal is clearly demonstrated by the increments in mean dosage of mepazine shown in Figure 1. Although the mean daily dose of mepazine given to patients during the flexible dosage period was 190 mgs., in the final weeks of the study, approximately a third of these patients were receiving the maximum amount allowed by the study protocol (300 mgs.) and side effects were minimal. In the light of current knowledge, it may be assumed that the unit dose of mepazine used in this study should have been approximately that of chlorpromazine.

The interpretation of the finding that the 4 remaining phenothiazines did not differ significantly is not an obvious one. Statistical logic does not permit the conclusion that these compounds are identical in action. Interpretation must be guided by the experimental conditions which produced the results. The purpose of random assignment of patients to treatment, the double blind procedure and statistical adjustment for initial differences was to prevent one treatment group from having an advantage over any other except in terms of the treatment being evaluated. The flexible dosage schedule was chosen to allow each drug to be evaluated at approximately optimal dosage. The choice of criteria of clinical effectiveness was intended to encompass a large portion of the domain of psychopathology. The reliability of the MSRPP was investigated and considered satisfactory. However, some may feel that such measures are either too insensitive to capture the subtle nuances of drug differences or have missed important areas of behavioral change. Within the limitations of this design, the findings are consistent and are considered reliable.

The high dropout rate (168 patients, 26%) in this study raised two questions. First, was there any evidence of selective dropout related to treatment group? In terms of total number of dropouts in each treatment group from all causes, there were no significant differences between the groups. However, a disproportionate number of patients on trifluprom azine were out of the hospital (26 of a total of 85) prior to the end of the treatment period. It is difficult to evaluate this as a biasing factor, in that 16 of these patients left against medical advice or without permission, which may not necessarily relate to the results of treatment. A disproportionate number of patients on phenobarbital and mepazine (16 of a total of 23) were dropped because of lack of improvement or worsening of their condition. This situation was consistent with the clinical findings and did not constitute a source of obscuring bias. Second, were these patients different in any way from those completing the study? Patients who left the hospital prior to the end of the study for whatever reason were in general not as ill initially as those remaining until the end of the study. Patients leaving without medical approval, the greatest number of whom were in the trifluprom azine group, had lower morbidity scores, were less depressed and withdrawn and showed less disturbance in thinking before treatment than did those who remained in treatment for the entire period.

When this study was conceived, the controlled evaluation of side reactions and abnormal laboratory results during therapy with phenothiazine drugs was considered potentially more important than therapeutic differences between the drugs. In some respects this prediction was true, though not in the manner thought. The most outstanding finding was the comparative paucity of severe abnormalities, accounting for only a 3% loss in the total sample. Next in interest was the lack of difference in prevalence of abnormal symptoms, signs, and laboratory tests between the phenothiazines and, surprisingly, phenobarbital. In the case of phenobarbital, these abnormalities included such adverse behavioral effects as depression or agitation, autonomic effects such as blurred vision or dry mucous membranes, such presumed central nervous effects as akathisia, as well as eosinophilia, leucocytosis, leucopenia and abnormal hepatic tests. In many instances, these abnormalities probably represented manifestations of schizophrenia or spontaneous fluctuations completely unrelated to drug

therapy. The failure to encounter any instance of frank jaundice or agranulocytosis in 530 patients treated with phenothiazine derivatives suggests that these complications may have been more feared in the past than was warranted. In view of the frequent abnormalities associated with phenobarbital therapy, especially those not commonly attributed to this drug before, one must be cautious in ascribing all that happens during drug therapy to the drugs being used. The original intent to discover some index between therapeutic effectiveness of the drugs and side reactions or laboratory abnormalities was not feasible with so little difference between the agents in either regard.

Although this study offers considerable information regarding the clinical effectiveness, side effects, and toxicity of 5 phenothiazines used under the described conditions, the data necessary to guide drug therapy of individual schizophrenic patients are not provided. With the data from this and other studies and his personal experience with drugs as background material, the physician must still select a specific drug for an individual patient, taking into consideration such factors as speed of action; dosage schedules; treatment goals; combinations, potentiation, and sequences of drugs; duration of effects; calculated risks and safety; convenience; cost; subjective patient response; compatability with other treatments; and any special features or unique advantages of a given drug.

Summary

Six hundred forty newly-admitted schizophrenic men in 35 VA hospitals were randomly assigned to chlorpromazine, triflupromazine, mepazine, prochlorperazine, perphenazine and phenobarbital groups. Treatment followed a double blind procedure for 12 weeks. Patients were started on low "equivalent" doses of each drug which were gradually increased in a predetermined manner during the first 4 weeks. During the final 8 weeks, each prescribing physician adjusted the dose for each of his patients in order to evoke an optimal therapeutic response.

Average daily doses during the flexible period were: chlorpromazine, 635 mg.; triflupromazine, 175 mg.; mepazine, 190 mg.; prochlorperazine, 90 mg.; and perphenazine, 50 mg. Clinical evaluations using two rating scales provided 24 criteria of change. For each criterion, the mean of each of the 6 treatment groups adjusted for the net effect of 12 control variables was compared by analysis of multiple covariance with the mean of every other treatment group at each of three evaluation periods; first month, the following 2 months, and over the entire 3 months. Side effects, hematologic and hepatic function data were also recorded during the course of treatment. One hundred sixty-eight patients failed to complete the study.

In general, the results indicated that all 5 phenothiazine derivatives were therapeutically more effective than phenobarbital. Mepazine was less effective than the other 4 drugs at the doses employed. No significant differences in therapeutic efficacy were noted between chlorpromazine, triflupromazine, prochlorperazine, and perphenazine. Criterion measures showing change toward improvement after treatment with phenothiazine derivatives included resistiveness, belligerence, thinking disturbance, and degree of illness. Other criteria affected favorably, especially by the 4 more potent phenothiazines, were motor disturbance, paranoid projection, perceptual distortion and withdrawal.

Only 21 patients (3%) were discontinued from treatment because of side reactions or deviant laboratory tests. Most side reactions, especially the extrapyramidal syndromes, were produced by perphenazine and prochlorperazine. Phenobarbital was associated with a number of side reactions ("turbulence," autonomic symptoms) commonly attributed only to the phenothiazine derivatives. Abnormal hematologic tests including eosinophilia, leucocytosis and leucopenia were neither frequent nor severe. The distribution of the 36 patients with leucopenia was not significantly different among the treatment groups. Continued treatment with the drugs in 31 leucopenic patients produced no case of agranulocytosis. Although abnormal hepatic tests occurred in 88 patients, these were sporadic. No clear-cut case of jaundice or hepatic dysfunction was encountered during treatment.

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ABNORMAL SYMPTOMS, SIGNS, AND LABORATORY TESTS DURING TREATMENT WITH PHENOTHIAZINE DERIVATIVES

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Abnormal symptoms, signs, and laboratory tests during treatment with phenothiazine derivatives

Complications were neither frequent nor severe in 599 newly admitted schizophrenic patients treated for 12 weeks with chlorpromazine, trifluprομazine, mepazine, prochlorperazine, perphenazine, and phenobarbital. Twelve patients were dropped from treatment because of adverse symptoms or signs, 5 because of hematologic abnormalities, and 4 because of deviant hepatic tests.

Many abnormal symptoms and signs generally thought to be associated with phenothiazine drug therapy also occurred during treatment with phenobarbital. Leucopenia was not significantly more frequent from phenothiazines than from phenobarbital. No significant differences in abnormal hepatic tests were noted between the 6 agents. Most abnormal tests were isolated and sporadic. No frank case of intrahepatic obstructive jaundice was observed. Changes in body temperature, pulse rate, and blood pressure were uncommon, with no significant differences in frequency between the drug regimens.

Not all abnormalities in symptoms, signs, and laboratory tests which occurred during treatment can be attributed to it. At least some must be spontaneous fluctuations in the population studied.

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Wide experience with the phenothiazine derivatives in clinical use has delineated the prevalence of undesirable effects or abnormal laboratory tests, as they are studied under varied conditions. A controlled study by the Veterans Administration suggests that the incidence of reactions and abnormal laboratory findings may be smaller than is generally believed, and these must be evaluated against a background of behavioral, hematologic, hepatic, and autonomic nervous system variability inherent in a schizophrenic population.

Six drugs (chlorpromazine, trifluprομazine, mepazine, prochlorperazine, perphenazine, and phenobarbital) were given for a 12 week period to 599 newly admitted

Staff from 35 hospitals participating in Project No. 3, Veterans Administration Cooperative Studies in Chemotherapy in Psychiatry, collected the data used for this study.

schizophrenic men in 35 Veterans Administration Hospitals.[1] A double blind control was employed, using "equivalent" doses of each of the 6 agents in both an initially determined and later flexible dosage schedule. Biasing factors were that the sample was composed of men under the age of 51 years, some of whom had previously received phenothiazine derivatives. Except for their mental illness, the patients were generally in good health.

Methods of study

Four specific types of information were sought: (1) the prevalence of clinical symptoms or signs frequently reported as occurring with phenothiazine derivatives[2,5,7,11]; (2) the prevalence of abnormalities in hematologic measures, especially total leukocyte count, absolute neutrophil count, and eosinophil count; (3) the prevalence of positive hepatic findings; (4) the occurrence of aberrations in body temperature, pulse rate, or blood pressure.

A symptom-sign check list for each of 14 specific items was completed weekly by the attending physician on each patient. Thus information was obtained about the prevalence, the time of onset, and the duration of each of these manifestations.

Total and differential leukocyte counts were obtained on each patient prior to and during each of the 12 weeks of treatment. If other hematologic tests were deemed necessary, these were obtained at the discretion of the attending physician. For purposes of this study leukocytosis was considered to be present if the total leukocyte count exceeded 13,500 per cubic milliliter. No lower limit was imposed on the total leukocyte count for determining the presence of leukopenia; rather this was deemed to be more accurately represented by a calculation of the absolute neutrophil count (total leukocyte count times per cent of neutrophils). An absolute neutrophil count of 3,000 per cubic milliliter was considered as the lower limit of normal. A patient was regarded as leukopenic when the absolute neutrophil count dropped below 1,800. Absolute neutrophil counts of less than 1,500 per cubic milliliter were considered to represent a potentially dangerous situation, but the decision as to whether or not treatment should be continued was left to the attending physician. Eosinophil counts of 7 per cent or more were considered to be elevated. All these data were tabulated on an appropriate form for each of the 12 weeks of treatment.

The study protocol also recommended that each patient have hepatic tests performed prior to and during the first 5 weeks of treatment. Recommended as preferential screening hepatic tests were the alkaline phosphatase determination and the serum glutamic oxalacetic acid transaminase (SGO-T) test. If either of these tests was abnormal (over 8 Bodansky units for the alkaline phosphatase test and over 40 units for the SGO-T test), other hepatic tests were to be performed. These included determinations of the total serum bilirubin, cephalin flocculation, and Bromsulphalein (BSP) retention. The upper limits of normal were set at 1.2 mg. per 100 ml., 3+ at 48 hours, and more than 8 per cent retention, respectively, for each of the tests.

Each participating hospital was requested to make daily measures of patients' temperatures during the entire treatment course and daily measures of blood pressure and resting pulse rates during the first week of treatment. Naturally, great variations occurred in conditions under which these measures were made in various patients.

Results of study

Control values for total neutrophil count, alkaline phosphatase and SGO-T determinations. Data on the total leukocyte count of 475 patients prior to treatment were tabulated. The mean control leukocyte count was 8,200 per cubic milliliter with a standard deviation of 2,750. Ninety-seven patients (more than 20 per cent) had control total leukocyte counts of over 10,000 per cubic milliliter. In 80 of these 97 patients the total leukocyte count

Table I. *Comparison* between drugs in occurrence of clinically noted side effects during 12 week treatment period*

Perphenazine	Produced *more* drowsiness and extrapyramidal effects (impaired associated movements, rigidity, tremor, and akathisia) than *phenobarbital* or *mepazine*; *more* extrapyramidal effects (rigidity, tremor, and akathisia) than *triflupromazine*; *more* extrapyramidal effects (impaired associated movements, rigidity, and akathisia) than chlorpromazine; and *more* akathisia than *prochlorperazine.*
Prochlorperazine	Produced *more* drowsiness, extrapyramidal effects (impaired associated movements, rigidity, tremor, akathisia) and nausea or vomiting than *phenobarbital*; *more* drowsiness, extrapyramidal effects (impaired associated movements, rigidity), weakness or fatigue and nausea or vomiting than *mepazine.*
Chlorpromazine	Produced *more* drowsiness, extrapyramidal effects (rigidity, tremor) than *phenobarbital*; *more* drowsiness, impaired associated movements, and weakness or fatigue than *mepazine.*
Triflupromazine	Produced *more* extrapyramidal effects (impaired associated movements) than *phenobarbital*; *more* impaired associated movements than *mepazine. Complete absence of side effects was more common* than with *prochlorperazine* or *perphenazine.*
Mepazine	Produced *more* blurred vision than *phenobarbital* or *triflupromazine.*
Phenobarbital	Produced *more* excitement and agitation than *mepazine, triflupromazine, chlorpromazine,* or *prochlorperazine. Complete absence of side effects* was *more common* than with *prochlorperazine* or *perphenazine.*

*Only differences significant at the 5 per cent level using chi square comparisons of the drug pairs are stated.

was in the 10,000 to 13,500 range, in 11 between 13,500 and 16,000, and in 6 over 16,000 per cubic milliliter. The maximum control leukocyte count observed was 22,500 per cubic milliliter. Nineteen patients had control leukocyte counts of less than 5,000 and only 3 of these 19 patients had total leukocyte counts of less than 4,000 per cubic milliliter. Thus leukocytosis by ordinary standards was comparatively common in this schizophrenic population but leukopenia was neither frequent nor severe.

Determination of control values for alkaline phosphatase was more complicated because they were reported in 4 different kinds of units. The largest sample consisted of reports in Bodansky units which were available on 256 patients. The mean value in Bodansky units for control alkaline phosphatase determinations was 4 units with a standard deviation of 1.8 units. Six patients had control values for alkaline phosphatase greater than 8 units.

SGO-T determinations were performed on 154 patients. The mean value for this determination was 24.8 units with a standard deviation of 19.4 units. Nineteen patients showed control elevations of SGO-T titer to more than 40 units.

Abnormal signs and symptoms. Data on the occurrence of abnormal symptoms and signs were available for the entire sample of 599 patients. Twelve patients were dropped from treatment because of side reactions. No abnormal symptoms or signs were reported in 167 patients. These 167 patients were not distributed among the 6 treatment groups as might have been expected by chance, so each drug group was compared individually with every other drug group and tested for significance by the chi square test. Each symptom or sign was evaluated in the same manner. If a patient was reported as manifesting a particular symptom at any time during the study period, he was tallied once regardless of whether the symptom occurred during one or more weeks. When a significant difference among the 6 groups was observed for any symptom, the groups were then compared by pairs. Ten symptoms showed significant differences between the treatment groups.

Table I compares the drugs with regard to clinical evidence of side effects during the 12 week treatment period. Perphenazine and prochlorperazine, both piperazine derivatives, produced more reactions than

the other drug. The two aliphatic derivatives, chlorpromazine and trifluprom azine, produced more reactions than the piperidine derivative, mepazine, or phenobarbital.

Table II indicates the number of patients showing any abnormal symptom in each of the drug treatment groups. The median daily dose at which drowsiness was produced varied considerably (prochlorperazine, 35 mg.; perphenazine, 48 mg.; trifluprom azine, 60 mg.; mepazine, 75 mg.; phenobarbital, 96 mg.; chlorpromazine, 200 mg.). The majority of adverse behavioral effects appeared during the first 3 weeks of treatment; their persistence was comparable for each of the drugs. Mental depression and "turbulence" (anxiety and agitation), usually considered adverse effects of phenothiazine derivatives, were equally common with phenobarbital.

Extrapyramidal effects were more frequent from the piperazinylphenothiazines

Table II. *Number of patients in each drug group showing clinically observed side effects*

Symptom or sign	*Total N = 599*	*Phenobarbital 99*	*Prochlorperazine 100*	*Trifluprom azine 96*	*Mepazine 103*	*Prochlorperazine 100*	*Perphenazine 101*
Adverse behavior							
Drowsiness	232	28	48	38	28	44	46
Depression	103	18	15	13	15	23	19
Anxiety	198	38	29	26	28	41	36
Agitation	181	44	20	26	30	27	34
Central nervous system							
Extrapyramidal effects	52	0	8	6	2	15	21
Impaired associated movements	57	2	8	10	1	16	20
Rigidity	62	0	9	9	2	15	27
Tremor	47	2	10	5	5	10	15
Akathisia	110	12	16	16	12	20	34
Dystonia (spasm)	16	1	2	3	1	3	6
Weakness, fatigue	135	16	28	18	16	29	28
Seizures	4	0	0	1	1	1	1
Autonomic nervous system							
Fainting	16	2	4	1	2	4	3
Blurred vision	90	10	16	8	24	14	18
Nausea, vomiting	60	6	13	10	5	17	9
Dryness of mouth	107	13	20	11	24	20	19
Constipation	89	10	17	14	23	12	13
Allergic effects							
Dermatitis	21	3	7	4	2	4	1

Table III. *Changes in leukocyte and eosinophil counts during 12 week treatment period*

Drug	*Eosinophilia*		*Leukocytosis*		*Leukopenia*	
	No. of patients	*Total No. counts*	*No. of patients*	*Total No. counts*	*No. of patients*	*Total No. counts*
Phenobarbital	20 (4)*	40	16 (3)	40	9 (5)	19
Chlorpromazine	18 (3)	34	12 (2)	13	7 (6)	23
Trifluprom azine	11 (0)	22	11 (3)	32	3 (3)	4
Mepazine	17 (4)	37	12 (4)	25	8 (5)	29
Prochlorperazine	16 (1)	42	19 (1)	42	2 (3)	5
Perphenazine	16 (4)	31	16 (2)	33	7 (4)	14

*Numbers in parentheses indicate patients with abnormal control values.

than the others. As might be expected, no patient treated with phenobarbital was believed to have the complete extrapyramidal syndrome. These effects were most frequent in the third week of treatment, at daily doses of 48 mg. of perphenazine, 75 mg. of prochlorperazine, 150 mg. of trifluprom azine, and 600 mg. of chlorpromazine. Patients receiving phenobarbital reported as having akathisia probably reflected the difficulty in distinguishing this symptom-complex from the ordinary manifestations of psychosis. Similarly, an instance of dystonic syndrome with phenobarbital must have reflected an error in clinical judgment, as this syndrome is unique for phenothiazine derivatives.

As extrapyramidal syndromes are frequently said to correlate with clinical improvement, such a relationship was sought in the case of perphenazine and prochlorperazine. Substantial clinical improvement was arbitrarily defined as a reduction of 25 per cent or more from the initial total morbidity score (measured by the Multidimensional Scale for Rating Psychiatric Patients) at the end of 12 weeks of treatment. Any change less than this was considered insufficient improvement. These two categories of improvement were then grouped according to the presence or absence of extrapyramidal syndromes. No statistically significant differences were noted between groups showing substantial improvement and those not, either with or without extrapyramidal effects, in the case of either drug.

Although autonomic nervous system effects are not related to the pharmacologic action of phenobarbital, a surprising number were recorded. Presumably these represent normal variations in the state of the patients, rather than drug effects. They tended to occur later in the course than with the phenothiazine derivatives, which usually produced these effects immediately and at low doses.

Cases of dermatitis were too few to show much distinction between the drugs. The occurrence of this complication with phenobarbital was not surprising as allergic eruptions with barbiturates should be expected.

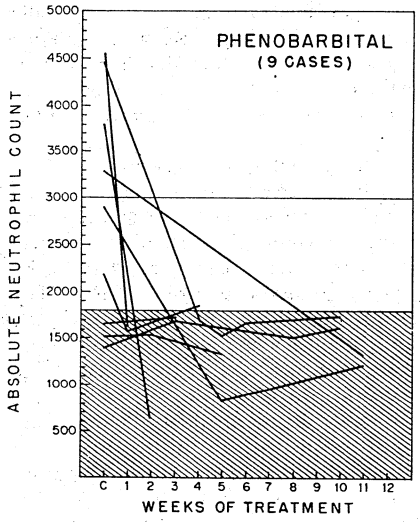
Changes in leukocyte and eosinophil counts. The occurrence of eosinophilia, leukocytosis, and leukopenia is shown in Table III. None of the differences between drug groups were statistically significant.

Eosinophilia was most frequently noted, being highest for phenobarbital (even when corrected for 2 abnormally elevated counts in the control period) and lowest with trifluprom azine. The total number of

Table IV. *Occurrence of abnormal hepatic tests during 12 week treatment period*

Drug	*Patients with abnormal tests*	*No. with 2 or more abnormal tests*	*Total serum bilirubin over 1.2 mg. %*	*SGO-T titer over 40 units*	*Alkaline phosphatase over 8 units (Bodansky)*	*Cephalin flocculation 3 plus or more in 48 hours*	*BSP retention over 8 per cent in 45 minutes*
Phenobarbital	20 (10)*	6 (5)	4	10	4	6	3
Chlorpromazine	19 (5)	3 (1)	4	9	5	5	0
Trifluprom azine	11 (2)	6 (2)	2	10	4	3	0
Mepazine	16 (8)	5 (3)	6	9	3	3	1
Prochlorperazine	17 (4)	3 (1)	0	11	6	1	2
Perphenazine	14 (7)	3 (1)	2	9	2	3	1
Total	97 (36)	26 (13)					
		Range of values	1.3-2.7 mg. per 101 ml.	40-177 units	8.2-14 units	3-4 plus	9-17%

*Numbers in parentheses indicate patients with abnormal control values.



Figs. 1 to 5. Course of absolute neutrophil counts in patients who developed leukopenia during treatment with five phenothiazine derivatives and phenobarbital. (After initial count, only counts in leukopenic range are shown, preceding or succeeding counts being above the leukopenic level.)

abnormal counts paralleled the number of patients showing such abnormalities. The degree of eosinophilia was comparable among various treatment groups, generally being mild. In 77 per cent of patients, counts were below 10 per cent. Although eosinophil counts as high as 20 per cent were observed, these were comparatively rare, only 17 counts of 13 per cent or more being observed. The frequency of abnormal eosinophil counts was rather evenly distributed through the 12 weeks of treatment and the control week.

The next most common hematologic abnormality was leukocytosis. The total number of elevated counts paralleled the distribution of patients with leukocytosis. Elevated counts were evenly distributed throughout the 12 weeks of treatment and the control week. The degree of leukocytosis observed was surprisingly high; over one-half the counts exceeded 15,000 per cubic milliliter, the median range being 15,000 to 16,500.

Leukopenia was comparatively infrequent in this group. Of 36 patients with leukopenia 5 were dropped from treatment. This abnormality was observed most frequently in patients treated with phenobarbital and least frequently in patients treated with prochlorperazine and trifluprom azine. The course of leukopenic counts in such patients is shown in Figs. 1 through 5. Although the absolute neutrophil count decreased to less than 1,500 per cubic milliliter with each of the 6 drugs, in those cases in which treatment was continued without interruption, counts subsequently returned to higher levels.

Abnormal hepatic tests. Abnormal hepatic tests occurred in 97 patients without statistically significant differences between the treatment groups (Table IV). In 36 of these 97 patients abnormal tests were present during the control period. Only 26 patients had more than a single abnormal test during the 5 week period of measure-

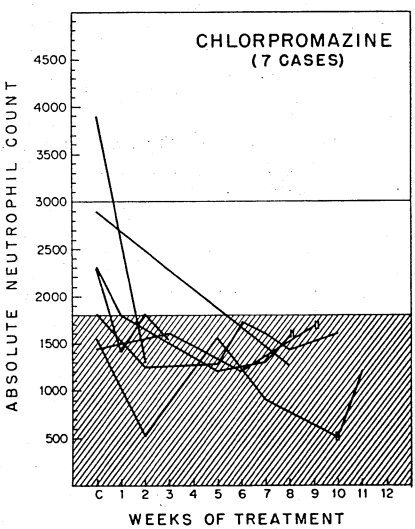


Fig. 2.

ment. Most abnormalities were found in the SGO-T titer, alkaline phosphatase determinations, and serum bilirubin levels. However, these tests were performed most frequently. As can be seen from the table, the range of abnormal values was not great, few tests being at the upper limits.

Interpretation of such abnormal tests, occurring sporadically and infrequently, was extremely difficult. In no instance was there a distinguishing pattern of persistent abnormal tests as occurs ordinarily in hepatic dysfunction following administration of phenothiazine derivatives. Prodromal symptoms or the appearance of clinical jaundice was not reported in any patient. Four patients were dropped from treatment because of abnormal hepatic tests without other abnormal clinical signs or laboratory findings. One patient treated with perphenazine had several abnormal control tests with persisting abnormalities through the early part of his treatment period. These tests were only mildly erratic but indicated pre-existing parenchymatous liver damage which was not aggravated by drug therapy.

Changes in temperature, pulse, and blood pressure. Temperatures which changed significantly were lower. Only oral temperatures of less than 97° F. were considered abnormally low (Table V). The distribution of this type of abnormal body temperature varied between the treatment groups. A few patients in each treatment group showed persistently low body temperatures ranging between 95° and 97° F. The frequency and persistence of these low temperatures throughout treatment (and often through the control period) suggested that these individuals had low body temperatures normally. In other instances the lowering of body temperatures was sporadic. No single sharp elevations of temperature occurred such as have occasionally been reported with phenothiazine derivatives, nor was any sustained elevation of temperature reported.

Table V. *Changes in temperature, pulse rate, and blood pressure during 12 week treatment period*

Drug	*Temperature less than 97° F.*	*Pulse rate over 110 per minute*	*Blood pressure decline: 30 mm. systolic and/or 20 mm. diastolic*
Phenobarbital	8	0	3
Chlorpromazine	7	1	5
Trifluprom azine	8	1	2
Mepazine	12	2	2
Prochlorperazine	8	1	8
Perphenazine	7	1	5

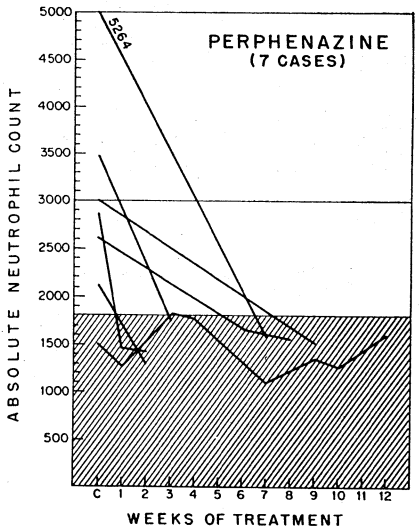


Fig. 3.

Changes in pulse rate were surprisingly rare. Patients who had tachycardia did not have it persistently, only occasionally. On the other hand, in a number of cases pulse rates declined under drug treatment, perhaps because of some abatement of anxiety.

Changes in blood pressure were uncommon. In practically all cases the blood pressure never fell below the usual physiologic limits. The usual pattern was a fall from an initially elevated or borderline level of blood pressure to a physiologic level either in the middle range or at the low side. The

varying conditions under which these measurements were obtained detract from their significance.

Discussion

Well-controlled studies for determining abnormal symptoms, signs, and laboratory tests associated with drug therapy take spontaneous occurrence into account and tend to eliminate the biasing factor of clinical expectation. The disadvantages of our technique are that the ranges of drug dosage are arbitrary during the critical early part of therapy and that the technique of observation of patients varies greatly. The dosage schedule in this study was therapeutically efficacious, simulating usual clinical conditions. Differences between observers should have been equally distributed among the 6 treatment groups, not constituting a major biasing factor.

Consideration of the occurrence of abnormal signs and symptoms in the 6 treatment groups led to three possible conclusions: (1) Their occurrence with phenothiazine derivatives has been greatly overestimated. (2) Phenobarbital produces more side effects than is ordinarily believed. (3) Many phenomena represent spontaneous fluctuations in schizophrenic patients or manifestations of the illness itself. Of these, the last has probably not been stressed enough. Examples of the first possibility were the relatively infrequent occurrence of extrapyramidal syndromes (less than 10 per cent), seizures, and skin eruptions in patients treated with phenothiazine derivatives. Examples of the second and third possibilities were the occurrence of depression, anxiety, agitation, akathisia, and autonomic nervous system side effects during therapy with phenobarbital. The abnormal behavioral symptoms were probably manifestations of schizophrenia rather than drug effects.

Leukocytosis, leukopenia, and eosinophilia are known to be consequences of treatment with phenothiazine derivatives.[3,8,12] However, each hematologic abnormality was present in control counts and just as frequent during treatment with phenobarbital as with the other drugs. The development of leukopenia during drug therapy is especially important. Twenty-five of the 36 patients in this study with leukopenia (absolute neutrophil counts

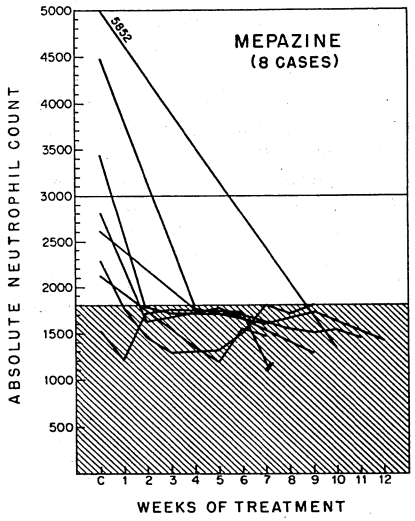


Fig. 4.

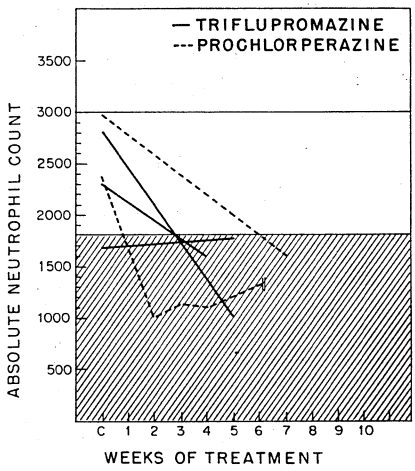


Fig. 5.

below 1,800 per cubic milliliter) had absolute neutrophil counts of less than 3,000 per cubic milliliter during the week preceding treatment. This suggests that patients beginning with low neutrophil counts are more prone to further depression during treatment. On the other hand, leukopenia from phenothiazine derivatives was not significantly more frequent than that from phenobarbital. Still more remarkable was the return to normal levels of considerably depressed absolute neutrophil counts despite uninterrupted treatment. Continuation of treatment did not produce agranulocytosis, but was succeeded eventually by normal counts. Obviously, the decision to continue or abandon treatment in the face of leukopenia must be made on more factors than a declining leukocyte count. In view of the occurrence of leukopenia with phenobarbital, it may be assumed that some patients may have spontaneously occurring cyclic leukopenia unrelated to drugs.

Abnormal hepatic tests were common in all treatment groups. More than one-third of patients with abnormal tests had them during the control period. More significant was the fact that no patient developed a clinical or laboratory picture compatible with jaundice as usually encountered with phenothiazine derivatives. The relatively few equivocal abnormal hepatic tests were probably not related to drug treatment, as these were sporadic, isolated, or not corroborated by other tests. Clinically important hepatic dysfunction from phenothiazine derivatives is usually associated with recognizable jaundice preceded by fever and prodromal symptoms, and easily corroborated by appropriate laboratory or histologic tests.[6,9] What is important is that abnormal hepatic tests occurring during drug therapy should not always be attributed to subclinical manifestations of drug-induced hepatic dysfunction, as has been done.[4,10]

The interpretation of the changes in temperature, pulse rate, and blood pressure was quite difficult. The infrequency of such changes, despite careful efforts to detect them, was surprising. Some patients had lower than usual body temperatures which varied from occasional to sustained low readings. These low body temperatures may have represented a normal variant for some schizophrenic patients rather than drug-induced hypothermia. Changes in pulse rate were few. None of the recorded blood pressures were below normal physiologic limits, the most frequent change occurring when the initial readings were somewhat higher than usual.

The untoward effects recorded in this controlled study were relatively uncommon and appeared in many instances to be manifestations of spontaneous variations in schizophrenic patients or not due to specific actions of the phenothiazine derivatives. Despite rather careful scrutiny for detecting these abnormalities, their occurrence in the various drug treatment groups was neither frequent nor troublesome. Only 21 of 599 patients were dropped from treatment because of side effects or abnormal laboratory tests, none of which were serious in degree.

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A Clinical Trial of Five Phenothiazines Using Sequential Analysis*

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Although there are now many examples of the use of sequential analysis in medical research,[4, 8, 13] as well as several excellent discussions of the method,[1–3, 5, 7] it has not often been applied to psychiatric problems. It seems particularly appropriate for clinical trials of new therapeutic agents. This paper describes an application of sequential analysis[14] to data gathered in a large-scale controlled study of newly admitted schizophrenic males treated with selected phenothiazine derivatives. Following a statement of the experimental design, the results of an analysis of multiple covariance will be presented to serve as a basis for evaluating the results of the sequential tests. The relevance of both analyses to this study will also be discussed.

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* Part of project III of the Veterans Administration Cooperative Studies of Chemotherapy in Psychiatry. Portions of this paper were presented at the Third Annual Research Conference in Psychiatry, Veterans Administration Hospital, Downey, Ill., June 10, 1958, the Fourth Annual Research Conference in Psychiatry, Veterans Administration Hospital, Memphis, Tenn., May 20, 1959, and the Gordon Research Conference on Medicinal Chemistry, New London, N. H., August 7, 1959.

METHOD*

Six medications were randomly assigned to 640 schizophrenic males as they were successively admitted over a six month period to 35 cooperating hospitals. The drugs used were chlorpromazine,† mepazine,‡ perphenazine,§ prochlorperazine,† and trifluprom azine.|| Phenobarbital was used as an active control substance. Treatment was carried out under double-blind conditions, and dosage followed a fixed-flexible schedule. Dosage was progressively increased at a specified rate during the first four weeks until it reached the following levels: prochlorperazine, 75 mg.; mepazine and trifluprom azine, 150 mg.; phenobarbital, 96 mg.; chlorpromazine, 600 mg.; and perphenazine, 48 mg. A flexible dosage schedule was used during the remaining 12 weeks of the study, during which period the physician adjusted the dosage, within limits, to meet the optimal chemotherapeutic needs of his individual patients. The daily dosage in mg. during the flexible period was as follows: prochlorperazine, 25 to 150; mepazine and trifluprom azine, 50 to 300; phenobarbital, 32 to 192; chlorpromazine, 200 to 1200; and perphenazine, 16 to 96.

At the beginning of the study, the average patient was 34 years old and had first been treated for mental illness about 7 years prior to current hospitalization. Eighteen per cent had never been hospitalized previously, and one third had been hospitalized more than three times. Fifty-six per cent had received some variety of ataractic drug previously.

Clinical changes in patients were measured by two rating scales: the Multidimensional Scale for Rating Psychiatric Patients[9] (M.S.R.P.P.), and the Clinical Estimate of Psychiatric Status Scale (C.E.P.S.S.). The M.S.R.P.P. yields scores for 11 factors or symptom clusters as well as an over-all score called Total Morbidity. The C.E.P.S.S. required judgments from psychiatrists on 12 items referring to psychopathology and prognosis. Patients were evaluated by both rating devices before treatment and after 4 and 12 weeks of treatment. Detailed laboratory studies were also conducted.

The statistical model used to evaluate the relative therapeutic effectiveness of the drugs studied was analysis of multiple covariance (simple randomized design). Each of the 24 criterion measures (12 from the M.S.R.P.P. and the 12 C.E.P.S.S. items) was analyzed for relative changes in clinical status during the first month, the second two months, and over the entire three month study period. Final criterion mean scores in each analysis were

* A more complete description of project III has been prepared for separate publication. The study protocol, reproduced in its entirety in the *Transactions of the Third Annual Research Conference on Chemotherapy in Psychiatry*, edited by Clyde J. Lindley and published by the Veterans Administration Department of Medicine and Surgery, April, 1959, contains considerable detail concerning selection of patients, the randomization procedures, precautions, restrictions, laboratory controls, and forms. A statistical appendix in the *Transactions of the Fourth Annual Conference on Chemotherapy in Psychiatry*, edited by Clyde J. Lindley and published by the Veterans Administration Department of Medicine and Surgery, May, 1960, presents the results, as well as other data, in great detail.

† The trade name of Smith, Kline & French Laboratories for chlorpromazine is Thorazine, and for prochlorperazine is Compazine.

‡ The trade name of Warner-Chilcott Laboratories for mepazine is Pacatal.

§ The trade name of Schering Corporation for perphenazine is Trilafon.

|| The trade name of E. R. Squibb & Sons for trifluprom azine is Vesprin.

adjusted for initial status on the criterion being analyzed, as well as for the net effect of 11 control variables such as age, number of previous hospitalizations, and initial weight.

Briefly, the results were as follows. Total morbidity scores were significantly ($p < 0.05$) reduced, after 4 and 12 weeks of treatment, by prochlorperazine, chlorpromazine, perphenazine, and trifluprom azine as compared with either mepazine or phenobarbital. There were no significant differences among patients treated with the first four drugs named during any of the evaluation periods. The difference between patients treated with mepazine and phenobarbital was not significant after four weeks but was significant after 12 weeks. The results on the remaining criteria essentially followed this same pattern.

The Sequential Analysis. Data were collected by the cooperating hospitals and forwarded to the central laboratory over a period of about nine months. Each set of data consisted of the requested information on 6 patients, to each of whom a different treatment had been assigned at random. The decision to be arrived at with each pair of treatments represented in the set was whether one drug was superior to the other or whether there was no important difference between them.

Reduction in total morbidity score was selected as the best single criterion of the clinical effectiveness of the drugs. In a particular pair of patients receiving different treatments, if the patient on drug A showed greater reduction in morbidity over the time period being considered than did the patient receiving the second drug, that pair of patients was scored a plus and plotted 1 unit vertically on a previously prepared graph containing a sequential channel. If drug B was superior, the pair was scored a minus and plotted 1 unit horizontally. The occasional ties were omitted. These plus and minus outcomes were plotted in serial order as data were received and evaluated, sampling being continued until the serial record of plus and minus pairs crossed one of the decision lines or until the number of available patient pairs was exhausted.

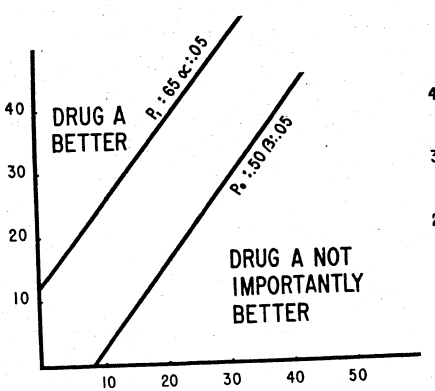

FIG. 1. Sequential channel: one-sided alternative.

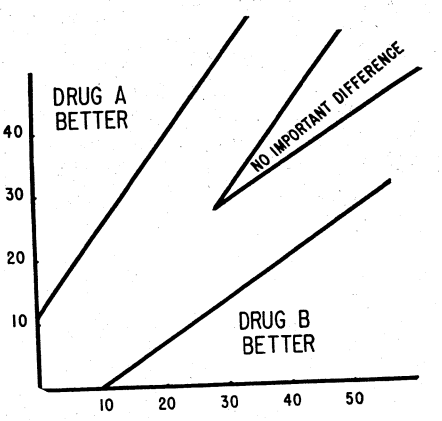

FIG. 2. Sequential channel: two-sided alternative.

If the two drugs were equally effective, it would be expected that half the pairs would be scored plus and the other half minus; that expectancy is represented by the lower decision line labeled P_0 in figure 1. For this case, the serial record of plus and minus pairs would ascend at about a 45° angle, crossing P_0 after perhaps 30 or 40 pairs had been evaluated. How soon the decision line would be crossed would depend upon the vagaries of sampling.

An alternative hypothesis must also be specified. If drug A were superior, the members of the pairs receiving that drug should, on the average, show greater improvement and the proportion of pairs scored plus should be greater than 50 per cent. A percentage that is felt to be clinically meaningful has to be designated for the upper decision line. The alternative hypothesis, labeled P_1 in figure 1, that 65 per cent or more of the pairs should favor drug A, was formulated after consulting several psychiatrists who were especially knowledgeable concerning patients' response to drugs. Calculation of the average sample number necessary to reach a decision also showed that, with this value, a decision could be expected to be reached before the number of observational units available were exhausted. A coefficient of risk of 0.05 was attached to both of these alternative hypotheses and is indicated as alpha and beta in figure 1. With these four values, the slope and intercept of these lines can be quickly calculated.[11]

It has been indicated what should happen if the two treatments were equally effective. If drug A were superior in 100 per cent of the pairs, the serial record of plus and minus pairs would go straight up to cross P_1 after 11 pairs had been evaluated. If the superiority of drug A were not quite that great, it might require additional pairs, again depending upon the sampling. If drug B were superior in 100 per cent of the pairs, the serial line would be plotted horizontally and cross P_0 after eight pairs of patients had been evaluated. In this event, it would be concluded that drug A was not importantly better than drug B. Again, if the percentage in favor of B were less than 100 per cent, more pairs might be required to reach this decision.

Using this sequential channel does not adequately provide for the contingency that drug B is better than drug A. Only the two decisions shown are permitted. If, however, another channel is superimposed on the first, as is shown in figure 2, the test is extended to include this additional possibility. The two lines defining the zone of no important difference should extend downward and to the left, although this is not shown in figure 2. If the sampling line of plus and minus pairs crosses both of these extended lines, the decision is that of no important difference. A number of instances in which such a decision was reached in this manner will be found in subsequent figures. The same graph shown in figure 2 served all of the drug comparisons.

RESULTS

Figures 3 through 6 present the results after one month of treatment on a fixed dosage schedule. Figure 3 contains five channels, one for each phenothiazine compared to phenobarbital. The following decisions were reached: prochlorperazine, chlorpromazine, perphenazine, and trifluprom azine were better than phenobarbital in reducing morbidity; mepazine was not importantly different from phenobarbital. Figure 4 compares mepazine

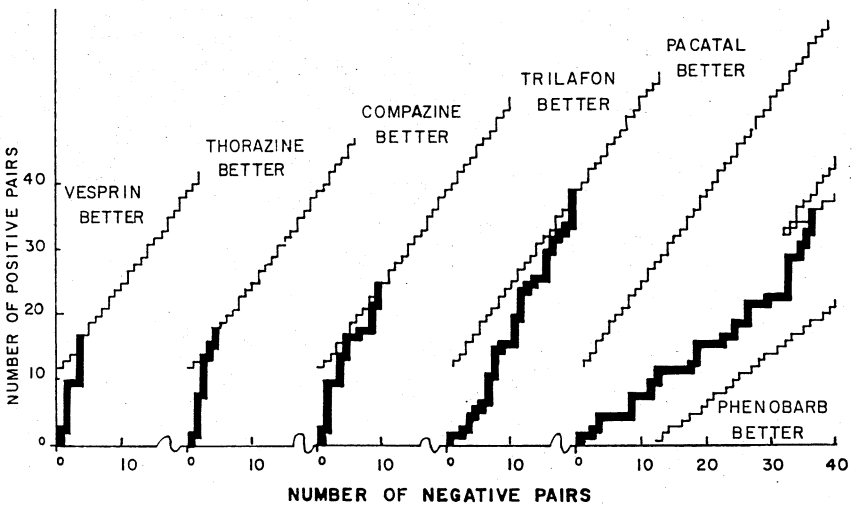

FIG. 3. Five phenothiazines compared with phenobarbital after one month of treatment.

with the four other phenothiazines. They were all better than mepazine. Figure 5 compares chlorpromazine with prochlorperazine, perphenazine, and trifluprom azine. No decision was reached in the trifluprom azine-chlorpromazine comparison before the cases available for evaluations were exhausted. Although trifluprom azine did have a tendency towards superiority at this point (59 per cent), it was not significantly better ($\chi^2 = 2.84$, $p > 0.05$).

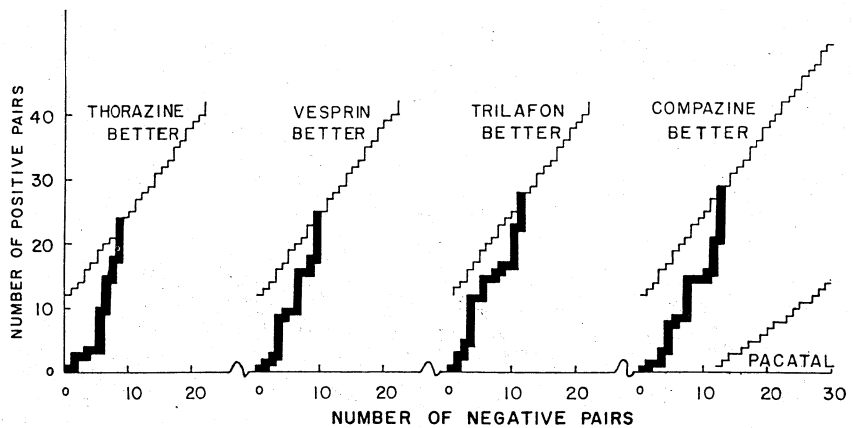

FIG. 4. Mepazine (Pacatal) compared with four other phenothiazines after one month of treatment.

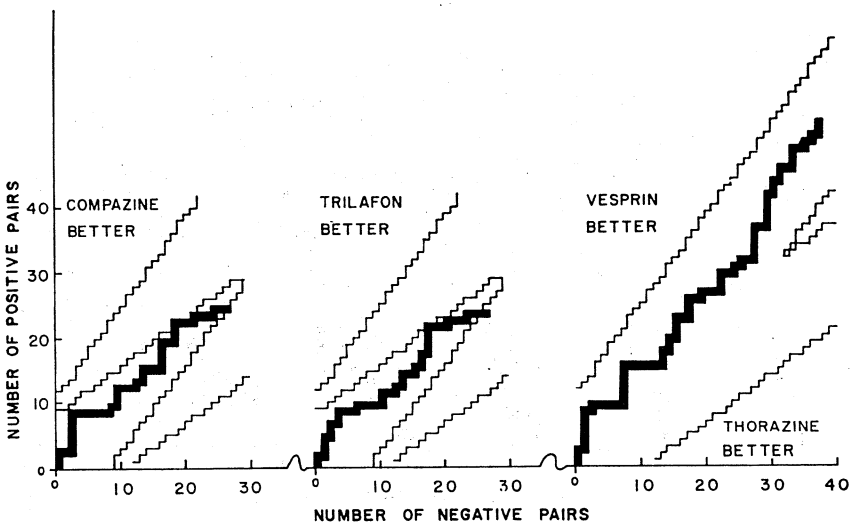

FIG. 5. Chlorpromazine (Thorazine) compared with prochlorperazine (Compazine), perphenazine (Trilafon), and trifluprómazine (Vesprin) after one month of treatment.

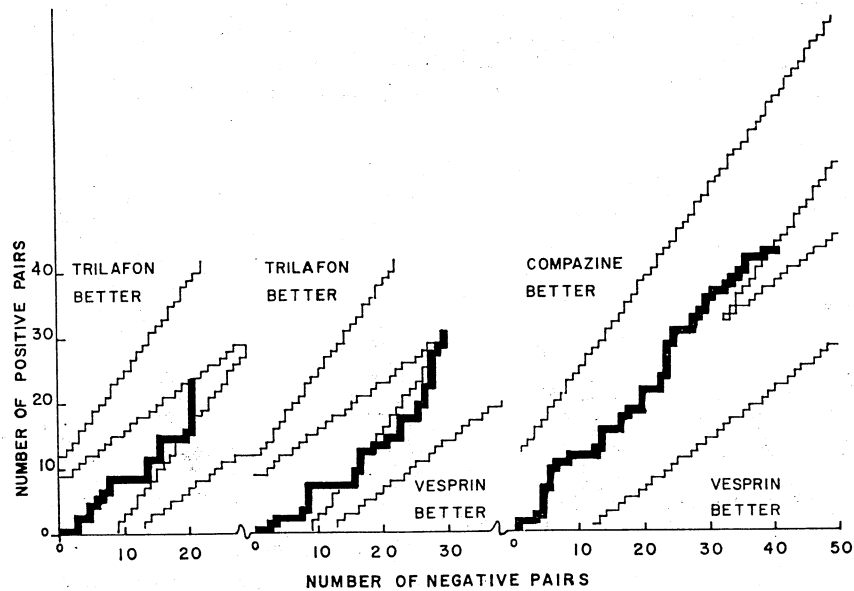

FIG. 6. Comparison of perphenazine (Trilafon), trifluprómazine (Vesprin), and prochlorperazine (Compazine) after one month of treatment.

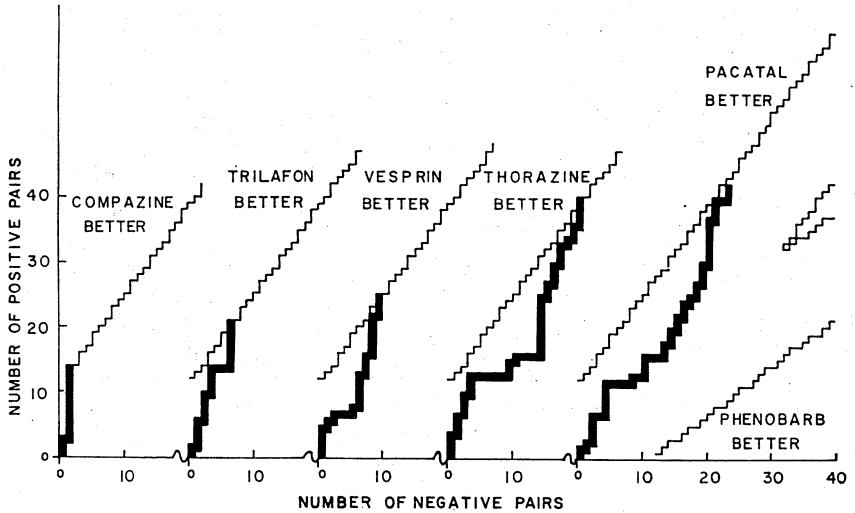

FIG. 7. Five phenothiazines compared with phenobarbital after three months of treatment.

The decisions reached in the other two comparisons were that neither prochlorperazine nor perphenazine is importantly different from chlorpromazine. Figure 6 shows the remaining three phenothiazines compared with each other, and in each comparison the decision was the same—no important difference. This completes the comparisons after one month of

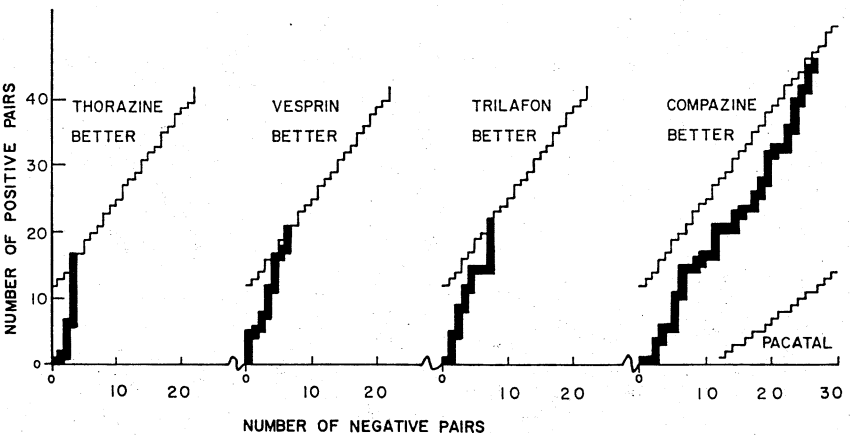

FIG. 8. Mepazine (Pacatal) compared with four other phenothiazines after three months of treatment.

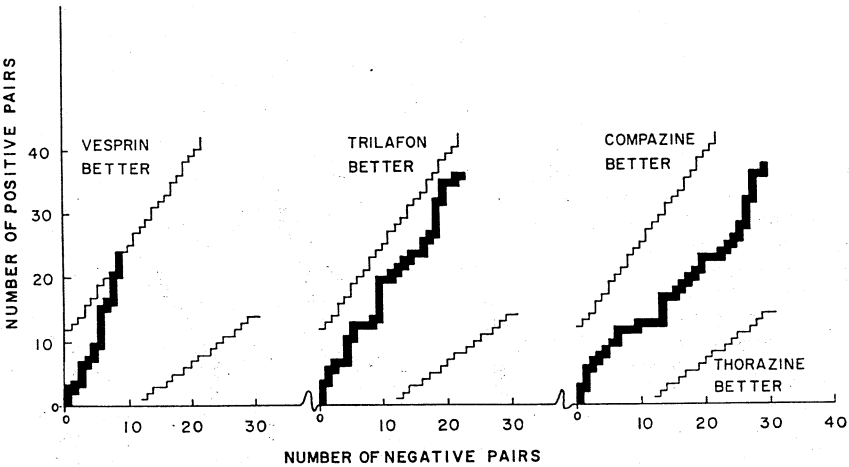

FIG. 9. Chlorpromazine (Thorazine) compared with triflupromazine (Vesprin), perphenazine (Trilafon), and prochlorperazine (Compazine) after three months of treatment.

treatment. The decisions are completely consistent with those yielded by the analysis of multiple covariance.

The remaining figures deal with the three month data. The first four channels in figure 7 yielded the same decisions as the one month data. However, mepazine, which was not importantly different from phenobarbital after one month of treatment was almost superior

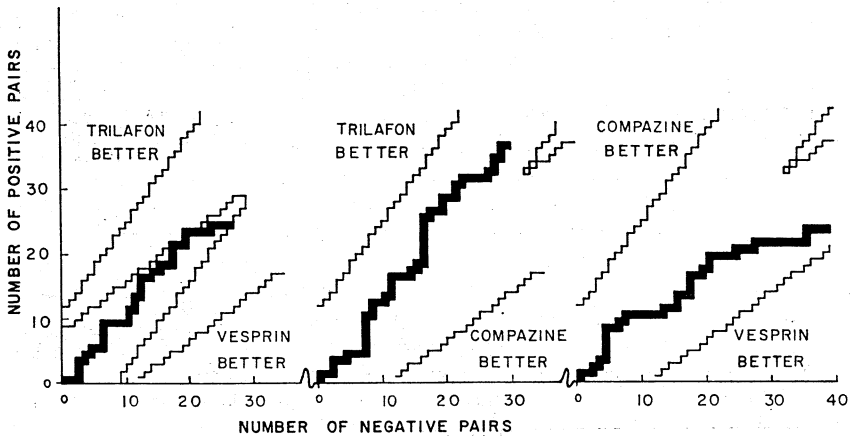

FIG. 10. Comparison of perphenazine (Trilafon), triflupromazine (Vesprin), and prochlorperazine (Compazine) after three months of treatment.

TABLE I

Total Number of Random Pairs Available for the Sequential Analysis and the Final Percentage Scored Positive

Comparison	After 1 month		After 3 months	
	Number of pairs	% positive pairs	Number of pairs	% positive pairs
Chlorpromazine vs. phenobarbital	94	63	60	67
Prochlorperazine vs. phenobarbital	96	70	67	73
Triflupromazine vs. phenobarbital	92	64	56	80
Perphenazine vs. phenobarbital	98	71	63	86
Mepazine vs. phenobarbital	98	53	64	64
Chlorpromazine vs. mepazine	96	65	69	67
Prochlorperazine vs. mepazine	99	65	71	63
Triflupromazine vs. mepazine	90	64	58	81
Perphenazine vs. mepazine	98	72	63	75
Prochlorperazine vs. chlorpromazine	96	51	65	55
Triflupromazine vs. chlorpromazine	90	59	55	71
Perphenazine vs. chlorpromazine	95	55	57	61
Prochlorperazine vs. triflupromazine	90	48	61	38
Perphenazine vs. triflupromazine	90	50	51	47
Perphenazine vs. prochlorperazine	97	57	65	55

to phenobarbital after three months. The number of available pairs was exhausted at a critical moment in this comparison. The final proportion of pairs in favor of mepazine was 0.64; significantly better than chance ($\chi^2 = 5.06$, $p < 0.05$). Thus, this result might be interpreted as being consistent with the covariance analysis, which did show mepazine to be superior to phenobarbital after three months. Figure 8 is similar; prochlorperazine at 63 per cent was another near miss but significant ($\chi^2 = 5.55$, $p < 0.05$). Figure 9 contains the one clear inconsistency with the analysis of covariance. Triflupromazine is shown to be better than chlorpromazine. The final proportion of pairs in favor of triflupromazine was 0.71. The covariance analysis did not distinguish between these two drugs, but inspection of the adjusted means shows that the triflupromazine group had the lowest mean morbidity score after treatment followed by perphenazine, chlorpromazine, prochlorperazine, mepazine, and phenobarbital, in that order. In the other two channels in this figure, perphenazine approached a decision line but no decision was reached in either comparison. The last figure is self-explanatory. Again the serial plot almost reached a decision in favor of triflupromazine over prochlorperazine, but did not disagree with the covariance analysis.

Table I presents the total number of random pairs available for the sequential analysis and the final percentage of them scored positive.

DISCUSSION

Although analysis of variance and this sequential model are quite dissimilar, in that the former tests the significance of the difference between adjusted means whereas the latter

tests the deviation from chance expectancy in the proportion of random pairs, both analyses led to essentially similar decisions and both analyses were relevant although they served different purposes.

The sequential analysis provided a simple cumulative summary of the progress of the study, which was very useful for purposes of information. In marked contrast in terms of time to this always current graphic record, the analysis of covariance provided findings only after six months of sample build-up, three months of treatment, and three months of data preparation and analysis. Most of the decisions yielded by the sequential analysis were reached while some hospitals were still accumulating their complete quota of patients for pretesting. If sampling could have been terminated as decisions were reached, considerable economy of effort would have resulted. In this study, however, other objectives, such as a determination of the incidence of side effects and an evaluation of laboratory data in large quantity, made it desirable to complete data collection on the entire sample.

On the other hand, analysis of covariance possesses certain advantages, the most important of which is that it is a more powerful statistical method than this nonparametric sequential model. Initial differences between groups in respect to 12 control variables were adjusted by covariance. This adjustment provided statistical equality of the treatment groups prior to treatment and reduced the error term used in evaluating mean differences. The problems introduced by making multiple comparisons was handled by use of a multiple range test.[6] Sequential analysis lacks both of these highly desirable advantages.

Sequential analysis is usually recommended because it is economical in terms of the number of observational units, since only that number of units necessary to reach a decision is evaluated. It has already been pointed out that in this study other objectives made it undesirable to suspend sampling and take advantage of whatever economy the method has to offer. Another feature of this application of sequential analysis that reduced the efficiency of the method was the use of pairs of patients as the observational unit. Although some decisions were reached after evaluating a small number of patient pairs, this was not generally true, and in several comparisons the cases available for evaluation were exhausted before a decision could be reached.

There are some alternative sequential models that may lead to more economical decisions but that were not adopted for use in this study because of other special requirements. One of these is the sequential *t* test. For example, previously collected data had shown that the median change in morbidity score over a six week period for phenobarbital and a lactose placebo group was zero, and that the change scores approximated a normal distribution. Using the sequential *t* tables developed by the Bureau of Standards,[12] it was possible to test whether zero would fall within or outside a one standard deviation limit for each of the drug groups at a specified level of confidence. Mepazine and phenobarbital were found to be noneffective agents by this criterion; the remaining four phenothiazines were found to be effective. The number of patients necessary to reach these decisions ranged from 7 to 12. In using this model, four values had to be designated at the outset: the two coefficients of risk (alpha and beta), the expected mean change of zero, and the amount of change which would be of interest (one standard deviation). The normative data that provided the ex-

pected change of zero was derived from a chronic schizophrenic sample and was not felt to be representative of the newly admitted patients.

Armitage[1] has discussed two models applicable to patient pairs. In the case where there is an "all or none" therapeutic outcome, e.g., death or infection, each pair of patients is classified as $++$, $+-$, $-+$, or $--$. The $++$ and $--$ pairs are disregarded, and the remaining pairs plotted in the order of their evaluation. To calculate his decision lines, it is necessary to specify two alternative hypotheses and their associated coefficients of risk. Armitage bases his alternative hypotheses on the known success rate of the control treatment and his judgment of what would constitute a meaningful increment of successes for a new treatment. One not-so-apparent disadvantage of this method is that the number of discarded pairs can be quite large, e.g., in his sample problem, a decision was reached after 14 pairs had been evaluated but 31 additional pairs were tied and therefore disregarded.

In the case where there is a quantitative measure of the success of treatment available for each member of the pair, Armitage recommends the sequential t test. The expected mean difference under the null hypothesis would be zero, and the alternative hypothesis can be set by the experimenter so as to represent a clinically important difference. This latter value can be determined from normative data obtained in previous investigations if they are available.

A variation of these two methods has been presented by Sainsbury and Lucas,[10] who used each patient as his own control in an evaluation of prochlorperazine in outpatients suffering from acute anxiety. The patients in their trial received either prochlorperazine for one week followed by placebo for a week, or the reverse order, determined at random. The outcomes were plotted as suggested by Armitage.

Finally, it is worth noting that, in all of these models, the experimenter must decide what constitutes a clinically important difference and what degree of risk he is willing to tolerate in reaching his decisions. Although the latter should not be determined without careful thought, convention leads us to set these at 0.05 or 0.01. Defining the difference that is considered to be important enough to detect is more difficult. It is possible in some instances to base this definition upon previously collected data or, as Armitage suggests, to select a value that, if present, has a reasonable chance of being detected with the cases available for evaluation. As he points out,[1] "Eventually a compromise will be reached between the requirements of sensitivity in detecting small differences (which tend to increase the length of the trial) and those of economy (which tend to decrease the length)."

SUMMARY

An application of sequential analysis in a clinical trial of phenothiazine derivatives is described. The results were found to be reasonably consistent with those obtained from a more conventional statistical approach. Advantages and disadvantages of the method as well as alternative models are discussed.

RESUMEN

Se describe en este trabajo una aplicación del análisis secuencial en una prueba clínica

con derivados de la fenotiazina. Los resultados se hallaron razonablemente paralelos con los obtenidos mediante un estudio estadístico más convencional. Se explican también las ventajas y desventajas del método así como los de otros estudios.

RESUME

L'auteur décrit l'application du procédé dit d'analyse par la méthode des probits séquentielle ou progressive dans un essai clinique de dérivés de la phénothiazine. Les résultats correspondaient d'assez près avec ceux obtenus par une méthode statistique plus courante. L'auteur examine les avantages et les inconvénients de cette méthode ainsi que ceux d'autres systèmes.

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(Thereupon, at 12:10 p.m., the hearing in the above-entitled matter was concluded.)

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

MONDAY, AUGUST 17, 1970

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

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

Present: Senator Nelson.

Also present: Benjamin Gordon, staff economist; Elaine C. Dye, clerical assistant; and Keith A. Jones, minority counsel.

Senator NELSON. The hearing of the Monopoly Subcommittee will come to order.

The committee is pleased to welcome you here this morning, Admiral Etter, and your associates. For purposes of the record, it might be helpful if you would introduce those who are with you from left to right or right to left, and then I would suggest that any time anyone wishes to make a comment, please identify yourself so that the reporter will have the correct identification in the record.

Admiral, we are pleased to have you here this morning.

STATEMENT OF REAR ADM. HARRY S. ETTER, MC, USN, CHAIRMAN, DEFENSE MEDICAL MATERIEL BOARD, AND ASSISTANT CHIEF FOR PLANNING AND LOGISTICS, BUREAU OF MEDICINE AND SURGERY; ACCOMPANIED BY COL. M. E. McCABE, MC, USA, OFFICE OF THE SURGEON GENERAL, DEPARTMENT OF THE ARMY; CAPT. L. M. FOX, MC, USN, CHIEF OF MEDICINE, NAVAL HOSPITAL, NATIONAL NAVAL MEDICAL CENTER; COL. E. J. CLARK, MC, USAF, OFFICE OF THE SURGEON GENERAL, DEPARTMENT OF THE AIR FORCE; COL. J. P. FAIRCHILD, MC, USA, DEPUTY COMMANDER, WALTER REED GENERAL HOSPITAL, AND CHAIRMAN, THERAPEUTIC AGENTS BOARD; CAPT. S. C. PFLAG, MSC, USN, CHIEF, FIELD BRANCH, BUREAU OF MEDICINE AND SURGERY, NAVY DEPARTMENT; AND COL. A. J. SNYDER, MSC, USA, CHIEF, MEDICAL PROCUREMENT DIVISION, DIRECTORATE OF PROCUREMENT AND PRODUCTION, DEFENSE PERSONNEL SUPPORT CENTER

Admiral ETTER. Well, Senator, it is a pleasure to be here. I am Rear Adm. Harry S. Etter, MC, U.S. Navy, Chairman of the De-

fense Medical Materiel Board and Assistant Chief of the Bureau of Medicine and Surgery for Planning and Logistics. It is a pleasure to appear before this subcommittee to describe and discuss the manner in which the Department of Defense procures pharmaceutical products. My formal statement has been previously submitted to the subcommittee for your review and study. With your permission I will, therefore, summarize it only and request that the full statement be inserted in the record.

Senator NELSON. The statement will be printed in full in the record.[1] You may present it however you desire and if you wish to elaborate on it in any way or extemporize, just feel free to do so.

Admiral ETTER. At the end of World War II the Army and Navy medical departments established the first consolidated standardized procurement office to serve the needs of both services. From that example has evolved our present DOD medical supply system. As it exists today our system includes a specific sequence of events.

Senator NELSON. May I interrupt a moment? I think it might be better if you would read it, and when we come to those parts that we have covered as a consequence of questions, you could skip them. That way it will be easier to follow your statement. In other words, would you just read your statement.

Admiral ETTER. The full statement, sir?

Senator NELSON. Yes. We will come to some questions which I have keyed to various parts of your statement, and in exploring these questions, we will cover other parts of your statement. Those parts that we cover you can just skip as you go along.

Admiral ETTER. It is a statement, as you know, quite lengthy.

Senator NELSON. I think some of our questions will cover fair parts of your statement, so you will be able to skip large parts of it later.

I have some questions, for example, on "Type Classification" starting under the title "Initial Action." Perhaps if you could present part of that, we can then raise some questions.

Admiral ETTER. Initial action. Type classification is a term applied to the adoption of a drug as a standard item, and its subsequent inclusion in the Department of Defense Medical Materiel Section of the Federal Supply Catalog. Type classification is a responsibility of the Defense Medical Materiel Board, but the action must be sponsored by one or more of the services.

Some drugs are type classified as standard because the worldwide commitments of the Armed Forces make it imperative that these items be readily available at all times, regardless of usage or consumption rates. Our usual motivation, however, is the dollar savings which accrue through our centralized purchasing and distribution system. Consequently, although type classification action may be initiated as a result of the recommendation of an individual, a presentation by industry, or a proposal by DMMB, most actions follow a determination that the volume of local purchases by field activities indicates that economies will result.

For several years, for example, we have been stock listing calcium carbonate and aminoacetic acid tablets (FSN 6505–890–1658). Type

[1] See information beginning at p. 7578.

classification was requested by the Air Force in 1963. The item is a commercially available antacid which was marketed under the trade name of "Titralac tablets" by Riker Laboratories, Inc., Northridge, Calif. It is used primarily in the treatment of peptic ulcers (gastric and duodenal) and gastric hyperacidity.

In 1963 the Air Force used a statistical sampling technique to evaluate usage of nonstandard drugs. Upon noting that over $2,500 was being spent on this antacid that year by a selected group of 21 hospitals, the Air Force marked the drug for review. Air Force professional and logistic personnel concurred that there would be a continued requirement for a drug of this type, and that demand and use rates could be expected to increase, or at least remain constant. As a result of these preliminary actions, the Air Force submitted to DMMB a recommendation "to stock list an antacid comparable to Titralac tablets."

DMMB advised the Army and Navy of the Air Force action, and requested service positions.

Working from the Air Force recommendation, Army and Navy personnel reviewed their own reports, consulted their specialists, concurred with the Air Force and the item was standardized. These reviews include consideration of such data as local purchase statistics, professional needs and uses, patient acceptance, comparison with items already stock listed, and an evaluation of known sources of supply.

ESSENTIAL CHARACTERISTICS

Since the Air Force request named only the one commercial product, it was necessary for DMMB to request Riker Laboratories for detailed information on Titralac. Riker advised that the product was patented, but agreed to provide that information—physical and chemical characteristics, test protocols, clinical and stability studies—which specifically identify the item produced by that manufacturer.

The board used these data in the preparation of tentative essential characteristics for calcium carbonate and aminoacetic acid tablets. The essential characteristics (or EC's) are defined as those mandatory qualities required of an item to accomplish a specific professional, therapeutic, technical, or military purpose. For drugs, they include, but are not limited to a description of the item, and its application or use; components of the formula, when appropriate; quantification, as required; unit of issue, type of container, package size, and any special packaging instructions; and labeling requirements, identification data, and necessary instructions for use.

Initial proposals for type classification on an item are recorded on a "coordination worksheet for medical items pending adoption" (DMMB form 1, Exh. 1).[1] DMMB distributed this form 1 concurrently to the services and to DPSC. Comments were solicited from all addresses. The services annotated the form 1 with their initial, and 12 months replenishment requirements.

Within DPSC, the form was reviewed in the technical and supply operations divisions of the medical directorate to hasten availability of the drug through the DOD wholesale distribution depots. Having

[1] See exhibits beginning at p. 7588.

determined that the EC's were adequate for preparation of a competitive specification or purchase description, DPSC returned the form 1 to the Board.

Had it been determined that no further data could be acquired, and that total available information was inadequate for preparation of a competitive specification, the case would have been returned to the services. Upon their recommendations, a determination would have been made to discontinue action, or to process the item indicating a limited source of supply.

Parenthetically, a recommendation for a limited source of supply may originate with a service, DPSC or DMMB. This action may be taken only in those instances where it has been professionally determined that the product of a specified supplier or suppliers is required to provide for the health and welfare of Armed Forces personnel or their dependents. The decision must be concurred in by all three military medical services. Such determinations normally derive from an accumulation of clinical experience, and may relate to experience prior to type classification of the drugs, or to those in the system which have accumulated a significant complaint history. I shall speak again of limited source items when I reach the statistical portion of my presentation.

Mr. GORDON. May I ask a question at this point? Turn back to Titralac, which you mentioned before. You said that Riker advised that the product was patented but it agreed to provide information you wanted.

Now, for one thing, did anybody examine the patent to see if it was a valid patent or if it, at least on the surface, looked like a valid patent? Or did you just take the word from Riker that they had a valid patent?

Admiral ETTER. Mr. Gordon, I cannot answer that from personal knowledge, but I would assume that when they said it was patented it was, but they provided the information which was necessary to write the specification. This satisfied the requirements of the DPSC and the board.

Mr. GORDON. With respect to the physical and chemical characteristics, is it not correct that when somebody files for a patent, that person has to give a sufficient amount of information so anybody in the field could duplicate it once the patent expires? In fact, as I understand it, disclosure is one of the reasons why we give a patent.

I cannot understand why you had to go to them and get this information when it should have been available in the patent application itself.

Admiral ETTER. Mr. Gordon, I cannot answer that question directly.

Mr. GORDON. Do you have anybody here who can?

Admiral ETTER. I would like to ask if Colonel Snyder or Captain Pflag could provide any information on that subject.

Colonel SNYDER. I am Colonel Snyder, Chief of the Medical Procurement Division, DPSC. Generally speaking, when a solicitation is made like this, or an offer is made, I cannot speak for the first inquiry when they are closing EC's, and so on, but when a solicitation is made and a patent reported on the solicitation, it is then referred to DSA Headquarters.

Mr. GORDON. Do I understand that you do not try to determine, at least on a preliminary basis, whether that patent may be or may not be valid—whether it looks valid or not?

Colonel SNYDER. At that point in time the procurement function is not aware of any patent that is reported and whether royalties are involved or payments. They are referred to DSA Headquarters where they are verified with the Patent Office. The patent involves many things, from processes to the compound itself. I think it would be imprudent for me to try to go into this. This is a very specialized field.

Mr. GORDON. You stated that you requested Riker Laboratories for detailed information on Titralac. Riker advised that the product was patented but agreed to provide that information.

Now, I thought that this information was provided when the patent is applied for. This is the justification for granting a patent monopoly. It is an exchange. We give you a patent monopoly for 17 years, you give the people of the United States information. So, anybody in the field could reproduce it once the patent expires.

Colonel SNYDER. Mr. Gordon, if I may, I would like to defer and get that information. I do not have the specifics.

Admiral ETTER. Could we provide it for the record?

(The subsequent information was received and follows:)

Patent data alone is inadequate for preparation of Essential Characteristics by the Defense Medical Materiel Board, or specifications by the Defense Personnel Support Center. Patents contain only those data on constituents and procedures that were available when the patent was filed. During the seventeen years of patent protection, processing or fabricating developments by the patent holder or licensees often significantly improve the product, but do not require modification of the patent. Additionally, patents do not provide data such as clinical studies, stability or packaging. If industry can be persuaded to provide this information, it results in a real dollar saving in development of procurement documentation.

Senator NELSON. May I ask a question? I am not exactly clear what the phrase "type classification" means actually. What does the word "type" mean as used in that phrase?

Admiral ETTER. Well, the type classification in this regard is a description of the drug, its ingredients, and in effect, its intended use. It is a type of drug, and we were standardizing, or asking for standardization of a type or class of antacid.

Senator NELSON. Are you using the word "type" in the generic sense? Does it refer to all drugs of the same compound regardless of how many there might be by various brand names and generic producers?

Admiral ETTER. It can be used in the generic sense but there are other things, as you well know, Senator, that take them out of the particular generic field and put into a local—into another source of drug, and in this instance, I think this applies here.

Captain Pflag, can you add any information? This is Captain Pflag of the Field Branch, Bureau of Medicine and Surgery, formally medical technical director of DPSC.

Captain PFLAG. Type classification in the generic sense, we are referring to standardization of a product.

Senator NELSON. But as I understand it, the branch or some com-

ponents of the branch of the service may request a type classification, is that correct?

Captain PFLAG. It means requesting standardization of the product for central procurement vis-a-vis local procurement.

Senator NELSON. That is what I do not understand. In this case we are talking about Titralac, right? Did one of the services or components of one of the services ask that Titralac become the type classification?

Captain PFLAG. Yes. In other words, the Air Force, in this instant case asked that the item be standardized so that it could be procured centrally.

Admiral ETTER. Senator, in that regard, could I add that they did this as a result of their survey, which indicated a large usage of this particular drug in their hospitals to support local practices. It had not been standardized. Therefore, they foresaw a saving to the Government—to the Air Force—if this could be type classified and standardized so that it could be bought in bulk and, therefore, the price to the user—the Air Force, in this instance—would be brought down. It is strictly an economy measure, sir.

Senator NELSON. So that I understand it correctly, the situation in this case or perhaps in many cases, is that at some various hospitals, a particular drug, in this case Titralac, is being locally procured.

Admiral ETTER. Correct.

Senator NELSON. And as you review the usage of drugs in your various installations, you see that a particular drug is being used a number of times.

Admiral ETTER. Right.

Senator NELSON. Then because of that, the service in which the drug is being used, in this case the Air Force, requests a type classification of that particular item under that particular name. At that stage, what is your procedure?

Admiral ETTER. Our procedure then——

Senator NELSON. Once you get a request from the service for a type classification, for example, in this case Titralac——

Admiral ETTER. Then the board writes the essential characteristics, which I have outlined in my statement, and forwards them to the Defense Personnel Center for technical characteristics. When these are approved, they go out on a purchase requirement to the industry.

On the other side of the coin, I can also say that we get quite a number of requests from our hospitals. Most of these—I am familiar because of my Navy connections—are requests for type classification of drugs because they think they are using a lot and it would result in a saving to them. When we canvass the rest of our hospitals, we find this is not the case. It is not in general use, and, therefore, type classification is not requested in this instance, and we ask that they continue to get it on local purchase.

Senator NELSON. In this case, as I understand it, Titralac is the brand name for an antacid.

Admiral ETTER. It is, sir.

Senator NELSON. Do you require the service to submit any clinical evidence as to the superiority of this antacid, for example, to the antacids that would be listed in the U.S. Pharmacopeia or National Formulary?

Admiral ETTER. I think that here we did not ask for anything other than the fact that it had been found to be a drug which their physicians have preferred to prescribe over other types of antacids, or the physician's own particular desire in that regard. The patient's acceptance, the doctors being satisfied that this produces the desired results, all of these things enter into the use of these drugs at the local level when the drug is not standardized.

Senator NELSON. But if you do not evaluate it at the top level in terms of its comparative value for the purpose it is used, vis-a-vis all other antacids, vis-a-vis what is in the U.S. Pharmacopeia or the National Formulary—in neither of which this is listed—what, if any, justification do you demand of the service or the hospitals to demonstrate their need to have this brand name drug over and against what is listed in the official compendia of the United States?

Admiral ETTER. My only answer, sir, is that it had been found to be the drug of choice by the local practicing physicians and I do not think that we, sitting up in the Bureau level or top of the organization, have any way at all to evaluate the use of a drug in a field that the physician feels is the drug he wants to prescribe.

Senator NELSON. What qualification does the individual physician have to make a judgment that some particular brand name drug is superior and he would prefer using it rather than one listed in the official compendia of the United States?

Admiral ETTER. I think, primarily, this would result from patient acceptance, and the fact that it has been found to be effective in his hands.

Now, how he particularly picked this one over another one is up to the individual physician, and this is something which we certainly cannot control.

Senator NELSON. That is the question I am getting at. Why can you not control it? For example, you say it is up to the individual physician to decide. Well, I think everybody knows that regardless of how good a physician is, most of them are not qualified to make a judgment as to one antacid or one drug versus another because all he can do is give a testimonial. He does not have any clinical evidence or any controlled tests to demonstrate it. This is the reason that the profession, the medical profession, takes the position that there ought to be formularies established and that anybody who wants to use something outside the formulary should have some kind of justification.

What I am getting at is how do you avoid, then, the prescribing of drugs which are ineffective?

Admiral ETTER. Well, any drug which is used in our hospital system (and I think this applies to all three services), that is not on the standard list—the request for purchase of that drug must go to the pharmacy-therapeutic committee for approval.

Senator NELSON. Excuse me. Is this at the hospital?

Admiral ETTER. This is at the hospital level, sir.

Senator NELSON. Well, does each one of the military hospital installations have a therapeutics committee?

Admiral ETTER. They do, sir.

Senator NELSON. And does each hospital have a formulary?

Admiral ETTER. They do, sir.

Senator NELSON. And I will get to that later, but I am just curious to know how some of these drugs get on their formulary when all the medical experts—the best expertise in the country say—they are ineffective or at best not better than other drugs.

We had similar testimony from the Veterans' Administration, that they have to listen to what the individual doctor says. You have a situation, then, in which the military has the authority to follow the soundest conceivable prescribing practices and the power to establish the best formulary, with the guidance of the best medical experts in the United States but the Veterans' Administration position was, "yes, but we have to do what the individual doctor says" and I understand that to be your response also.

Admiral ETTER. That is, sir, and I would like to have one more comment on that, Senator. Then I want to toss this one over to Colonel Fairchild.

I think that this is very pertinent to the issue today. As you well know, the military medical services are all having a desperate time keeping enough qualified physicians in the hard core of the services to practice medicine. As a result, we try to do everything we can to make service life just as attractive, and as professionally rewarding to them as we possibly can, particularly when young doctors first come into the service. One of the first things that can really tee him off is the old man or skipper says you cannot prescribe that drug. And why not? Because I say you cannot.

Now, this is the old man speaking up against the young man just out of medical school, just out of residency, or internship, who wants to try his wings and is on his own. Certainly physicians are individualists, as I am sure you are well aware, and if you try to restrict their practice or you try to keep them from prescribing in the way they think best, it certainly can be one added way to make service life unattractive and that man is going to leave the service.

Senator NELSON. Well, that is like saying we will let him practice bad medicine because we do not want to lose him.

Admiral ETTER. I do not think it would be practicing bad medicine when the pharmacy-therapeutic committee has to pass on this particular drug.

Senator NELSON. Apparently the pharmacy-therapeutics committee takes the same position you do because they have passed a lot of drugs—I have a list here—which the National Academy of Sciences-National Research Council or the Medical Letter simply says are ineffective or that there is no proof that they are any better—and this is the pattern we get all over the country.

Now, the young doctor, as you know, has a modest course in pharmacology the second year in medical school. What is his qualification when he comes to your hospital to tell a therapeutics committee or to tell any distinguished authority that he knows better about the use of a particular drug. You say you are afraid to interfere for fear you will not make his practice comfortable and he will not stay in the service? It does not seem to me that that is an efficient way to run a professional organization.

Admiral ETTER. I think many of the people we are talking about

are those who have finished their residencies, have had considerable practice, and in their hands these are the drugs they have found to be accepted by the patients and which give them the results they desire.

Senator NELSON. I am sure that you are well aware we had the same thing with all the fixed dosage antibiotic combinations. Doctors all over the country used them and said they were effective despite the fact that the chairman of the AMA's Council on Drugs and a distinguished list of clinicians who were nationally known for their expertise, wrote an editorial in the AMA Journal as far back as 1957 decrying the use of these antibiotic combinations.

It has been the traditional position of the AMA's Council on Drugs that fixed combination antibiotics should not be used, that their use is poor medical practice, irrational prescribing. Then finally, the NAS–NRC comes to exactly the same conclusion, and recommends their removal from the marketplace.

Now, what are the qualifications for an individual doctor to say that he wants to use the fixed combination antibiotics because his experience indicates that it works and it is good for the patient and he knows better than the chairman of the Council on Drugs of the AMA and his associates which took that position 13 years ago and the National Academy of Sciences-National Research Council which took that position in 1968.

Admiral ETTER. Well, in that regard, Senator, I think certainly all these drugs which now have been proven to be ineffective or at least have, in their reasoned judgment, been declared ineffective by the NRC and NAS Council, will not be prescribed in our military hospitals. We are certainly—we are dedicated, Senator, to providing the best possible drugs we can for the treatment of our active duty and dependents personnel and retirees—the best possible drugs at the least possible cost, because cost is a real consideration for us now at the present time. This is where I get into it on one of my jobs. My main job is as Assistant Chief, Planning and Logistics, where I can control the budget for all hospitals. I am interested in economies, as we all are, but at the same time, not economy at the expense of the patient.

Senator NELSON. But what I am trying to get at here is, how do you get the best medicine for your patients—at the best economy—if the prescribing physician is going to have the kind of influence he does at the hospital—an influence contrary to the best medical expertise in the United States?

Admiral ETTER. We are not now in the position, Senator, of thwarting their advice. We are taking the advice of the experts at the present time.

Senator NELSON. Well, let me just read a couple to you. Here is a drug called Fiorinal. You purchased in 1968, $238,383 worth of Fiorinal, which is an APC plus butalbital. It is an analgesic.

Now, here is what the Medical Letter says about Fiorinal, volume 3, page 21:

> It has never been convincingly shown that the combination of aspirin, phenacetin, and caffeine as in Fiorinal has greater analgesic effectiveness than aspirin alone.

Volume 9, page 38, "If aspirin alone is not effective, a sedative drug, in place of or in addition to aspirin, can be tried". For example, phenobarbital, as an alternative to Fiorinal. You have the Medical Letter saying it has not been shown that in combination it is better.

The price for aspirin is 70 cents a thousand, for phenobarbital $1.10 a thousand, for Fiorinal $8.58 a thousand. If you had followed the advice of the Medical Letter, instead of spending $238,383, a comparable amount of the aspirin would have cost $19,504, a saving of over $200,000, or the comparable cost of phenobarbital would have been $30,000, a savings of $208,000.

Now, what clinical evidence was given by those who asked at the hospital level that Fiorinal be on your list, to prove that it was a better analgesic than aspirin or a better sedative than phenobarbital?

Admiral ETTER. Colonel Fairchild, do you have a response to the Senator here?

Colonel FAIRCHILD. I will try, Senator. I am Colonel Fairchild, president of the therapeutic agents board of Walter Reed. If I may stick to Fiorinal as an example, I personally am concerned that it is in the formulary. I would like to see it not in there. However, the young doctors coming from schools in other parts of the country, have been using a drug, for example: Fiorinal. They want to continue to practice as they have practiced where they came from. They put in a request to our therapeutic agents board through their chief of service. Then a search is made at that time to find comparable items. Our pharmacists at the same time will be checking prices now. The prices would be compared. The requesting physician would have to present his case to the chief of service, and then the chief of service and the man himself would have to present it to the therapeutic agents board, which meets once a month. If he can convince the group of the therapeutic agents board that he, in fact, needs this medication to continue his practice, then it is purchased locally.

This acceptance is following a sometimes relatively heated discussion whether or not a medication really has any value over, as for example, aspirin or phenobarbital.

And then as I understand from this particular point or, as the hospital uses more and more of a given medicine, whether or not it is justified as the hospital uses it and it becomes a high-cost item, a request is made for standardization of the Army.

Senator NELSON. How are we ever going to accomplish the objective of the higher standards of the profession in terms of rational prescribing unless we are going to require that the young people who come into the medical practice in your jurisdiction or the Veterans' Administration be required to prescribe rationally? I am astonished to think that a young doctor coming into the hospital would sit down with the therapeutics committee where you had a clinician with many years of experience, where you could produce the Medical Letter, where you could produce the evidence of what the drug was and what it was used for, and show him that he was advocating one which cost much, much more and that there was no proof that it was superior and if he could not produce any proof himself—I think it would be astonishing for him to take the attitude

he wants to prescribe it anyway. If he did, I do not think he ought to be practicing medicine. I just do not understand that.

Colonel FAIRCHILD. It is not only young doctors.

Senator NELSON. When I went into the Army, they did not allow me any of my idiosyncracies for very long.

Colonel FAIRCHILD. Not only the young doctors. We are getting in older doctors who come into the service. They have their own likes and dislikes, too.

Senator NELSON. I understand your position: you do not believe you should have Fiorinal in the formulary. But, I think we have demonstrated quite clearly over a period of time in our hearings, that even when you get to a physician with all the authority the military has over its hospitals and personnel, including the capacity to establish the best formulary and the best guidelines for medical practice in hospitals according to the best standards that can be established, that even the Army cannot do it. It seems to me, then, the possibility of really achieving rational prescribing by doctors on a whole series of complicated drugs and me-too drugs and duplicative drugs is out the window. It cannot be done. You might as well admit it. I have a list here of drugs. They run the same. Here is Zactirin, which is a fixed combination drug consisting of ethoheptazine citrate and aspirin. The National Research Council of the National Academy of Sciences states: "Zactirin is possibly effective as an analgesic but only because it contains aspirin."

Well, you spent $472,131 on Zactirin in 1968 and 1969. The amount you would have spent on aspirin is $22,467. It would have been a saving of $450,000 in view of the National Academy's statement that it is effective only because it contains aspirin. The NAS–NRC concludes:

> This combination may be no more effective as an analgesic than the amount of aspirin present.

How do we justify spending an extra $450,000 when the National Academy of Sciences states that it is no more effective than the aspirin it contains?

Colonel FAIRCHILD. May I speak to that?

Senator NELSON. Yes.

Colonel FAIRCHILD. Although it is, I think, relatively difficult to defend, I would like to cite a case, if I may, of a lady. Let us take a 55-year-old who has had for years a disfiguring rheumatoid arthritis, and over the period of years she has tried this drug, that drug, and another drug. One day she meets Zactirin, and Zactirin seems to hit the spot with her. It is difficult then after a period of 4 or 5 years of success with Zactirin for the physician to withdraw that particular drug and say aspirin is just as good. And that is the position we are put in, the relationship between the physician and the patient.

Senator NELSON. You are not telling me, are you, that in every case this drug is used, the Military Establishment had first tried aspirin or some other analgesic for years, and then went to Zactirin because Zactirin worked? I assume, because of the purchase, that this drug is now on your type classification list, is it not?

Colonel FAIRCHILD. It is; and it is in our formulary, but the drug is not in our pharmacy. It just was an example that we could use——

Senator NELSON. Well, you know better than I, that an inexpensive analgesic which works for 99.9 percent or more of the people may not in some rare instance for some reason that no one understands. In which case you might have to go to another drug which works but costs more. This, however, is not the position of the National Academy of Sciences, and that is not how the drug is being prescribed in the military installations. It is a type classification and it is being prescribed instead of aspirin in the face of the judgment of the National Academy of Sciences and in the face of Defense Department claims of budget squeezes.

Here is where you could have saved at least $400,000 and still bought it for this little old lady who had the problem you are talking about.

Colonel FAIRCHILD. I think you will find that we are gradually getting these things out and that the relative use of them is becoming smaller and smaller.

Senator NELSON. Well, that was $400,000 worth.

Let me take one that is very substantial. In 1968–69, your figures indicate an expenditure for Ornade of $4,373,147. Ornade was bought for the treatment of upper respiratory infections. The National Academy of Sciences-National Research Council panel says it is unaware of any evidence that Ornade is effective for congestion or hypersecretion associated with the common cold. Furthermore, several carefully controlled studies, in which different antihistamines were tried, disclosed no alleviation of symptoms or shortening of duration of symptoms of cold. NAS–NRC said that Ornade and other antihistamines may be beneficial in the treatment of allergic rhinitis but allergic rhinitis is being treated in that instance, not the upper respiratory infection.

Here you have the National Academy of Sciences taking a position against the use of Ornade and $4,373,000 worth of the drug has been purchased. What is the explanation for that?

Admiral ETTER. Well, in this regard I am not sure when these purchases for Ornade particularly were made relative to the NRC–NAS recommendations. As I am sure you are well aware, Senator, these recommendations are now just coming off the press in fairly voluminous numbers, and these all will be taken into consideration in all of our future purchases. Up to now our system just has not caught up with the NRC–NAS studies.

However, I will say this about Ornade in particular. I was chairman of the therapeutics committee 3 or 4 years ago in the Portsmouth Naval Hospital, at which time it was not on the table. There was, as Colonel Fairchild indicated before, quite a heated discussion, and our ENT people were bound and determined that this drug should be type classified because of the large usage of it in the pharmacy. They were convinced at that time that it was a good nasal decongestant. They were convinced at that time it was the best one they had available. Based on that, the Navy went along with the type classification, and I said we could put it in the formulary. But here you are putting yourself—in this instance the chairman of the group is putting himself up against the clinician who has observed the drug. At least, his objective feelings about Ornade were that he

felt that his patients were getting relief by having been given Ornade. Whether this treatment would have been just as good with Benadryl or others I cannot say, but they were convinced this was the drug of choice.

Senator NELSON. NAS–NRC said it was good for rhinitis. But that was not what the procurement was for in the Defense Department requirements. The specifications state: "Shall be suitable for use in the treatment of upper respiratory infections"—that is the specification demanded by your Department in purchasing.

What I am saying is, what evidence did anybody ever produce that Ornade was of any value for upper respiratory infections?

Colonel FAIRCHILD. It actually does not help the infection, sir.

Senator NELSON. Pardon?

Colonel FAIRCHILD. It actually does not help the infection, but it relieves the congestion so the individual can carry on his work at the time he has a cold. That is the difference between keeping a man at his job and losing him to stay home and blow his nose.

We brought Ornade up before our Board several months ago and just because of the extra expense we felt this was a drug that we could perhaps do without and use something else instead. And we asked all our chiefs to justify the continued use in our formulary of Ornade and those who were for it were in the majority. So we had to continue the use of Ornade. But we reviewed it just recently for this very thing that you bring out today.

Senator NELSON. Despite what the individual doctors' testimonials were respecting Ornade, the NAS–NRC panel said that several carefully controlled studies in which different antihistamines were tried disclosed no alleviation of symptoms or shortening of duration of cold symptoms. So, you have a situation where a doctor is giving testimonials and you are stocking the drug without evidence that it does what it is alleged to do. For this the Government is spending a large amount of money.

I just keep getting back to the question, how can we have rational prescribing in this country if the military cannot achieve it, although they are in total control of what should be purchased and what should be prescribed and they can call upon the best expertise in the United States to help them make the judgment both within and without the service. How much credence would you give to a doctor who would say he does not agree with the Medical Letter, with the Drug Council of the AMA, with Dr. Dowling and Dr. Modell, and with the expert clinicians on the various panels of the U.S. Pharmacopeia and the National Formulary? You have all that expertise available to you. Why don't you use it and say, this is our formulary, we are going to practice good medicine here?

Admiral ETTER. Senator, I think we are making progress in this regard. I sincerely do. I think as a result of many of these authorities you quote, that we are going to be in a much better position in our local hospitals to evaluate these drugs on possibly a little more rational basis, but it is very difficult to evaluate a drug entirely rationally when the physician himself feels that this has been a useful tool in his hands.

I would like to ask Captain Fox if he has anything to add to the

discussion so far from his experience at Bethesda. He is the chief of medicine, Naval Hospital, Bethesda, and is the chairman of their pharmacy-therapeutics committee.

Captain Fox. Senator, I agree with Colonel Fairchild, that I personally would not prescribe many of the items that have been mentioned here so far this morning. I do not think I have ever prescribed Zactirin. Ornade, on the other hand, remember, Ornade is a combination drug. I gather that the NAS–NRC study was referring to the antihistamine part of the Ornade and I think that probably is true, although a few years ago there was general thinking that an antihistamine did have a drying effect on the nasal passages. I think this idea is not being adhered to and people are now beginning to believe antihistamines are ineffective for nasal congestion.

On the other hand, Ornade does have other agents, strictly decongestant agents, and I think it is effective in that sense, but not in combination with the antihistamine.

Senator NELSON. Of course, there are lots of cheap decongestants in terms of nose drops, et cetera, rather than using Ornade.

Captain Fox. Yes, sir.

Senator NELSON. I will recite another case for the record. Darvon is an analgesic. Its established name is propoxyphene HCL. Total expenditures for Darvon were $4,360,784. The comparable cost of aspirin would have been $172,380, a savings of $4,188,404.

Yet, the Medical Letter, volume 12, page 5, says there is no evidence to "establish the superiority of 65-milligram doses of propoxyphene to two tablets of either aspirin or APC."

In the few studies which have been done, a 32- to 65-milligram dose of Darvon "has consistently proven inferior to aspirin."

Then why use Darvon?

Captain Fox. I agree, sir, but that volume 12 of the Medical Letter is the current volume. This information has not come out until recently, although the studies that they are basing it on have been accumulating over several years' time.

Senator NELSON. I understand. That is the issue dated January 23, 1970. But my question is: Since there are well-established, effective analgesics, does not the procedure that the DOD follows in acquiring drugs actually encourage this sort of thing, because you do not require proof of a new drug's superiority to established, effective, and less costly drugs before you give it a type classification or before you let it be used in your hospitals?

Captain Fox. Well, Senator, the Armed Forces do not practice a brand of medicine that is any different from civilian medicine. Most of our doctors are civilians who come in and spend a few years, 2 usually, and then go out, and our turnover rate is very high, as you know. We are just part of the civilian medical community, and I do not think that we can try to enforce standards that are not being enforced in the civilian practice.

Senator NELSON. There are some therapeutics committees in private hospitals in this country, in public general hospitals, that are tough and have established a high standard, and would not permit any of these drugs on their formularies and those are civilian hospitals. Why could not the military establish a therapeutics commit-

tee with, if necessary, outside consultants to secure all the guidance it can and then say we are simply not going to spend this kind of money on drugs that are either ineffective or not more effective than established drugs available in the marketplace, and if a physician wants to prescribe them, he must come up with a justification showing its superiority—something other than a testimonial?

That is done in many important hospitals in this country now. I recognize that there has been a vast accumulation of knowledge about drugs in the past 5 or 10 years, but it would seem to me that military installations ought to be leading the parade in the establishment of a standard for use of drugs that is not excelled any place in the country.

Captain Fox. I think we are headed in that direction, Senator. It is a slow process. It takes education at all levels.

Senator NELSON. Counsel calls attention to the testimony of Dr. Harry Williams, a distinguished pharmacologist from Atlanta, Ga., who is professor of pharmacology, Emory University School of Medicine, Atlanta, Ga. He testified on Librium and he says Librium costs somewhere around $50 a thousand:

> Faced with a choice between whether to use that drug or use phenobarbital, which we use at Grady Hospital, and which in many cases is equal to and in some cases superior to Librium, which costs us 9 cents per 1,000—

This is 9 cents versus $50—

> the average physician has nowhere to go to find out whether the statement made by the drug company that Librium is the successor to the tranquilizers is really true. He has no place to go.

This is a case where they replaced Librium, a drug costing $50 a thousand, with one that costs them 9 cents. The whole pattern over the past 3 years in our hearings indicates the same type of thing, that is, where expensive brand names of some kind or another are used for a purpose for which they either are not effective or no more effective than a well-established drug available in the marketplace at a much lower cost. I am concerned about establishing procedures, as I am sure the professional people are, procedures which would require the practice of good medicine. I can't accept the idea that somebody may resent it because he is used to prescribing something else; adoption of procedures to promote rational prescribing will enhance his medical education.

Here are the cases of Librium and Valium as tranquilizers: total purchases of a little over $6 million, $3,191,000 plus for Librium, $2,932,000 for Valium. Comparable cost for phenobarbital for the Librium would have been $132,976 instead of $3,191,442. Comparable cost of phenobarbital for the Valium would have cost $88,000 versus the Valium cost of $2,932,200. So, there would have been a savings of almost $6 million had phenobarbital been purchased instead of Librium and Valium.

The Medical Letter, in volume 11, says both drugs "are effective sedatives but it is still not clear that they have any important advantage over barbiturates."

This is another example, it seems to me, where physicians who want to use a more expensive drug ought to be required to produce

evidence that it has some superior qualification over and above testimonials of individual physicians.

I will put this material into the record and I will put the tetracycline case in the record also. They stated in the Medical Letter, "At recommended dosages and frequency of admission the different tetracyclines have similar clinical effectiveness."

Well, oxytetracycline was purchased by your Department. Chlortetracycline, demethyltetracycline were all purchased by the DOD at a cost of $2,959,000. Comparable cost of tetracycline hydrochloride would have been $610,000, with a savings of $2,349,000.

It has been argued for a long, long time by clinicians that there is no superiority of these other tetracyclines over tetracycline hydrochloride, which is the position of the Medical Letter. I think it demonstrates the problem of allowing a type classification to originate willy-nilly based upon the prescribing bias of individual physicians in miscellaneous Defense hospitals around the country, does it not?

Admiral ETTER. Well, that is awfully hard to argue against, Senator. It is very hard to argue against your position in this regard, but I think, as Dr. Fox pointed out, progress is being made, and many of these reports you are speaking about now are just now surfacing. A lot of this is just now coming to the attention of the hospital authorities and the board and DPSC, and I think there will be some changes in our customs and practices.

Senator NELSON. Is it not true, that unless the procedure is changed, this will be repeated over the years? Unless you establish a therapeutics committee, using the guidelines of the best expertise on drugs in the country, and unless you require the prescribing physician to prescribe from a formulary established in accordance with the best available knowledge, as new combinations or new variations of old drugs come out, there will be advertising and promotion, as a result of which there will be a new Librium, a new this, or a new that, for which there is an old established drug available. Under the system you follow, is it not true that you would end up with thousands of type classifications for drugs which are based solely upon usage at the local level with no proof that they are superior to available established drugs at all?

Admiral ETTER. Well, Senator, speaking about hospital pharmacy-therapeutics committees, I think that the ones in existence now at Walter Reed, Bethesda, and at Andrews certainly represent some of the best professional talent in this country in the medical field. All the specialty fields are covered, and they are noted in their fields. I think as it is, these people—these boards—will become aware of these things, and will make the changes. It has to be, I feel, an evolutionary thing rather than revolutionary thing.

You just cannot dictate to doctors summarily how they are going to practice medicine. It just does not work. They are not that breed of cat. As Dr. Fox pointed out, these that we have are a cross section of the civilian physicians, and as long as they want to do these things, they are doing these things in their own way. We have to go along with them up to an extent.

Now, we can put on the brakes, and brakes are being put on. As

Colonel Fairchild said, some of the drugs which are more expensive have been questioned at Walter Reed, but I certainly think you could put Walter Reed's committee up against any group in the country. They are eminently qualified physicians in their own right and in their fields. Put them up against any board, and I would go along with the Walter Reed group.

Senator NELSON. I have no basis for making a judgment one way or the other, but if I understand you correctly, you take the position that you cannot tell the doctors what to do. Therefore, even if you have the best experts in the world available to you, you can still get into your formulary drugs that the therapeutics committee say are no good, besides costing a lot more, because no one wants to offend the individual doctors. So it ends up that you can have a superb therapeutics committee and yet have a formulary that is not superior.

Now, I do not know what the Walter Reed Hospital formulary is and I would not be qualified to judge it. It may be one of the best in the country, but I still do not understand why you should worry about a doctor saying he has been using Librium, or any one of these other drugs, for many, many years and he finds it effective and wants to use it, while at the same time the therapeutics committee finds that the particular drug he wants is not superior and, in fact, is ineffective. The committee has the Medical Letter statements of the best clinicians and medical panels which have studied it. Certainly the therapeutics committee can say: here is what the panel of the USP and NF have decided to put into the official compendia for this purpose, unless you can produce some evidence based upon controlled clinical studies, you will have to use the drug in the formulary.

The physician is not much of a scientist if he is going to insist on using something if there is no scientific evidence of its superiority, is he?

Colonel FAIRCHILD. I believe that if we stick with Librium and Valium for a moment, that as the drug is evaluated and presented to the medical profession in the literature, that these articles, this evidence, is then used by the individual physician interpreted as absolutely correct and it is not until later after they have had a chance to evaluate the drug over many millions of patients can they state it is not as effective as, and it is at this particular point in time that the therapeutics agents board is presented with the request by the doctor to add it to his armamentarium.

So, at the time he presents his original request for Valium, Librium, et cetera, he has evidence or could not get it through the committee.

Senator NELSON. What is his evidence?

Colonel FAIRCHILD. His evidence is articles in the literature that support his particular need. Or perhaps—as I had the good fortune, I grew up with Dr. Dowling, rather, under Dowling, and I worked with him over here in D.C. General, so I had an experience with sulfisoxazole before it was known as Gantrisin while it still had a—it was called NU 445 at the time. And I had this experience and when I was ready to go out, I liked this drug. I had some fine experiences with it by a well known man, and I wanted to use it. And I thought at that particular time I had a right and justification to use it.

Senator NELSON. You say they cannot get the drug in the formulary unless they have some evidence from the literature. What do you mean by that?

Colonel FAIRCHILD. They have to have some evidence, sir.

Senator NELSON. Well, would the evidence be controlled studies?

Colonel FAIRCHILD. Alleged controlled studies, that as time goes on perhaps they find that they are not as controlled as the original——

Senator NELSON. These drugs that the Medical Letter and the National Academy of Sciences were commenting on did not have any controlled studies that demonstrated their superiority. The fixed combination antibiotics, the best known of which was Panalba, are good examples. The studies which the manufacturer of Panalba performed, or had contracted for, simply showed that the ingredients of the mixture tetracycline and novobiocin were not synergistic, were not additive, but were actually antagonistic. And yet this drug was one of the most widely prescribed drugs in this country. So, when it was included in the hospital formulary, there had not been any controlled studies to demonstrate its superiority to tetracycline alone.

Now, how would that particular drug get on the formulary if such an action is based upon controlled studies and when the controlled studies that were done by the company did not support the claims that were made for it? I think that including it in a formulary and using it extensively is due to the advertising and promotion.

Colonel FAIRCHILD. I was not on the board at Walter Reed at the time Panalba was brought in. I was on the board when it was taken out, so I cannot make a statement as to what claims were made for Panalba.

I do know that when a request is made of my board, that request must include justification for that drug over known drugs, and particularly if that drug is a more expensive drug than the known drugs. So, you must speak to this and convince the committee that in fact they need it, there is justification for the use of it.

Mr. GORDON. May I interrupt just a moment? You mentioned sulfisoxazole a few moments ago. That drug is in the USP and we were not discussing that particular drug, isn't that correct?

Colonel FAIRCHILD. I was just bringing this up as an example of my own personal experience with a drug before it was on the market.

Senator NELSON. Sulfisoxazole was included in the U.S. Pharmacopeia after that?

Colonel FAIRCHILD. Yes. Back in 1943, I think it was.

Senator NELSON. Let us see. I suppose we have covered a fair amount of what follows.

I had some questions, Admiral, on page 10. Would you want to start reading there, 10 and 11, at the top.

"Pure, safe and therapeutically effective drugs".

Admiral ETTER. It starts on page 9.

Senator NELSON. Yes, go ahead.

Admiral ETTER. In the preparation of medical specifications, every effort is made to delineate the essential needs of the Government in an effort to procure pure, safe, and therapeutically effective drug products, yet maximizing efforts to seek competitive procurement.

It must be recognized that military needs frequently involve requirements which transcend those of some commercial products on the market. For example, military medical materiel is subjected to worldwide distribution under adverse conditions. Product stability is, therefore, a very essential element in assuring that the product is suitable when it is ultimately consumed. As a result, the standards described in DPSC specifications are at times more stringent than commercial standards in anticipation of adverse storage and transportation, and long-term storage.

Senator NELSON. May I ask a question there? The first sentence is, "It must be recognized that military needs frequently involve requirements which transcend those of some commercial products."

As I read your statement, you seem to be referring to packaging here, not composition of the finished product. Am I correct?

Admiral ETTER. The stability of the product itself for long-term storage, and this can come particularly in the tablet form of certain drugs. Tablets must be made in a particular fashion so that they will remain stable longer under high temperatures or high humidities or freezing or cold. Packaging is certainly part of that, too.

Senator NELSON. Fine.

Admiral ETTER. It will be noted that the method of specification preparation is responsive to the rapidly changing need of the medical services. The division operates closely with the procurement personnel and obtains rapid feedback from industry on recent technological advances. Technical reviews and evaluations of such data permit updating and upgrading medical specifications. Valuable information is obtained via the complaint reporting system which involves evaluation of complaints, classification of the types of complaints, and determination of whether specifications require modifications in order to circumvent further complaints of a similar nature.

DPSC procures approximately 1,100 drug items, of which about 560 are monographed in the current issue of USP XVIII and NF XIII. About 50 percent of these items include standards that exceed those of the official compendia.

Senator NELSON. In what way do you exceed the standards of the official compendia? It is the position of the USP and NF that these standards are as high as they can be for any useful medical purpose.

Admiral ETTER. For example, it is my understanding that with some of the antibiotic preparations, DPSC requires both high and low limit concentrations of the available active ingredients in that drug. NF and USP did not, and now I understand they have incorporated some of the higher standards as I indicated before, because of certain storage requirements and certain requirements which make them last over a longer period of time under adverse conditions.

Senator NELSON. Just so that it is clear in the record, you are not saying that because it has something that makes it store for a longer period, that that makes it a therapeutically more effective drug?

Admiral ETTER. No, sir.

Senator NELSON. I just wanted to get at the question of superiority, to be clear on what you mean by standards that exceed those of the official compendia and if you intend to say they exceed them in terms of therapeutic effectiveness.

Admiral ETTER. This next sentence, I think, also speaks to this.

Requirements specified include color limits for liquid products particularly for parenterals; expiration dates, refrigeration requirements for many items not required by the USP and NF; dissolution tests, animal tests, accelerated aging, and some clinical requirements. Also, special packaging is required for greater assurance of stability. These areas include inner and outer seals, leakage tests, special closures, label adhesion, tin plating, and vacuum packing.

In this regard, Senator, I would like to ask Captain Pflag if he has anything to add to this matter of exceeding the USP and NF standards.

Captain PFLAG. No, sir. I think, Admiral, that was covered in the statement in a very general way, unless the Senator wants some specific, more specific data.

Senator NELSON. Well, I am not exactly sure what the Admiral is saying, when you talk about packaging and the longer life because of a different method of compounding or formulating. We have made it clear that this does not make it superior therapeutically.

Frequently, the drug companies say, well, our drugs meet a higher standard than the U.S. Pharmacopeia and/or the National Formulary. The best expert testimony that we could get, not only from USP and NF, but also from outside experts, such as Dr. Modell, with whom you are familiar. Dr. Modell states:

By and large, purification or modification beyond these standards—

That is, USP or NF—

doesn't make any practical difference, but as I have already stated from time to time there are improvements made occasionally by the industry, occasionally by workers outside of the industry, and as soon as the USP learns of this, it changes its own standards and requirements.

Thus, there may be a gap, but in general, there is no practical difference between all drugs that live up to USP standards.

Then on page 303 Dr. Modell states:

They—

Referring to USP standards—

they are not minimal standards by any means. U. S. Pharmacopeia has the highest standards of all pharmacopeias in the world. They are standards that are so high that further purification would provide nothing more than additional costs.

The primary requisite is the establishment of the standards necessary for the most effective use in medicine. It is, therefore, explicit in the decision of the U. S. Pharmacopeia Committee to set specific standards for a drug that further purification or higher standards will accomplish nothing in medicine. If the industry wants for one reason or another to go far beyond this, of course, it has every right to do it, but it does not mean that it has accomplished anything in so doing.

This is the aspect that I was referring to, and I take it that you are not saying that you require standards higher than USP or NF in the context in which I was reading the statement of Dr. Modell? [1]

Captain PFLAG. Senator, we find it absolutely necessary that a drug be as potent at the time it was procured as it would be at the end of a long-term storage period. It might be, for example, 5 years.

[1] See testimony of Dr. Walter Modell, Part 1, pages 283–305.

The drugs procured commercially generally meeting USP standards, which are minimum in many instances——

Senator NELSON. But Dr. Modell says no.

Captain PFLAG (Continuing). Are not subjected to extremes in temperature and climatic conditions.

May I give you an example, a specific example, sir.

Several years ago we purchased reserpine tablets from a certain company on the west coast. These tablets met the NF disintegration test which at the time was 30 minutes, at the time of procurement it met it nicely. At the end of 5 months, as this material laid on our depot shelves, the disintegration time ranged from 30 minutes to 2½ hours, and had this been in the system any longer it might have even gone beyond that.

So we have to make absolutely certain that an item that we procure at one point in time is in a condition to be used on a patient several years later if it is stored in prepositioned war reserve stocks.

Senator NELSON. Or if it is an item that can be preserved that long without losing its potency.

Captain PFLAG. Yes. We have other instances where material is put on the beaches, for example, in Vietnam, i.e., dextran. When it is in an ambient atmosphere fluctuating from 120 degrees Fahrenheit to 50 degrees Fahrenheit, you get particulation in this material.

Senator NELSON. So you aren't saying, really, if I understand you, that you require standards higher than USP because obviously that drug that was on the shelves on the warehouse for 5 months and did not disintegrate for 2½ hours did not meet USP standards——

Captain PFLAG. Did not meet NF standards——

Senator NELSON (Continuing). At that time.

Captain PFLAG (Continuing). At the time we picked it up, but at the time we purchased it, it met NF standards.

Senator NELSON. That's right.

Captain PFLAG. And, sir, as a result of that, what we do is, we reexamine our specification and attempt to introduce tests and tighten specification so that we can prevent this from ever occurring again.

Senator NELSON. Yes; but what you are saying is that you wish to insure that it meets USP standards, not superior standards.

Captain PFLAG. That it would meet NF standards or USP standards.

Senator NELSON. Or USP.

Captain PFLAG. Yes, sir; at the time the drug is to be used.

Senator NELSON. Correct.

Captain PFLAG. Yes, sir.

Senator NELSON. But at no stage were you demanding that the drug meet a standard higher than NF or USP. You are just demanding that it meet the NF or USP standard, and under certain storage conditions, it didn't meet it. I would like to know what that standard is if it is higher than USP or NF.

Captain PFLAG. We have a case in penicillin, in a penicillin injectible, in which we require a color standard which is higher——

Senator NELSON. A color standard?

Captain PFLAG. A color standard; that the injectible be of a certain clarity, have an absence of yellowness or color.

Senator NELSON. Do you have evidence that that is more effective therapeutically?

Captain PFLAG. Yes, sir; to this extent, sir. We have found that as penicillin injectible ages, that there is an increase in yellow color, or it darkens, and, therefore, since we purchase some of this for long-time storage, it seems prudent to get the lowest color value that one possibly can, so that as it ages there would be less color, and, therefore, less degradation. The color is synonymous with degradation. Generally, where there is a color change, it is generally associated with degradation of the product.

Senator NELSON. All right, go ahead.

Admiral ETTER. In qualifying drug manufacturers, facilities of prospective contractors are inspected to determine the company's potential to produce a specification item under acceptable conditions of quality control and housekeeping. The DPSC drug standards are used as a guide in determining the acceptability of the firms. Disqualifications are usually in the areas of inadequate quality control, unacceptable housekeeping, or deficiencies in technology.

Preaward samples are requested in those instances where the capability of the firm to produce an item in conformance with the specifications has not been established. Our medical laboratory performs the necessary analyses to determine compliance with specifications, and from these findings judges whether the manufacturer has the potential to produce the item specified. Other Government laboratories, such as FDA and U.S. Army Medical Research Laboratory at Fort Knox, are utilized to augment DPSC testing capability.

The medical laboratory is an essential segment of the total quality assurance effort. The laboratory represents an independent source of analyses by highly qualified, trained scientific personnel intimately acquainted with tests and standards of chemical, physical, and bacteriological testing. The analyses performed on preaward samples, first articles, preacceptance samples, and depot surveillance samples represent a critical part of the effort toward the quality objective. The laboratory also serves as a checkpoint for inspectors when they wish to have company results verified independently.

During production, every drug product is inspected by a qualified chemist, pharmacist, or chemical engineer of the Defense Contract Administration Service of DSA. These personnel are specifically and formally trained for this function by DPSC.

Senator NELSON. May I ask a question here. I think I could cover these next few pages.

Do DOD personnel inspect the plants of all suppliers?

Admiral ETTER. Of all the prospective suppliers, they inspect all plants of those with whom we have contracts, sir.

Senator NELSON. Those with whom you have direct contact. You aren't referring to purchases made at the local level?

Admiral ETTER. No, sir.

Senator NELSON. What is the qualification of your inspectors? What are their technical qualifications?

Admiral ETTER. They all undergo training in DPSC, and they have all—I think I am correct, Captain Pflag—a baccalaureate degree, usually in one of the sciences.

Captain PFLAG. Yes, sir.

Admiral ETTER. And are chemists or other similar type trained personnel such as pharmacists.

Senator NELSON. Are these full-time personnel? Is this their full-time assignment?

Captain PFLAG. Yes, sir.

Senator NELSON. And how many are there?

Captain PFLAG. There are approximately 80 inspectors full time. This is the Defense Contract Administration Services inspectors who have a baccalaureate in one of the sciences, chemistry, pharmacy, and they are all civilians as the admiral has pointed out; yes, sir.

Senator NELSON. They are civilians whom you have hired?

Captain PFLAG. Yes, sir. And they have been trained by the Defense Personnel Support Center in a special course in drugs and chemicals.

Senator NELSON. Is there any coordination between the inspecting agencies or exchange of information with them, for example, the Veterans' Administration?

Captain PFLAG. Yes, sir.

Senator NELSON. Is there any coordination among these inspection teams?

Captain PFLAG. Yes, Senator. Through the Intragovernmental Professional Advisory Council on Drugs and Devices, we have an arrangement whereby information is transmitted from us to FDA to VA and back again. So that we are all kept aware of any deficiencies that we may encounter, any violations of the law, and so forth.

Senator NELSON. Where is that information filed or kept? In other words, is there some central place that one could go to see all the inspections made of whatever number of plants by DOD personnel, Veterans' Administration, Food and Drug Administration?

Captain PFLAG. Yes, sir. We have, of course, in the Defense Personnel Support Center that information available. In the FDA that is available, and in the VA it is available. And we incorporate the intelligence that relates to our contracts into the procurement history files of the other item history files that we have.

Senator NELSON. What is the basis of your inspections? That is, do you routinely inspect those who are regular suppliers, or do you just get a contract and then inspect before you accept the product, or what is the procedure?

Captain PFLAG. When an offeror of material bids, of course, he is inspected and he is given what we give a preaward survey. However, each time there is a contract in a plant, our inspectors are inspecting as they are accepting lots of material. Each lot must be inspected.

Senator NELSON. When the drug is supplied, is there any assay of the drug to determine whether it meets the standards?

Captain PFLAG. Yes, sir. Every lot is assayed either by the contractor with the inspector witnessing it, or the inspector himself will perform the assay. And in many instances we will require a verification assay that is done at the Defense, is performed at the Defense Personnel Support Center. So there is a check-and-balance system, sir.

Senator NELSON. Then, for procurement of drugs overseas, which I take it you occasionally do, you have inspectors there, too?

Captain PFLAG. Yes.

Senator NELSON. How many do you have? Are they permanent civilian or military personnel?

Captain PFLAG. We have two civilians who are there on temporary additional duty assignments, and we have a full-time Medical Service Corps officer who has received special training at the Defense Personnel Support Center.

Unlike our contracts in the United States, in Europe we have a full-time resident inspector while production is going on.

Senator NELSON. Here, in this country?

Captain PFLAG. No, sir.

Senator NELSON. No; there.

Captain PFLAG. There.

Senator NELSON. So, if you make a purchase there, you have one of your personnel present at all times?

Captain PFLAG. Full-time resident inspector, sir; yes.

Senator NELSON. I think you covered that, Admiral. So maybe you could start on page 14. I think you have covered everything up to that, or the last sentence on page 13, unless there is something that you wish to add.

Admiral ETTER. No, sir.

The basic statute governing procurement by the Department of Defense—title 10, United States Code 2304—directs that purchases shall be made by formal advertising and authorizes the use of negotiation in 17 specifically enumerated situations.

Formal advertising operates most effectively where (1) an adequate number of qualified suppliers have actively competed for Government contracts; (2) they are willing to price competitively; (3) definitive specifications are available for the required product; and (4) there is sufficient time to carry out the inflexible formalities of the formal advertising process——

Senator NELSON. May I interrupt at this point, Admiral.

On item 2, what does that mean, "They are willing to price competitively"?

Admiral ETTER. Could I ask Colonel Snyder to respond to this part, sir.

Colonel SNYDER. To make a formal advertising meaningful, you must have competition. Otherwise, there is no basis of comparison. Now, to take that by itself would be most difficult to define. I cannot think of a single instance, other than a sole source supplier, where firms have been unwilling to price competitively.

The essential element of formal advertising is that you have some variance in price. Otherwise, there is no ability to differentiate one from another. On a supposition, if I may, if we were to solicit competition on a particular product, and if three firms came in with an identical price, unless there was some strange and unusual circumstances—I can't even think of an example offhand—we would be required to report them to the Federal Bureau of Investigation for possible collusion.

Now, I cannot remember, in my limited experience, of it ever happening, because all of the firms are well aware of this provision of law where they would be investigated very painfully if this

happened. But this is only there as an element that would be essential to formal advertising.

As I say, we have never used this as a reason for not using formal advertising.

Senator NELSON. There is, as I understand it, a provision in the law—section 1498 of title 28 of the United States Code—that provides that Federal agencies are not bound by patents issued by the Federal Government, so if there is a sole source here in the United States and other sources in Europe and if you are not satisfied with what you can negotiate with the American sole source, you may purchase in Europe; is that not correct?

Colonel SNYDER. That is correct.

Senator NELSON. And as I understand it, you have done that from time to time?

Colonel SNYDER. Yes, sir.

Senator NELSON. Is it a matter of policy in negotiating with sole source suppliers in this country to maintain a listing of the world price, so to speak, versus the sole source offering price here so that as a regular part of purchasing policy you would use the world price to guarantee that you were getting a reasonable price offering from the American sole source?

Admiral ETTER. I think that is correct, sir.

Senator NELSON. Is it a part of regular policy to do that? In other words, every time you have a sole source supplier in the United States, do you as a matter of policy check the price listing of European suppliers of the same drug?

Colonel SNYDER. No, sir. First, I would like, if I may, to define "sole source."

Admiral ETTER. This is single source here.

Colonel SNYDER. Sole source, we have very, very few. I think there are only eight or nine drug items. If you are speaking of single source, we do not solicit only one firm on a single source drug, even though it may have been historically supplied by a single source during some extended period of time.

Senator NELSON. Sole source being a case where there is no other producer in this country; right?

Colonel SNYDER. No. Sole source would be a situation where the Defense Medical Materiel Board would designate the source as the only source from which we might procure the item.

Senator NELSON. Though there may be other sources.

Colonel SNYDER. Yes. Though there may be other sources, many more. Single source is where traditionally or historically there has been the one supplier, either for reasons of price, patent, Federal authorization such as an NDA or a form 6, or whatever, even though there may have been some limited degree of competition, only one source has been successful over an extended period of time.

Senator NELSON. So it is in single-source situations where you have bought from the world market, right?

Colonel SNYDER. Generally speaking, yes.

Senator NELSON. My question is, in those situations do you always check the world price to be sure that you are at arms' length in your negotiations with the single source here?

Colonel SNYDER. Not specifically, because on each of our single-source procurements we do solicit competition. Rest assured, there are a number of suppliers of foreign material; all of the major drug firms in Europe watch our procurements very carefully. As you know, each procurement that we make is advertised in the Commerce Business Daily and it is in several of the trade journals. They watch us very closely.

Now, one thing you should know is because of our Buy American Act, there can be what appears to be a substantial price differential in a lower price that may be available in Italy or Germany, or whatever, and the price, but because of our Buy American Act we have a 50-percent differential which would immediately set them somewhat apart. We are prohibited from spending our Defense appropriations money without allowing this differential.

Senator NELSON. Well, is that 50-percent differential in the law? Is that a rule of the Defense Department?

Colonel SNYDER. It is in the Armed Services Procurement Regulations. I would presume that there was some legislative guidance. We don't just arrive at these things—it is the Buy American Act, which is our guide. I am not sure of the intricacies of the actual legislation, but I am sure that this was not something that we arrived at unilaterally.

Senator NELSON. You are saying that even if there is a single source, that you are required to accept the American single source if it does not exceed the world price available drug by more than 50 percent; is that it?

Colonel SNYDER. Well, that is over-simplifying it, but, generally speaking, that is true. It is a little more involved in the evaluation than that. We do not, though, specifically investigate the world price, other than what we may have read in our professional reading, ancillary reading, that would indicate something of this sort.

Senator NELSON. But you are saying that if there is a single source you do advertise automatically for bids in any event?

Colonel SNYDER. We always ask for competition regardless of the traditional history of buying it from one source; yes, sir.

Senator NELSON. And even when you have a negotiated contract with a sole source you ask for bids regularly?

Colonel SNYDER. No, sir. Now, sole source, if we are directed by the Defense Medical Materiel Board to buy a specific agent or drug from one firm, we only contact that firm. But there are only, I think, nine items of that nature, and those are under constant review where the state of the art advances or where it no longer can be designated, for professional reasons, as a sole-source item. On all items, of which there are over 500, which are single source, we do solicit competition. And the fact it isn't successful is due to any one number of reasons.

There is no single reason which you can categorically say that we could correct this situation so we would immediately have competition.

Mr. GORDON. Mr. Chairman, as I understand it, the Executive order which governs the statutory Buy American provisions sets alternative standards by which the price of products of domestic origin is deemed to be unreasonable or inconsistent with the public

interest. That is, the American price is presumptively unreasonable if the U.S. bid or offered price exceeds the sum of the bid price for materials of foreign origin, plus a differential consisting of (1) 6 percent of the bid or offered price of materials of foreign origin, or (2) 10 percent of the bid or offered price of materials of foreign origin exclusive of applicable duty and all costs incurred after arrival in the United States.

However, the Armed Service Procurement Regulations adds a 50-percent evaluation factor in favor of goods of American manufacture. It is quite different from the Executive order; in other words, there is an addition of about 40 percent there.

I am reading from a staff memo:

> The Armed Services Procurement Regulation (ASPR), for instance, adds a 50 percent "evaluation factor" in favor of goods of American manufacture. This procedure originated as a gold flow correction, but since the agreement among the world's central banks in 1968 whereby a two-tier gold system operates to end the monetary gold flow problem, the practice has been continued as a balance-of-payments correction. Thus, instead of a 10-percent alternative Buy American calculation, the Defense Department applies a 50-percent balance-of-payments factor.

Senator NELSON. I would like to skip to the bottom of page 15, Admiral, and the following sentence:

> It is the policy of the Department of Defense to place a fair proportion of its total contracts for supplies and services with small business concerns.

and you go on beyond that.

What methods do you follow to place a fair proportion of the contracts with small business?

Admiral ETTER. Well, we encourage them in every way to bid on all solicitations. When they have failed to submit bids for one reason or another, because, possibly, of some of the difficulties of the manufacturing processes, the representatives of these small business firms are counseled at DPSC. They are advised as to what they might be able to do to put them in a better bidding position. Every effort is made in this regard to try to give them a fair share of the business.

Senator NELSON. What is the definition of a small business that is used by the Defense Department?

Colonel SNYDER. It is 750 employees in total. That includes all affiliations, firms under a common executive board or control.

Senator NELSON. Seven hundred and fifty or less employees?

Colonel SNYDER. Yes, sir.

Senator NELSON. Do you know how many there are with whom you have done business who fit the small business category?

Colonel SNYDER. I do not have that information specifically.

Senator NELSON. Could you supply it for the record?

Colonel SNYDER. Yes, sir.

Admiral ETTER. There is, in the backup data—in the exhibits there are some listings of the small businesses, and the ones that have been given contracts recently.

Senator NELSON. Where is that?

Admiral ETTER. Captain Pflag says he can name a few offhand.

Captain PFLAG. The Endo Laboratory, Knoll Associates, the Strong Cobb Arner Laboratories, Day-Baldwin—these have all been successful suppliers in the small business category, sir.

Colonel SNYDER. I would like to add, though, that each of those has been acquired by large business in the last 2 years. This is one of our great difficulties, and I know because of your interest in small business, Mr. Gordon has commented informally as to your distress over the apparent shift from small to large. Really, there is no shift as such. We are still buying, generally speaking, from these very successful small firms, but they have in the main been acquired by one of the conglomerates or one of the larger holding companies.

Now, as we—it is very interesting, because of the assistance that is given—and there may be some difference as to the word "assistance", but because of the monitoring of the procurement and the manufacturing practices and the quality control actions of these small companies, they become more skilled, and as they become successful in participating in our Defense procurement, they are watched very carefully. And I think, really, that it is kind of a kiss of death on a small business; as we get a small business to the point where they are supplying successfully and kind of get them on their feet, they are immediately acquired by one of the larger firms.

It speaks well for our system in one way in that it is a mark of success that they can succeed with us. It is distressful in that we must again start all over in our efforts to obtain small businesses to participate in our effort.

As you know, we are given a goal of a certain amount of our procurement must be given to small business, and we spend a great deal of time in this effort. But it is very difficult.

Senator NELSON. Do you have a set-aside provision? Five percent is it?

Colonel SNYDER. Our goal for this year, for fiscal year 1971, is 20.1 percent. And this is very difficult.

Mr. GORDON. So far it is only 8 percent, isn't it?

Colonel SNYDER. I am sorry, sir.

Mr. GORDON. So far the small business set-aside program is only 8 percent, isn't it?

Admiral ETTER. It was 8 percent, I think, in 1969. In 1970 it is, as I remember, 17 percent.

Colonel SNYDER. It varies substantially between segments of the industry. We get much more small business success in the metal-bending or in the hospital equipment area than we do in the drug business. The nature of the drug business, because of the requirements for a very substantial quality control staff, sales staff, manufacturing staff, makes it very difficult for a small business—that is, it is more difficult, comparably speaking, for a small firm to succeed in the drug field than it is in one of the other fields.

Mr. GORDON. Isn't it generally true that a small business can do better in the drug industry as far as capital equipment goes? It is not a capital intensive industry, and it seems to me that a small business could do better in that field, especially in selling to the Government.

Colonel SNYDER. Well, this has not been my experience, sir. There is a very substantial investment, unless you are going to be just a tableting firm or do one very specific operation where it may be more successful, or they may be more successful in working as a subcontractor somewhere.

Mr. GORDON. I would like to ask about the bidders' list you submitted. You say here on the top of the bidders' list:

> This list represents those organizations which are presently listed as bidders for drug products. The list does not purport to indicate the capability of the bidder, nor is it a listing of suppliers of drugs to DPSC.

Colonel SNYDER. That is true, sir.

Mr. GORDON. That is right on the list. However, the Armed Services Procurement Regulations; paragraph 2.205(b) says:

> All eligible and qualified suppliers who have submitted bidders' mailing list applications or whom the purchasing activity considers capable of filling the requirements of a particular procurement shall be placed on the appropriate bidders' mailing list.

Is this that list?

Colonel SNYDER. That is true, sir.

Now, any firm can submit a form 129, which is a request for inclusion on the bidders' mailing list, by indicating those products which he feels he is qualified and capable of supplying.

Now, the only qualification that he must furnish at the time of that submittal is one as to his financial capability, which is a very broad thing, the number of employees, square footage, and so on. I am sure you are familiar with the form. We do not really investigate his capability and qualifications until such a time as he is the low bidder on a specific offer. And at that time the people from our technical division would investigate him as to his, the housekeeping, his manufacturing capabilities, capacity, his quality control methods, all of the things that go into qualification as a supplier to the Government.

Mr. GORDON. Does this list include eligible and qualified suppliers?

Colonel SNYDER. Using your word——

Mr. GORDON. That is what the ASPR regulation requires.

Colonel SNYDER. Using your word "include", it does, sir. It includes also those who, in my personal view, are certainly not qualified. We have no way of rejecting them until such time as a specific evaluation is made as to their technical, total capacity requirements.

Mr. Gordon, you must understand that anyone is eligible to participate in a Government procurement. We take their applications but we do not spend a great deal of money investigating each of these until such time as they are the low offerer.

Mr. GORDON. The regulation says that a list should be established which includes eligible and qualified suppliers, or the alternative, suppliers considered capable of filling the requirements.

Colonel SNYDER. Yes, sir.

Mr. GORDON. Now, is this such a list? That is what I want to know.

Colonel SNYDER. I haven't stopped beating my wife, either.

Mr. Gordon, you must understand that there is no facility—and we do not have the funds nor the ability—to evaluate every person who submits a form 129 unless he is the low bidder on a specific offer.

Now, it does include—include, using "include" in its very strict definition—all those eligible and qualified, but it also includes some who are not eligible and qualified. When we get down to the specifics of an examination of their plant——

Admiral ETTER. But it does include all those eligible and qualified.

Colonel SNYDER. Yes, sir.

Admiral ETTER. The answer is yes.

Senator NELSON. Would you like to skip to page 17. I think we have covered everything up to there.

Admiral ETTER. Start with the paragraph, "The procurements"——

Senator NELSON. No; I wanted to discuss the drug Titralac. Is that an antacid?

Admiral ETTER. The Titralac; yes, sir.

Senator NELSON. Titralac. And that is for gastrointestinal problems, peptic ulcer? Is that the area that we are talking about?

Admiral ETTER. Yes, sir.

Senator NELSON. And that was a sole-source procurement item?

Admiral ETTER. No, sir. It was not. It was a single-source procurement.

Senator NELSON. Single source?

Admiral ETTER. It was single source from the time that it was first standardized in 1964 up to 1968. Since 1968, there have been two or three other bidders, and Riker Laboratories, which originally had the contract, has not had it since that time. Chase Laboratories has had the contract, and I think Abbott has one at the present time.

Senator NELSON. I couldn't find it in USP or NF as an antacid. Dr. Burack doesn't mention it.

What does this antacid have that any number of others don't have?

Admiral ETTER. As I think I tried to point out earlier, Mr. Chairman, this one was originally recommended for type classification because of its use, and of prescribing by a large number of physicians in Air Force hospitals. At the same time, the Navy and the Army, because of their experience with the drug, agreed that this was a good agent. This happened to be one that they felt had a high degree of patient acceptability, and in which the doctors who were prescribing had confidence. This is only one of 18 or 19 antiacids which are on our standard listing, so that we have a choice. The doctor can pay his money and take his choice in these particular antiacids family compounds.

Senator NELSON. You have 18?

Admiral ETTER. Eighteen or 19, I think, sir.

Senator NELSON. Are there any clinical studies to indicate that they do anything the drugs listed in NF and USP don't do?

Admiral ETTER. Most of them are listed in the NF and USP—the other ones to which I spoke—the other list of 17 or 18. And here, again, we are back to the matter which we discussed earlier—the physician's choice and patient acceptability of this particular one.

In this regard, Colonel Clark has not had an opportunity to say much yet, and he is an internist. I would like to know if Colonel Clark from the Air Force Surgeon General's Office would like to comment on this particular item.

Colonel CLARK. I am not sure I can add anything to Admiral Etter's statement. I think the number of antacids required reflects the gamut of physician training, each physician being trained in the use of different drugs, and it also reflects the fact that this is a chronic problem we are talking about—many of the patients have been taking drugs for many years and they are reluctant to switch to a different one even though they might get a good result.

Senator NELSON. Are you skipping to the last paragraph on page 19?

Admiral ETTER. I am starting "On 31 March"?

Senator NELSON. Yes, sir.

Admiral ETTER. On 31 March, 1 and 2 April 1969, the Drug Information Association, in collaboration with the American College of Clinical Pharmacology and Chemotherapy, American Medical Association, American Therapeutics Society, and the American Society for Pharmacology and Experimental Therapeutics conducted a symposium on "Formulation Factors Affecting Therapeutic Performance of Drug Products."

Dr. Don Harper Mills, M.D., JD, Clinical Professor of Forensic Medicine and Pathology, School of Medicine, University of Southern California at Los Angeles, presented a paper which stated most succinctly the problem of the medical practitioner. Dr. Mills notes the significant increase of malpractice suits in recent years, and speculates that certain statistics project that theoretically, "a physician who practices for ten years faces a 100 percent chance of being sued."

It is the duty of the physician to exercise judgment, to select, to choose—he determines what laboratory test, to consult or not consult, which consultant, what diagnosis, and finally, what therapy. It is the exercise of his judgment in the latter area which is of concern to us today. In his paper, Dr. Mills emphasizes that the duty of the physician to choose a drug which, of his own knowledge, is effective, safe and proper, is an affirmative one, and must be susceptible of proof in court. Dr. Mills includes as a fact requiring personal knowledge, the therapeutic equivalency—or biological availability—of the chemically equivalent drugs available.

Senator NELSON. May I interrupt.

Doesn't this indicate that your physicians in the hospital would be better off if a formulary was established by qualified people? In all these cases we named here, such as Darvon, Librium, and others, if we had a lawsuit, the doctor couldn't present any evidence about the therapeutic equivalency or biological availability because he does not have any. The basis of the selection of the drug for your type of classification is that the doctor uses it.

We have recited the examples here where the Medical Letter says in controlled tests they either are inferior or not superior.

In addition, how can the individual physician, as Dr. Mills says, depend on his own personal knowledge—susceptible to proof—to select from a therapeutic category the best drug for a particular purpose?

Obviously, of this list of available drugs I submitted, there is no test that proves that according to the Medical Letter or the National Academy of Sciences-National Research Council.

Admiral ETTER. No. I think here is a—it is primarily a matter of the physician having confidence in a particular drug for one reason or another. He has——

Senator NELSON. What I am getting at, the doctors who requested Darvon and these various other drugs I cited, didn't have any knowledge of therapeutic equivalency or biological availability. They just

had an impression or testimonial that they made for the drug. Isn't that correct?

Admiral ETTER. That, and the fact that they had prescribed that drug and had found that drug in their experience and in their feelings about it to be effective, in their own judgment. And this—we are getting down to one of the real problems here. As you well know, the practice of medicine, fortunately or unfortunately, is not a science, but it is an art, and it is frequently that art that goes along with the prescribing of the drug that does as much as the drug does. If a physician has confidence in that drug, whatever you may want to call it, he can impart that confidence to the patient. If the patient feels better on that drug—better on that drug than any other drug—that is the drug that that doctor is going to use because he has confidence in that drug. Charisma, or whatever you want to call it.

Senator NELSON. Well, I guess we went through it. I think the practice of prescribing drugs is an art, but there is some science to it, too. And the argument of the leaders of the profession, so far as I know, in every single medical discipline I know, is that we use all the best knowledge available, and all I am pointing out is that these doctors prescribing these drugs are not using the best knowledge available; they are using testimonials which, no matter how competent they are, doesn't compare with the controlled studies used by the Medical Letter or the NAS–NRC in making their determinations.

Admiral ETTER. They are doing it, Senator, as a result of prescribing this drug themselves. Certainly, no one on the basis of a testimonial from a drug company or anybody else, without having used that drug, is going to ask to have it put in the formulary, or request standardization. This follows a result of trial and error, if you will. This results in the use of the drug by that doctor in his practice of medicine.

Senator NELSON. I think, as all good doctors know, if you just prescribe diet and rest for patients, 90 percent of them get well, without any medication at all, so the fact that you gave them drugs and they got well does not prove that the drug is any good.

Admiral ETTER. I will not argue that one bit, sir. I think you are absolutely right.

Senator NELSON. Minority counsel would like to ask a question.

Mr. JONES. To what extent do you attempt to educate the individual physicians concerning the relative therapeutic efficacy of the drugs?

Admiral ETTER. There is continued education through their medical staff meetings, through the written word in the medical journals, through the Medical Letter, and any number of ways. Certainly, in our larger hospitals there are continuing medical education programs that they go through.

Mr. JONES. Is there an attempt to educate them directly through the Department, or are you relying primarily upon their own individual efforts at education? For example, take the Medical Letter concerning Darvon: How are they now to know that Darvon has been found to be no more effective than aspirin, if in fact, that is the case?

Admiral ETTER. I am glad you added that last phrase, "if, in fact, that is the case."

These are circulated and are read at the weekly and monthly meetings of the medical staff. Every effort is made to get as much information as possible to the practicing physician. Also, the headquarters divisions of the three services put out bulletins, put out monthly notices, at least, on all of the information which is put out by the National Research Council and NAS in an attempt to get this disseminated.

Now, you can lead a horse to water, I will admit, but you can't make him drink. But we do everything we can in the service to try to keep him abreast of the most recent advances in medical literature.

Could I ask Colonel McCabe if he could add to this. He has not had a chance to say anything yet.

Colonel McCabe from the Army Surgeon General's Office.

Colonel MCCABE. I think, in general, our physicians keep themselves up to date through their own devices, through the usual staff meetings.

I don't think it is practical for us to reduplicate an entire information-producing system that has grown by tradition as a way to educate physicians, namely, attendance at professional meetings and reading the available literature. It seems to me highly uneconomic to reduplicate all this.

So we expect our physicians who come to us as qualified physicians and remain with us for a long period of time, to maintain their own competence through the usual professional channels. We do provide a certain amount of information through DOD channels, but I don't think we should try to reduplicate the entire thing. It would not be economically feasible to do this.

Mr. JONES. As a practical matter, would you anticipate that the Medical Letter article concerning Darvon would affect DOD purchases of Darvon?

Colonel MCCABE. Well, I think with any of these things there is an evolutionary process and not a revolutionary process when there is change found in drug efficacy or drug use. Why does an individual physician want to use a drug or have it presented to a therapeutic agent board? One—he has read about it in the journals. Two—his colleagues have used it, perhaps, and told him they find it effective. Three—he has used it himself before he came into the service and found it effective, and, therefore, in his own best clinical judgment this is a drug which he would like to use. If he wishes this to be put in the formulary of the hospital, then he would present it to the TAB, again, who are, I think, conscientious individuals, not pharmacologists but practicing physicians.

This is not a rubber-stamp operation. There are many drugs presented that are not used, but they are in that situation that when someone is told, "No, we are not going to put this drug in the pharmacy," he is sitting in a room with these people who can discuss it, and it is not someone far distant who is, by fiat, practicing medicine for him. Someone in the same room is saying, "We don't think it is economic. We don't think it is good enough. We think there are better drugs, and better drugs you can use."

But if he is convinced it is useful and TAB feels it is probably useful, it may very well be put in the formulary. Now, many of these drugs that were put in the formulary by therapeutics agent board action, at the time they were put in there probably the consensus of medical people in the country would have been that they were useful. It is a considerable amount of time later now that the——

Senator NELSON. Which drugs are you talking about.

Colonel MCCABE. Many drugs that are now being claimed ineffective, when they were originally put on the drug list were probably considered effective.

Senator NELSON. Well, let's take a look at the biggest, most dramatic case of all, and that is the fixed combination antibiotics. The best authorities in the country were saying for the past 15 years, "It is bad medical practice to use fixed combination drugs," and that was the standard of the top medical experts in the country, in the teaching hospitals and the clinicians and the pharmacologists, and yet physicians continued right on using it.

Colonel MCCABE. That is correct.

Senator NELSON. So those were not considered by the best experts to have been the most effective drugs.

Colonel MCCABE. Another reason for the use of drugs is widespread use. In other words, if there is a large number of physicians who feel the drug is effective, that in and of itself is indication for use, perhaps. In addition to which, if these drugs are ineffective in fixed combination for the indication given, that doesn't mean the drug per se is an ineffective drug. It is just acknowledgement of the fact that when you use two drugs, you should use them, if you use them together, as individual drugs with their own dosage rather than just put them together in a fixed dosage.

Senator NELSON. Correct. But the problem of the fixed combinations was that they were not more effective than one of their ingredients, making other ingredients unnecessary and in the case of Panalba, some tests showed that the effect was antagonistic. Why expose a patient to two drugs when one will do the job.

By that test, the NAS–NRC was saying it was ineffective. They didn't mean to say that if you give somebody tetracycline and novobiocin in a fixed combination it might not affect the target organism. It probably would. But you were at the same time exposing the same patient to sensitizing with a drug he didn't need. It was not more effective than tetracycline alone.

But what I am saying is that all through the years the standard in the profession was you shouldn't use fixed combinations. But aren't we talking about something here that is kind of a mythology? We say the doctors are the ones who have to make that judgment about the drugs and that they are qualified to do so.

I have kept you past 12 o'clock, but I just want to read into the record from the HEW Task Force on Prescription Drugs and what they say on this issue we are now discussing is quite dramatic—page 26.

The Task Force said:

> Finally, it is assumed that he [the doctor] has the training, experience, and time to weigh the claims and available evidence, and thus to make the proper selections.

Everything, of course, hinges on the validity of this final assumption.

We find that few practicing physicians seem inclined to voice any question of their competency in this field. We have noted, however, that the ability of an individual physician to make sound judgments under these quite confusing conditions is now a matter of serious concern to leading clinicians, scientists, and medical educators. A distinguished pharmacologist, for example, has stated that the lack of knowledge and sophistication in the proper use of drugs is perhaps the greatest deficiency of the average physician today. Other medical leaders have pointed to the wide discrepancy in the prescribing habits of the average physician as compared to the prescribing methods recommended by panels of medical experts. Still others have commented on the continued use by the average physician of products which have been found unnecessary or unacceptable by specially qualified therapeutics committees in hospitals and clinics.

We note that the most widely used source of prescribing information is essentially a compilation of the most widely advertised drugs.

The responsibility for these and other deficiencies has been placed on various factors:

Inadequate training in the clinical application of drug knowledge during the undergraduate medical curriculum.

Inadequate sources of objective information on both drug properties and drug costs.

Widespread reliance by prescribers for their continuing education upon the promotional materials distributed by drug manufacturers.

The exceedingly rapid rate of introduction and obsolescence of prescription drug specialties.

The limited time available to practicing physicians to examine, evaluate, and maintain currency with the claims for both old drugs and newly marketed products.

The constant insistence on the idea that the average physician, without guidance from expert colleagues, does in fact possess the necessary ability to make scientifically sound judgments in this complicated field.

This is really a refutation of all the testimony made here today and by witnesses previously.

Now, Dr. Dowling, formerly chairman of the AMA Council on Drugs and a most distinguished authority, states in his recent book, "Medicines for Man, the development, regulation and use of prescription drugs"—I won't read all of the examples but I will put them in the record. I will start in the middle of page 281:

The first consisted of observations of the work of 88 general practitioners in North Carolina. Each doctor was rated on the various skills of general practice by an internist who watched him at work for three days, in the office, in the hospital, and in the patients' homes. Therapeutic skills were assessed for six common disease categories. Proper treatment was judged to have been given for anemias by only 15 percent of the doctors, for emotional problems by 17 percent, for congestive heart failure by 25 percent, for upper respiratory infections or obesity by 33 percent, and for hypertension by 43 percent.

So substantially less than half were meeting the best standards in prescribing drugs under direct observation.

Then, in Ontario, page 282:

The proportion of Ontario physicians whose work was considered unsatisfactory varied from 15 percent for the treatment of cardiac failure to 75 percent for the treatment of high blood pressure. Corresponding figures for Nova Scotia physicians ranged from 45 percent for drugs used to treat infections, to 75 percent for high blood pressure.

Then he concludes:

Under the circumstances, the number of doctors whose performance does not meet reasonable criteria of quality is too great to be tolerated.

Well, this is what we are dealing with in terms of prescribing drugs.

I shall just conclude by saying that it seems to me the Department of Defense is in a position in its hospitals to establish the highest standard and have the doctors comply. If it can't be done there, those statistics will be the same 10 years from now.

Admiral ETTER. Senator, could I make one remark here. I certainly hope that those percentages are not used to rate the physicians practicing in the military today.

Senator NELSON. Not what?

Admiral ETTER. They are not used to rate the physicians practicing in the military today. We are citing here a large number of cases of people who apparently have been judged by their peers to be found wanting. I do not think that we can certainly apply those same kind of percentages to the practicing military physician today, particularly in our military hospitals.

Senator NELSON. Well, yours are civilian doctors, you told us, and the HEW study was a general study. We are talking about prescription drugs in an area where it has been incredibly complicated. There is no criticism of the brilliance or intelligence of an individual physician. It is just the question of who knows what these claims stand for. If I were a doctor and read the Journal of the AMA, and I see Chloromycetin advertised with a bronchoscope, which gives the indication it is for upper respiratory treatment, which it is not, and see it promoted widely for a broad spectrum of anti-infective purposes, and when the Journal says that its regulations require proof that it is effective and meets proper standards, I would probably prescribe it.

There is no way for me to know, even if I were a most brilliant physician, that in fact Chloromycetin was being widely misprescribed and overprescribed in this country just because of the promotion of the drug. With respect to control of prescribing practices, it seems to be agreed upon by all the experts in the field, that we establish a formulary based upon the best knowledge there is. Neither the Veterans' Administration nor the Department of Defense in my judgment, has at least done as good a job as they ought to, based upon the procedure you have followed.

With that happy note—did you have anything you wanted to add? I do not have any objection to your arguing with me, if you had something you wanted to add to that.

Admiral ETTER. I have nothing to add.

Senator NELSON. You had some material on the names of small businesses and so on that we asked for.

Admiral ETTER. Yes, sir.

Senator NELSON. I want to thank you very much, gentlemen, for your patience today.

Admiral ETTER. Thank you.

(The complete prepared statement of Admiral Etter, above-referred to, follows, together with attachments:)

STATEMENT OF REAR ADM. H. S. ETTER, MEDICAL CORPS, U. S. NAVY, CHAIRMAN, DEFENSE MEDICAL MATERIEL BOARD

Mr. Chairman and members of the subcommittee, it is a pleasure to appear before this subcommittee to describe and discuss the manner in which the Department of Defense procures its drugs.

In the interest of brevity, I shall group those medical, dental, and veterinarian medicaments and drug products under the general term "drugs".

I will attempt to provide continuity by first presenting a brief historical background. Then I will trace a drug from a statement of requirement through its standardization and availability in the supply system, and examine its procurement files. With this approach, I can explain the inter-relationships between the users, the services, and the various defense activities involved. I have some statistics to present at the conclusion of this review, and will then attempt to answer questions by the subcommittee. Since I am a physician, and do not work directly in the procurement area, I am accompanied by specialists who can provide detailed information within their areas of expertise.

HISTORY

The Army and Navy Medical Departments pioneered the consolidated, standardized military supply systems we have today. As early as 1945, the Army-Navy Medical Procurement Agency was established by the two military Surgeons General to act as a common purchasing office for standardized medical, dental, and veterinarian supplies. In 1949, following establishment of the Air Force as a separate service, the Agency was chartered as the Armed Services Medical Procurement Agency. Subsequently, as military logistic support organizations continued to evolve, the activity was successively designated as a single manager agency (Military Medical Supply Agency); Defense Medical Supply Center; and most recently, Directorate of Medical Materiel, Defense Personnel Support Center, Philadelphia, Pa. It is a component of the Defense Supply Agency (DSA), and its acronym is "DPSC".

Medical and dental professional guidance to this Agency is provided by the Defense Medical Materiel Board (DMMB, or "the Board"). Its predecessors included most recently the Armed Services Medical Materiel Coordinating Committee, and the original Army/Navy Medical Materiel and Specifications Board.

INITIAL ACTION

"Type classification" is the term applied to the adoption of a drug as a standard item, and its subsequent inclusion in the Department of Defense (DOD) Medical Materiel Section of the Federal Supply Catalog. Type classification is a responsibility of the DMMB, but the action must be sponsored by one or more of the services.

Some drugs are type classified as standard because the worldwide commitments of the Armed Forces make it imperative that these items be readily available at all times, regardless of usage or consumption rates. Our usual motivation, is the dollar savings which accrue through our centralized purchasing and distribution system. Consequently, although type classification action may be initiated as a result of the recommendation of an individual, a presentation by industry, or a proposal by DMMB, most actions follow a determination that the volume of local purchases by field activities indicates that economies will result.

For several years, for example, we have been stock listing calcium carbonate and aminoacetic acid tablets (FSN 6505–890–1658). Type classification was requested by the Air Force in 1963. The item is a commercially available antacid which was marketed under the trade name of "Titralac tablets" by Riker Laboratories, Inc., Northridge, Calif. It is used primarily in the treatment of peptic ulcers (gastric and duodenal) and gastric hyperacidity.

In 1963 the Air Force used a statistical sampling technique to evaluate usage of nonstandard drugs. Upon noting that over $2,500 was being spent on this antacid that year by a selected group of 21 hospitals, the Air Force marked the drug for review. Air Force professional and logistic personnel concurred that there would be a continued requirement for a drug of this type, and that demand and use rates could be expected to increase, or at least remain constant. As a result of these preliminary actions, the Air Force submitted to DMMB a recommendation "to stock list an antacid comparable to Titralac tablets."

DMMB advised the Army and Navy of the Air Force action, and requested service positions.

Working from the Air Force recommendation, Army and Navy personnel reviewed their own reports, consulted their specialists, concurred with the Air

Force and the item was standardized. These reviews include consideration of such data as local purchase statistics, professional needs and uses, patient acceptance, comparison with items already stock listed, and an evaluation of known sources of supply.

ESSENTIAL CHARACTERISTICS

Since the Air Force request named only the one commercial product, it was necessary for DMMB to request Riker Laboratories for detailed information on Titralac. Riker advised that the product was patented, but agreed to provide that information—physical and chemical characteristics, test protocols, clinical and stability studies—which specifically identify the item produced by that manufacturer.

The Board used these data in the preparation of tentative essential characteristics for calcium carbonate and aminoacetic acid tablets. The essential characteristics (or EC's) are defined as those mandatory qualities required of an item to accomplish a specific professional, therapeutic, technical, or military purpose. For drugs, they include, but are not limited to—

A description of the item, and its application or use. Components of the formula, when appropriate.

Quantification, as required.

Unit of issue, type of container, package size, and any special packaging instructions.

Labeling requirements, identification data, and necessary instructions for use.

Initial proposals for type classification on an item are recorded on a "coordination worksheet for medical items pending adoption" (DMMB form 1, exhibit 1). DMMB distributed this form 1 concurrently to the services and to DPSC. Comments were solicited from all addressees. The services annotated the form 1 with their initial, and 12 months replenishment requirements.

Within DPSC, the form was reviewed in the Technical and Supply Operations Divisions of the Medical Directorate to hasten availability of the drug through the DOD wholesale distribution depots. Having determined that the EC's were adequate for preparation of a competitive specification or purchase description, DPSC returned the form 1 to the Board.

Had it been determined that no further data could be acquired, and that total available information was inadequate for preparation of a competitive specification, the case would have been returned to the services. Upon their recommendations, a determination would have been made to discontinue action, or to process the item indicating a limited source of supply.

Parenthetically, a recommendation for a limited source of supply may originate with a service, DPSC or DMMB. This action may be taken only in those instances where it has been professionally determined that the product of a specified supplier or suppliers is required to provide for the health and welfare of Armed Forces personnel or their dependents. The decision must be concurred in by all three military medical services. Such determinations normally derive from an accumulation of clinical experience, and may relate to experience prior to type classification of the drugs, or to those in the system which have accumulated a significant complaint history. I shall speak again of limited source items when I reach the statistical portion of my presentation.

Had DPSC or the services submitted conflicting recommendations regarding this particular standardization action, it would have been DMMB's responsibility to resolve them. There being none, comments were reviewed, data was finalized, and the results transcribed to an item review report (DMMB form 5, exhibit 2). Distribution follows that of the form 1, but the form 5 is an action document. It authorizes cataloging, preparation of specifications, procurement, and distribution. (This same form is used for any directed change in status, such as revised EC's or reclassification to limited standard or deleted.)

I will not describe in general terms the responsibilities and actions taken by personnel of the Technical and Supply Operations Divisions of the Medical Directorate upon receipt of an item review report.

SUPPLY OPERATIONS

A supply control study (DPSC form 2340) is developed by a supply operations commodity (item) manager to portray all data relevant to an appropriate

procurement. Such data includes considerations of the item's shelf life, the time needed to obtain an item, and the mobilization as well as operational (quantity) requirements. The supply control study, and the levels of approval that it goes through (depending on dollar values involved) becomes a backup document for DD form 1348 (DOD single line item requisition system document) used as the formal purchase request, which is forwarded from the DPSC Medical Supply Operations Division through the Medical Technical Operations Division, to the DPSC Procurement and Production Directorate (Medical Procurement Division) to obtain system stocks.

When a new item is adopted, and the item is not replacing an existing item, services estimate their initial requirements, and their 12 months replenishment requirements. These estimates are used to assist in determining the initial procurement quantity. Subsequent procurements are based on actual demands placed by customers. In the case of new items replacing items already in the system, requirements are computed from the demands applicable to the items being replaced. The announcement of the availability for issue of new items in the supply system is made to the services upon award of a contract and designation of a firm delivery date. This permits sufficient time for the services to disseminate the information to customers through service publications.

Once an item is stocked, the computation of future requirements is based on orders or demands received, as adjusted by accumulated professional information. DPSC receives an average of 3,500 to 4,000 requisitions daily from a total of about 3,700 military customers. On the basis of these demands, a monthly computerized demand forecast is constructed, and is used to compute projected system supply levels and requirements. For items centrally managed, procured, and stocked and issued, a 2-month safety level stock is needed to prevent possible depletion of inventory resulting from unavoidable delays in deliveries and/or due to surges in demands. A procurement cycle (PC) factor represents the periods between successive replenishments, or procurement frequency for an item, and takes into consideration the economic order quantity concept. The PC factor normally represents the quantity to be procured at the time the item reaches the reorder point. The procurement leadtime is expressed in months of demands anticipated to occur from dates of purchase requests to the point of delivery on the contract. When assets on hand and on order reach the level of the quantitative sum of demands anticipated during the safety level and the procurement leadtime periods, DPSC normally buys the procurement cycle quantity. Therefore, under an ideal situation, stocks should be received into the system when the quantity remaining on hand is at or just above the computed safety level quantities.

TECHNICAL OPERATIONS

The primary responsibility of the Division of Technical Operations is to conduct an effective quality assurance program to assure that medical materiel of suitable quality is procured, stocked, stored, and issued. To conduct this program effectively, it is necessary to prepare comprehensive and definitive specifications, perform preaward facility surveys of prospective contractors, analyze preaward samples to determine potential capability, participate with defense contract administration service in product inspections at contractors' plants, evaluate field complaints, and maintain an active liaison with the depots and military medical services.

DMMB provides the selection of items and the EC's to technical operations as the specification preparing activity. The Technical Operations Division seeks specification information from industry, the Food and Drug Administration, National Institutes of Health, professional committees of compendia such as the U. S. Pharmacopeia (USP) and National Formulary (NF), published literature, and military activities such as specialized service laboratories. DPSC is assisted in obtaining such data from other Government departments by using the lateral contacts developed under the Intragovernmental Professional Advisory Council on Drugs and Devices (IPADD). Required data includes, for example, chemical and physical characteristics of raw materials, dosage forms, stability and clinical studies or reports.

In the preparation of medical specifications, every effort is made to delineate the essential needs of the Government in an effort to procure pure, safe, and therapeutically effective drug products, yet minimizing efforts to seek competitive procurement. It must be recognized that military needs frequently in-

volve requirements which transcend those of some commercial products on the market. For example, military medical materiel is subjected to worldwide distribution under adverse conditions. Product stability is, therefore, a very essential element in assuring that the product is suitable when it is ultimately consumed. As a result, the standards described in DPSC specifications are at times more stringent than commercial standards in anticipation of adverse storage and transportation, and long-term storage.

It will be noted that the method of specification preparation is responsive to the rapidly changing need of the medical services. The division operates closely with the procurement personnel and obtains rapid feedback from industry on recent technological advances. Technical reviews and evaluations of such data permit updating and upgrading medical specifications. Valuable information is obtained via the complaint reporting system which involves evaluation of complaints, classification of the types of complaints, and determination of whether specifications require modifications in order to circumvent further complaints of a similar nature.

DPSC procures approximately 1,100 drug items, of which about 560 are monographed in the USP XVIII and NF XIII. About 50 percent of these items include standards that exceed those of the official compendia. Requirements specified include color limits for liquid products particularly for parenterals; expiration dates, refrigeration requirements for many items not required by the USP and NF; dissolution tests, animal tests, accelerated aging, and some clinical requirements. Also, special packaging is required for greater assurance of stability. These areas include inner and outer seals, leakage tests, special closures, label adhesion, tin plating, and vacuum packing.

In qualifying drug manufacturers, facilities of prospective contractors are inspected to determine the company's potential to produce a specification item under acceptable conditions of quality control and housekeeping. The DPSC drug standards are used as a guide in determining the acceptability of the firms. Disqualifications are usually in the areas of inadequate quality control, unacceptable housekeeping, or deficiencies in technology.

Preaward samples are requested in those instances where the capability of the firm to produce an item in conformance with the specification has not been established. Our medical laboratory performs the necessary analyses to determine compliance with specifications, and from these findings judges whether the manufacturer has the potential to produce the item specified. Other Government laboratories such as FDA and U. S. Army Medical Research Laboratory at Fort Knox are utilized to augment DPSC testing capability.

The medical laboratory is an essential segment of the total quality assurance effort. The laboratory represents an independent source of analyses by highly qualified, trained scientific personnel intimately acquainted with tests and standards of chemical, physical and bacteriological testing. The analyses performed on preaward samples, first articles, preacceptance samples and depot surveillance samples represent a critical part of the effort toward the quality objective. The laboratory also serves as a check point for inspectors when they wish to have company results verified independently.

During production, every drug product is inspected by a qualified chemist, pharmacist, or chemical engineer of the Defense Contract Administration Service of DSA. These personnel are specifically and formally trained for this function by DPSC. Inspection is performed against the applicable specifications and includes review of the laboratory analyses. The inspector may witness contractor testing or personally conduct check tests as necessary in the company laboratory.

Among the other features of the quality assurance program are: monitoring of inspection reports, participating in inspection operations, and maintaining a surveillance program over material in the system. Customer satisfaction with material supplied is evaluated by visiting depots, military hospitals and dispensaries. In this manner, DPSC maintains a direct line of communication with the medical/professional personnel with a view toward improving products and services wherever possible.

In offshore procurement of drugs further measures are taken to assure that plants and products comply with specifications. A specially trained medical service corps officer is assigned overseas for inspection of plants and surveillance of the inspection program. During production on DPSC contracts, a qualified inspector maintains residency at the plant. Prior to acceptance the active ingredients and finished product of each lot are forwarded for FDA testing in

Washington, D. C., or New York district offices. Only after such testing reveals compliance with our specifications does the inspector accept and ship the material.

In the context described above, the technical operations division completed action on this specific item review report and subsequently forwarded to procurement both the requisition from supply operations, and the definitive specifications.

PROCUREMENT

The DPSC organization is made up of a number of separate directorates, as shown in their organization chart (exhibit 3). The Directors of the Directorate of Medical Materiel and the Directorate of Procurement and Production are on an equal organizational level, and both report directly to the Commander. I point this out to show that at this point, the requisition passes from the control of a medical officer to the province of a medical procurement specialist.

Within the Directorate of Procurement and Production is a division of medical materiel which does the actual buying of drugs.

Drug purchases result from a team effort. Supply operations determines when and how much to buy. The technical staff looks at each buy and establishes the specifications. An advance copy of the purchase request is received in the procurement directorate for supply operations. This copy is utilized by the contracting officer to determine the method of procurement.

The basic statute governing procurement by the Department of Defense (title 10, USC 2304) directs that purchases shall be made by formal advertising and authorizes the use of negotiation in 17 specifically enumerated situations.

Formal advertising operates most effectively where:

(1) An adequate number of qualified suppliers have actively competed for Government contracts.

(2) They are willing to price competitively.

(3) Definitive specifications are available for the required product.

(4) There is sufficient time to carry out the inflexible formalities of the formal advertising process—preparing the invitation; permitting bidders time to prepare their bids; reviewing, opening and evaluating the bids received; and determining the responsibility and responsiveness of the low bidder.

When all of these conditions exist, formal advertising is the most successful means of securing for the Government the benefits of competition. In the absence of any one condition, however, formal advertising may be ineffective and negotiation must be used.

It should be noted that the benefits which flow from competition do not result exclusively from "formal advertising". Publicized negotiated procurements can actually become more competitive than procurements utilizing traditional invitation for bid format.

The contracting officer reviews the item's procurement history card and the bidders list for past procurement problems. Should the bidders list indicate only one known source of supply, or limited sources of supply, this would be a signal to the buyer or contracting officer that a negotiated procurement is in order. The buyer determines whether the delivery schedule allows time for formal advertising. If not, he negotiates with the supply operations division. If priorities permit, the delivery date is revised. If the urgency of need does not permit a reduction in the priority, negotiated procurement may be required to meet the required delivery date.

The hard copy of the requisition contains the specifications to be utilized for the procurement. Should the specification be new or a significant modification of an existing specification, this too could be a reason for negotiation of the procurement.

Once the contracting officer determines that negotiation or formal advertising is in order, a solicitation is issued. In the case of formal advertising, award is then made to the low responsive and responsible bidder. In cases of negotiated procurements, the contracting officer evaluates the responses received and makes a determination whether further negotiation is in order. In contrast to the formally advertised procurements, in negotiated procurements, an offeror's prices, terms and conditions are not revealed until after award.

It is the policy of the Department of Defense to place a fair proportion of its total contracts for supplies and services with small business concerns. Every

effort is made to encourage small business participation. The Defense Personnel Support Center has on the staff of the commander a group of small business specialists who, together with the resident representatives of the Small Business Administration, personally review every procurement action contemplated with an estimated value in excess of $2,500. This review for small business suitability contemplates historical evidence of small business competence and/or probability of developing small business capability. The review is documented in every procurement, reflecting all the factors considered, with negative or affirmative determinations in each case.

As is readily apparent from the statistics previously furnished by DPSC, and in spite of concerted efforts, DOD is unable to place a significant percentage of total dollars with small business. This is caused by two factors. First, the dominating high dollar value of the single source drug items, and secondly, the recent substantial acquisitions of successful small business by large corporations. It seems that as quickly as we develop responsible small business sources, they are acquired by large business. Their success with our agency appears to be *prima facie* evidence of desirability for acquisition. While the information is available in other places, experience during fiscal year 1970 reflects 17.8% of total medical procurement dollars going to small business, and 32.5% of total medical contracts. As an indication of the industry differences, the small business share of drug business in numbers of contracts is 7.7%. Conversely, in surgical instruments and dressings, it is 27%; and hospital equipment's share is more impressive at 38%.

The first buy of our example drug, calcium carbonate and aminoacetic acid tablets, was in January 1964. Following a pattern established to ensure rapid availability in the supply system, the first procurement was negotiated with the known commercial source: Riker Laboratories, Inc. All subsequent procurements have been publicized in advance, and based on the competitive specification.

The procurements, with one recent exception which was by formal advertising, have all been negotiated. Despite publication of the requirement in the business journals, DPSC had no bidders except Riker between the first buy and February 1968, although the patent (to which Riker was apparently the sole licensee) expired in October 1964. Two of our present generically-oriented bidders (Dorsey Labs and Chase Pharmaceuticals) were queried regarding their earlier failure to bid after the patent expired. The first indicated a general lack of interest in DPSC business until 1967. The latter had experimented with the tablet shortly after expiration of the patent. They were at first unable to locate a supply of the appropriate type of calcium. Later they had tableting problems. They have been active bidders since solving their production problems between late 1967 and early 1968.

Exhibit 4 depicts the detailed purchase history for 1968 and 1969. Since preparation of these data for earlier submission to this subcommittee, Abbott Laboratories has been awarded a contract at a unit price of $1.97.

During its presence on the stock list, the Drug's EC's have been modified but once, and that was in July 1968. Essentially, this revision established stated parameters for weight, content, and active ingredients.

Two specific subjects related to this drug require detailed examination: the selection of one of a family of drugs such as antacids, and the procurement of a product protected by a patent.

A recent article ("O.T.C. Antacids," by Richard P. Penna, handbook of nonprescription drugs, American Pharmaceutical Association, 2nd edition, October 1967, page 7), quotes the *Drug Trade News* to the effect that antacids on the market today include over 300 products in the form of tablets, gums, lozenges and wafers; about 175 liquid antacids; and over 100 in powder form. Most of these products are a combination of one or more of a half dozen antacids such as calcium carbonate or aluminum hydroxide, with another agent (such as magnesium carbonate) to prevent constipation which might be caused by the antacid alone.

Different patients and conditions preclude standardizing on a single generic product or dosage form. Conversely, the total numbers availab'e in the market are too great to consider standardization of all. Our supply system lists about 18 antacid products, including tablets, liquids and powder. This range allows the military physician a deliberate, reasoned choice in management of the individual patient.

Because the majority of antacids are used for treatment of chronic conditions, patient acceptability and psychosomatic considerations are particularly important. Many gastric problems originate with or are aggravated by stress. Having settled on a satisfactory prescription, the physician will frequently find that the patient becomes conditioned to the use of exactly that medication, and unexpected changes in its appearance can generate patient reactions of a magnitude not seemingly in direct relationship to that of the change. Consequently, our essential characteristics for these items are particularly sensitive to flavor, palatability, and color.

Other factors also have a major bearing on our choices among this family of drugs. I mentioned that we provide a range of antacids in order to allow a deliberate choice. We must do this because of the medicolegal responsibilities of the physician as they relate to drug usage.

Through the use of our individual hospital formularies, and the medical stock list, we encourage our physicians to prescribe generically. The Surgeons General endorse this procedure so long as we can exercise adequate quality control and quality assurance procedures throughout the entire supply system, from type classification of the item to consumption of the drug by the patient. We have, to the best of our ability, assured ourselves that these products are safe, efficacious, and economical. But what of the individual physician?

On 31 March, 1 and 2 April 1969, the Drug Information Association in collaboration with the American College of Clinical Pharmacology and Chemotherapy, American Medical Association, American Therapeutics Society, and the American Society for Pharmacology and Experimental Therapeutics conducted a symposium on "Formulation Factors Affecting Therapeutic Performance of Drug Products". Dr. Don Harper Mills, M.D., JD, clinical professor of forensic medicine and pathology, School of Medicine, University of Southern California at Los Angeles, presented a paper which stated most succinctly the problem of the medical practitioner. Dr. Mills notes the significant increase of malpractice suits in recent years, and speculates that certain statistics project that theoretically, ". . . a physician who practices for ten years faces a 100% chance of being sued." It is the duty of the physician to exercise judgment, to select, to choose—he determines what laboratory test, to consult or not consult, which consultant, what diagnosis, and finally, what therapy. It is the exercise of his judgment in the latter area which is of concern to us today. In his paper, Dr. Mills emphasizes that the duty of the physician to choose a drug which, of his own knowledge, is effective, safe and proper, is an affirmative one, and must be suceptible of proof in court. Dr. Mills includes as a fact requiring personal knowledge, the therapeutic equivalency (or biological availability) of the chemically equivalent drugs available.

We in the Department of Defense have been aware for some time of clinical indications that not all chemically equivalent drugs appeared to be therapeutically equivalent. Like most of the profession, we had originally no scientific documentation or studies. It was primarily a clinical impression supported by a large body of the profession over the same general time frame and substantiated by therapeutic experiences.

In 1966, we became sufficiently concerned that we began to search for a means of evaluating the question. The services are neither staffed nor funded for the conduct of formal clinical studies. In this connection, section 203 of title 2 of the fiscal year 1970 Defense Authorization Act (research and development) required a restriction on our medical R&D efforts to studies involving military-related diseases. The FDA did not at that time appear informed in this area, and we were somewhat reluctant to set ourselves up as experts purely on the basis of clinical indications. We chose a very small scale approach similar to that ultimately adopted by the National Academy of Science/National Research Council Task Force on drugs. We planned to obtain all possible clinical and stability data from the originator of a product and the FDA. We would then search the literature, and other possible sources such as the Intragovernmental Professional Advisory Council on Drugs and Devices (IPADD), and attempt to reach conclusions which would be supported by scientifically acceptable evidence. Limited resources precluded advancing beyond the planning stage.

DOD is grateful that it has been spared the necessity of conducting its own study. Recent widespread concern has resulted in the NAS/NRC study of drugs, which has now been reported to FDA.

FDA Commissioner Edwards is quoted in the July 1970 issue of the Journal of the American Pharmaceutical Association as follows:

"I refer, of course, to the problem of generic equivalence. It has become increasingly apparent that drug products which purport to be equivalent and which may satisfy chemical and other analytical tests of equivalence may not be therapeutically equivalent."

FDA has indicated that the problem is as complex as we had originally envisioned. They recognize that it is not presently possible to determine bioavailability in the entire armamentaria. DOD is not fully informed on all FDA action regarding bio-availability. We do know that the subject is under intensive study. We know also that the University of Michigan is currently under contract to FDA for a study titled "Generic Equivalency of Marketed Drug Products". As these data are developed, they will be required in new drug applications, and we, in turn will include them in our EC's.

In mentioning the NAS/NRC study, I have raised the collateral issue of the efficacy of drugs. This group reported to FDA that they could find no substantiating evidence that many drugs on the market are effective for treatment of the conditions for which they are labeled. DOD follows the actions of FDA very closely. It is our policy that central procurement of these drugs is suspended immediately upon FDA announcement that certification of the drug has been questioned. Unless there is an indication that the drug may be harmful, we do not suspend issues of the drug until FDA completes its administrative reviews and directs regulatory action. When that action is directed by FDA, DOD complies. Our immediate interest at the initial announcement, however, is a logistical one—we want to preclude further investments in an item which may be eliminated from the stock list.

Perhaps an example is the best explanation of our procedures when the efficacy of a drug has been questioned. Tolbutamide has been much in the news of late.

The University Group Diabetes Program (UGDP) has studied a 10 year period of the administration of tolbutamide in the treatment of diabetes. Their statistics suggest that patients on tolbutamide suffered a higher death rate from cardiovascular events than did patients on insulin or those without medication. The UGDP report was one of three presented at the meeting of the American Diabetes Association on 14 June 1970. Papers were also presented by Dr. Harry Keen, speaking for the British Diabetic Association, and Dr. J. Paasikivi of the Karolinska Institute of Sweden.

The UGDP findings were totally unexpected. No adverse effects were suspected by clinicians throughout the world.

The findings of Dr. Keen do not refute the UGDP data, since Keen's study is of shorter duration in years, and the UGDP study does not indicate an increased cardiovascular disease mortality in the tolbutamide group until about six years.

The study by Dr. Paasikivi is somewhat different design, and is difficult to compare with the UGDP work. However, the data to date are not conclusive, and other undetected risk factors may be involved.

The statement issued by Dr. Harding for the American Diabetes Association (exhibit 5), appears fully representative of the current attitude of diabetologists toward the use of tolbutamide, and the other oral agents. After consultation, DOD concurs that it would be wrong at this time to withhold tolbutamide from patients who need it. On the other hand, the indiscriminate use of this drug merely to correct mild blood sugar abnormalities must be discouraged.

To return to our example drug—when we first standardized calcium carbonate and aminoacetic acid tablets—may I digress to say that I hope the subcommittee is successful in its objective of simplified generic names. Dr. James E. P. Toman, Ph.D., of the University of Illinois College of Pharmacy has some particularly pungent and appropriate words on this subject in a 1964 McGraw-Hill book: "The Evaluation of Therapeutic Agents and Cosmetics". But, to return to my subject, when first type classified, this drug was patented, and was sold under the trade name of Titralac. Although the patent expired some months after our first purchase (October 1964), it affords us an opportunity to discuss this subject.

With respect to the patent aspects of DOD drug procurement, DPSC contracts for drugs incorporate the "authorization and consent" clause set forth in ASPR 9–102. Briefly, this clause authorizes and consents to any unnecessary

infringement of product or process patents by a contractor in the production of an item for the Government. The clause is used to take advantage of 28 U.S.C. 1498 which provides that when a contractor infringes a patent with the authorization and consent of the Government, the patent owner's only remedy is by suit against the Government. The effect of that statute on drug purchases has been considered by the Comptroller General of the United States. He has held that it would be improper to reject a low bidder's offer merely because the bidder was not licensed to manufacture a patented article. The basis for his view was that Congress enacted 28 U.S.C. 1498 specifically to enable the Government to obtain or use patented articles from any source subject to the payment of reasonable compensation to the patent owner.

In addition to the authorization and consent clause, the indemnity provisions prescribed by paragraph 9–103 of ASPR are usually included in DSA contracts for drugs. These provisions require the contractor to indemnify the Government for patent infringement liability assessed against the Government as a result of the contractor's performance. Including such provisions is generally considered to be in the Government's best interest since it enables bids to be evaluated on an equal basis. It tends to encourage suppliers to become licensees of the patent owner, and thus in a position to sell not only to the Government but to the public as well. However, DSA assumes the full financial responsibility for patent infringement by deleting the indemnity provisions from the solicitation where this would result in a lower overall cost to the Government.

Lest there be some implication from the above that DOD does not actively solicit competition in procurement of drugs, exhibit 6 is a copy of a letter which was distributed by DPSC to their entire drug bidders list. Exhibit 7 is a copy of that list.

As can be seen from exhibit 6, DOD placed no legal impediments in the way of possible bidders, whether considering patented or unpatented items. The lack of response to exhibit 6 can probably be best explained in terms of industry self-protection.

In DMMB development of EC's, and DPSC preparation of specifications, we have found that a patent is only one form of protection for a proprietary item. It is very common to develop trade secrets subsequent to the grant of a patent. These secrets need not be made available to other than a licensee of the patent holder, and may be of such significance that they affect the therapeutic capabilities of the drug.

Secondly, we find that in many instances, only one company manufactures a non-patented item. Exhibit 6 contains multiple examples of this situation. We attribute the lack of additional bidders to several factors:

1. The established bidders, by virtue of existing plant equipment, capacity, special competence, know-how, or production scheduling, is able to underprice prospective competition. (For example, a DPSC solicitation closing on 26 May 1970, contained a 50% set-aside for small business. The buy was for 376,104 bottles of glyceryl guaiacolate syrup, FSN 6505–064–8765. Small business did not bid, and we are convinced that this omission relates to inability to compete on the price.)

2. Industrial secrets are closely protected by their developers. Many of our single source items have generic EC's but we do not know the necessary manufacturing techniques. Such factors as the sequence of combining substances, humidity, working temperatures, etc., have specific effects on the finished product. Lack of knowledge in this area may preclude or delay competition (as it did with our example drug, calcium carbonate and aminoacetic acid tablets).

3. It may not be profitable to obtain a new drug application (NDA) for Government sales only, and many small manufacturers lack the resources for national distribution in the commercial market.

In summary, by using the "authorization and consent" clause, and by considering bids or offers from firms, whether or not they are owners or licensees of a patent, DOD and DSA do take advantage of and use the authority provided in 28 U.S.C. 1498 in the purchase of drugs. This practice is well known throughout the drug industry.

Gentlemen, this completes my formal statement. At your pleasure, we may now review the exhibits which are appended to the statement, or I shall endeavor to answer questions for the subcommittee.

EXHIBIT-1

Coversheet
DMMB Form 1
(Rev 10/69)

DEFENSE MEDICAL MATERIEL BOARD
TYPE CLASSIFICATION/USER TEST ACTION REQUEST

File:

From: Staff Director
To: OTSG, Department of the Army (MEDDD-SC) 3-3 Date:
OTSG, Department of the Navy (BUMED 4A) 6-3
OTSG, Department of the Air Force (AFMSHBA) 6-3

Subj:

Encl: (1) DMMB Form 1, Section A covering new item

DMMB CONTROL NUMBER

SECTION A - TYPE CLASSIFICATION (TO BE COMPLETED BY SPONSOR)

1. RECOMMENDED ITEM IDENTIFICATION: STRENGTH, PACKAGING, UNIT OF ISSUE

2. DESCRIPTION AND USE OF ITEM (FOR DRUGS, INCLUDE EFFECTIVE DATE OF NEW DRUG APPLICATION AND THERAPEUTIC CLASSIFICATION)

3. A. MANUFACTURER(S) AND ADDRESS(ES) | TRADE NAME | CAT. REF. | STRENGTH/PACKAGING | PRICE

B. FEDERAL SUPPLY SCHEDULE, CONTRACT NUMBER AND PRICE

C. LENGTH OF TIME ITEM HAS BEEN COMMERCIALLY AVAILABLE

D. $ SALES TO MILITARY ARMY NAVY AIR FORCE TIME PERIOD

4. PRELIMINARY MILITARY TEST, OR DEVELOPMENT (WHEN, WHERE, AND WHAT RESULTS)

5. SIMILARITY OR DIFFERENCE TO STOCK LISTED ITEMS (SHOW CURRENT DEMAND AND $ VALUE FOR SIMILAR ITEM)

6. WHAT ARE THE PROFESSIONAL, LOGISTIC OR COST ADVANTAGES OF THE ITEM

7. WHAT STOCK LISTED ITEMS ARE ACCEPTABLE AS SUBSTITUTES FOR ITEM IN WHAT RATIO

8. EXISTING ITEMS TO BE REPLACED(R) SUPPLEMENTED(S)	(R)	(S)	FSN OF SET, KIT, OUTFIT CONTAINING EXISTING ITEM	QUANTITY CONTAINED	REPLACEMENT RATIO (IF NOT DESIRED, ENTER NONE)

9. HAS ITEM BEEN PREVIOUSLY PRESENTED IF SO GIVE DATE, FILE REFERENCE AND COMMENT OF EACH SERVICE

☐ UNKNOWN ☐ SEE

10. RELATION TO STOCK LISTED ITEMS (REPAIR PART, COMPONENT, ACCESSORY, OR SUPPLY) AND FSN(S) OF RELATED ITEMS.

☐ NOT APPLICABLE ☐ SEE

11. EXISTING ITEMS WHICH MUST BE MODIFIED AND NEW ITEMS WHICH MUST BE CLASSIFIED.

☐ NOT APPLICABLE ☐ SEE

12. STATE REQUIREMENTS FOR SERVICE DATA, REPAIR PARTS PAMPHLET, HIGH MORTALITY PARTS TO BE SUPPLIED WITH ITEM AND MINIMUM PARTS TO BE TYPE CLASSIFIED

☐ NOT APPLICABLE ☐ SEE

DMMB FORM 1 TYPE CLASSIFICATION/RECLASSIFICATION SECTION A

CONTROL NO

SECTION C - TECHNICAL/LOGISTIC DATA (To Be Completed by DMMB Staff)

1. RECOMMENDED ITEM IDENTIFICATION, STRENGTH, PACKAGING, UNIT OF ISSUE

2. RECOMMENDED BY (LIST ALL PERTINENT REFERENCES AND WHERE FILED)

3. ESSENTIAL CHARACTERISTICS

4. REPLACED FSN | TO BE RECLASSIFIED TO | TO BE USED AS SUBSTITUTE FOR | RATIO

5. PROVIDE REPAIR PARTS PAMPHLET ☐ | SERVICE DATA ☐ | NEITHER ☐

6. OTHER

SIGNATURE AND DATE OF PREPARING OFFICIAL | SIGNATURE AND DATE OF APPROVING OFFICER

DMMB FORM 1 TYPE CLASSIFICATION/RECLASSIFICATION SECTION C

DMMB Form-5

EXHIBIT-2

DEFENSE MEDICAL MATERIEL BOARD ITEM REVIEW REPORT

TO: COMMANDER, DEFENSE PERSONNEL SUPPORT CENTER

FEDERAL STOCK NUMBER	AVAILABILITY	UNIT OF ISSUE	NOTES

ITEM IDENTIFICATION:

SUPPORTING DATA

CONTROL NO.	APPROVED FOR THE DMMB:	DATE:
FSN:	Staff Director	IRR SERIAL NO.

EXHIBIT-3

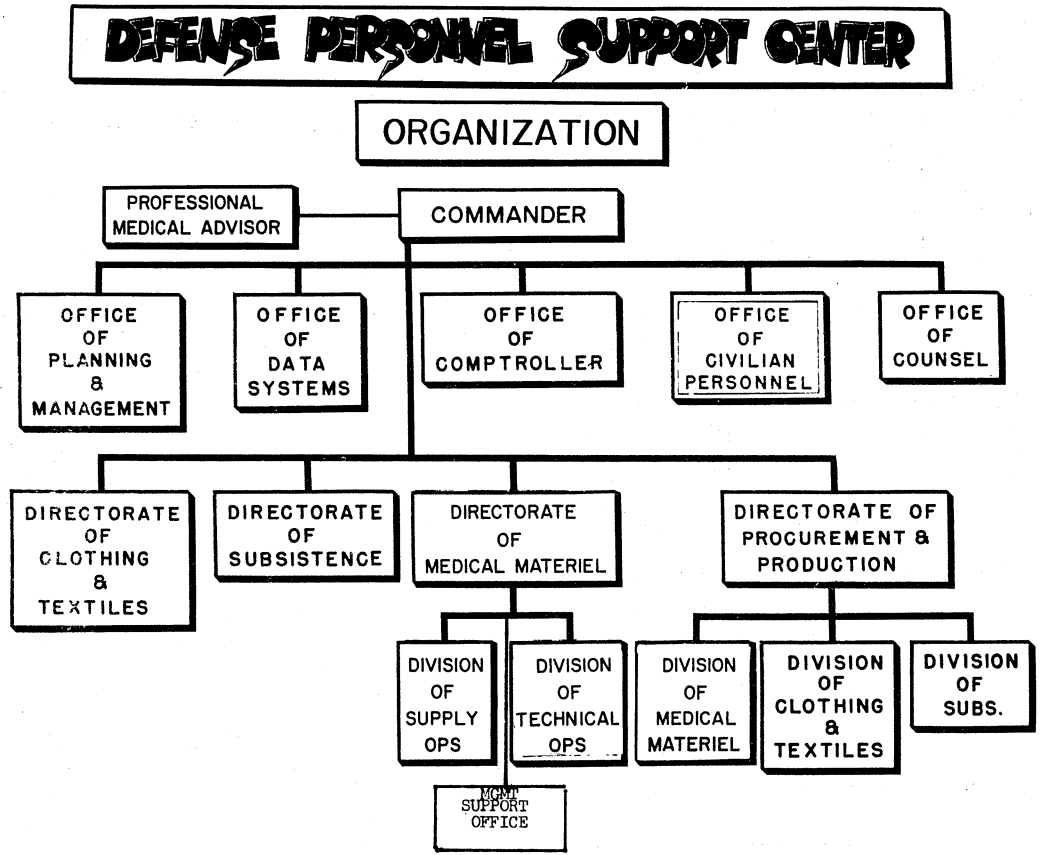
DEFENSE PERSONNEL SUPPORT CENTER
ORGANIZATION
PROFESSIONAL MEDICAL ADVISOR
COMMANDER
OFFICE OF PLANNING & MANAGEMENT
OFFICE OF DATA SYSTEMS
OFFICE OF COMPTROLLER
OFFICE OF CIVILIAN PERSONNEL
OFFICE OF COUNSEL
DIRECTORATE OF CLOTHING & TEXTILES
DIRECTORATE OF SUBSISTENCE
DIRECTORATE OF MEDICAL MATERIEL
DIRECTORATE OF PROCUREMENT & PRODUCTION
DIVISION OF SUPPLY OPS
DIVISION OF TECHNICAL OPS
DIVISION OF MEDICAL MATERIEL
DIVISION OF CLOTHING & TEXTILES
DIVISION OF SUBS.
MGMT SUPPORT OFFICE

EXHIBIT-4

FSN 6505-890-1658
CALCIUM CARBONATE AND AMINOACETIC
ACID TABLETS, 500s, BOTTLE

CONTRACT NUMBER	AWARD DATE	METHOD OF PROCUREMENT	QUANTITY SOLICITED	QUANTITY AWARDED	SUCCESSFUL BIDDER/ OFFEROR	UNIT PRICE	TOTAL PRICE	UNSUCCESSFUL BIDDERS/ OFFERORS	UNIT PRICE
68-C-2746	6 Feb 68	N	11,952	11,952	Riker	$ 3.48	$ 41,593	None	
68-C-2952	21 Feb 68	N	15,216	15,216	Riker	3.48	52,952	*Dorsey	$ 3.25
68-C-4568	20 Jun 68	N	11,904	11,904	Chase	2.84	46,076	Dorsey	3.15
								Riker	3.48
68-C-4633	26 Jun 68	N	16,224	16,224	Chase	2.84	46,076	Dorsey	3.00
								Riker	3.48
69-C-2118	13 Dec 68	N	11,280	11,280	Chase	2.75	31,020	Riker	3.48
69-C-2707	31 Jan 69	N	20,544	20,544	Chase	2.67	54,852	**Strong Cobb	.806
								Riker	3.40

* Low offer rejected due to an unsatisfactory pre-award survey.

** Low offer rejected in that the samples submitted failed to conform to the Government's requirements.

Titralac (Riker)

EXHIBIT 5

EXTRACT FROM AN AMERICAN DIABETES ASSOCIATION LETTER TO MEMBERS DATED 17 JUNE 1970, AND DISTRIBUTED FOLLOWING THE 30TH ANNUAL MEETING OF THE AMERICAN DIABETES ASSOCIATION, WHICH ENDED ON 14 JUNE 1970:

AT A PRESS CONFERENCE THAT FOLLOWED THE SCIENTIFIC SESSION, A STATEMENT GIVING THE ASSOCIATION'S POSITION WAS READ BY DR. ROBERT C. HARDIN, RETIRING PRESIDENT. SO THAT MEMBERS OF THE ASSOCIATION WILL BE FULLY AWARE OF THIS ORGANIZATION'S PRESENT VIEWPOINT ON THE SUBJECT, THE STATEMENT TO THE PRESS IS REPRINTED IN FULL BELOW:

THE AMERICAN DIABETES ASSOCIATION COMMENDS THOSE PERSONS WHO HAVE REPORTED STUDIES CONCERNING THE EFFECTS OF THERAPY ON THE COURSE OF DIABETES AND ITS COMPLICATIONS AT THIS ANNUAL MEETING.

NEW DATA HAVE BEEN PRESENTED, SOME OF WHICH RAISE QUESTIONS ABOUT THE EFFICACY AND SAFETY OF ORAL THERAPY. HOWEVER, IT IS DIFFICULT TO GENERALIZE FROM THESE UNPUBLISHED DATA. CAREFUL EVALUATION OF THE COMPLETE DATA AND FURTHER STUDY WILL BE NECESSARY TO REACH FINAL CONCLUSIONS.

AT THIS POINT, THE EVIDENCE PRESENTED DOES NOT APPEAR TO WARRANT ABANDONING THE PRESENTLY ACCEPTED METHODS OF TREATMENT OF DIABETES -- DIET, DIET WITH ORAL AGENTS, OR DIET AND INSULIN AS INDICATED.

EXHIBIT-6

DEFENSE SUPPLY AGENCY
HEADQUARTERS, DEFENSE PERSONNEL SUPPORT CENTER
2800 SOUTH 20TH STREET
PHILADELPHIA, PENNSYLVANIA 19101

IN REPLY REFER TO DPSC-PM

JAN 27 1969

MEMORANDUM TO: PROSPECTIVE MEDICAL BIDDERS

Government procurement officers are required by law and regulations to procure competitively to the maximum extent possible. This, of course, benefits all of us as taxpayers.

This Center is experiencing considerable difficulty in obtaining competition on many items. Enclosed you will find a partial listing of these items. I am requesting that you review the listing to determine if your company may possibly be able to participate in future solicitations for these items. Following your review, it is important that I have your reaction. Are you interested? If not, why? Are there aspects of our methods or contractual requirements that are not entirely clear to you?

I would welcome any comments that you may wish to submit in writing and am available at any time in my office for further discussion.

I am looking forward to your continued support and cooperation.

Encl

ALLAN J. SNYDER
Lt Colonel, USA
Chief, Division of Medical Materiel
Directorate of Procurement & Production

FSN & NOMENCLATURE

6505-045-3466
Sodium Iothalamate Injection

6505-050-3078
Mellaril Tablets

6505-052-1367
Vistaril Parenteral Solution, 50 mg, per cc, 10 cc (Hydroxyzine Hcl. Inj.)

6505-055-5716
Lidocaine-Hydrochloride

6505-059-9017
Chlordiazepoxide Hydrochloride Caps.

6505-064-8731
Sodium Diartrizvate

6505-065-4214
Phenergan Suppositories-Rectal

6505-066-4875
Sodium Liothyronine Tablets, USP, 1000's

6505-071-0610
Metostix Reagent Strips

6505-071-6547
Triamcinolone Acetonide Cream, 0.5%, 8 oz.

6505-074-2760
Iodipamide Sodium Injection, NF

6505-074-2981
Dioctyl Sodium Sulfosuccinate & Ferrous Fumarate Capsules, 1000's

6505-074-3169
Danthron and Calcium Bis

6505-074-4702
Dyshenoxylate Hcl. & Atropine Sulfate Tablets, 500s

6505-074-9914
(Hygroton Tablets - 100s) Chlorthalidone Tablets

6505-082-2651
Meperidine Hydrochloride Inj.

6505-082-2652
Meperidine Hydrochloride Inj., NF, 75 mg, Cartridge Needle Unit, 1 cc, 20s

FSN & NOMENCLATURE

6505-082-2659
Amitriptyline Hydrochloride Tabs.

6505-082-2658
Nitrofurantoin Oral Suspension

6505-082-2669
Measles Virus Vaccine, Live

6505-082-2672
Streptokinase-Streptodornase Tablets

6505-082-2684
Diethylpropion Tablets, 75 mg, 100s

6505-089-3424
Ephedrine Hydrochloride Phenobarbital Potassium Iodide

6505-104-5400
Corticotropin Injection, USP, 40 USP Units

6505-106-9000
Amyl Nitrite, NF Ampuls, 0.33 cc (5 minims), 12s

6505-108-4965
Atropine Injection, 2 mg, 1 cc

6505-108-8500
Dimercaprol Inj., USP, 10%, 5 cc, 10s

6505-110-6575
Blood Detection Tablets, 60s

6505-113-9295
Chlorquine Phosphate Tablets, 0.5 Gm

6505-113-9310
Chloroquine Phosphate Tablets, USP, 0.5 Gm, 1000s

6505-114-5025
Cocaine Hydrochloride, USP, 0.5 Gm (7-1/2 gr) 6's

6505-116-0100
M-Cresylacetate, 1 oz.

6505-116-0200
Crotamiton Cream, 10%, 60 Gm

FSN & NOMENCLATURE

6505-116-5495
Bishydroxycoumarin Tablets, USP, 50 mg (3/4 gr) 100s

6505-116-5498
Diethylcarbamazine Citrate Tablets, USP, 50 mg (3/4 gr) 100s

6505-116-8350
Diphenhydramine Hydrochloride Capsules, USP, 50 mg (3/4 gr) 100s

6505-116-9660
Dimenhydrinate Tablets, USP, 50 mg (3/4 gr) 100s

6505-116-9670
Dimenhydrinate Tablets, USP, 50 mg 1000s

6505-126-9425
Merceptomerin Sodium, USP, Sterile 1/4 gr

6505-128-5675
Thimerosol, NF, 1/4 oz

6505-129-5517
Merphine Injection, USP, 16 mg (1/4 gr) tube w/Needle

6505-129-5518
Morphine Injection, USP, 16 mg (1/4 gr), 5s

6505-130-1960
Nitrofurazone Ointment, NF, Water Soluble, 1:500, 1 lb (453:6 gm)

6505-138-4610
Protein Hydrolysate Injection, USP, 1000cc, 6s

6505-140-5010
Silver Nitrate Solution, Ammoniacal, 2 cc

6505-146-4425
Sulfisoxazole Tablets

6505-147-0300
Tar Compound, Ointment, Modified 1# Jar

6505-147-1860
Tetracaine Hydro Tabs, 100 mg, 1.5 gr, 100/Btl

6505-153-8223
Ethyl Chloride, NF, 100 Gm

FSN & NOMENCLATURE

6505-153-8728
Methiodal Sodium Inj., USP, 40%

6505-153-8774
Hexylresorcinol Pills, USP, 0.2 Gm (3 gr) 5s

6505-153-9719
Ergonovine Maleate Tablets, 0.2 mg 100s

6505-160-7000
Plague Vaccine, 20 cc, Potency 18 months

6505-160-7875
Rabies Vaccine, USP, 14 Doses, Potency 6 months

6505-160-8200
Scarlet Fever, Streptococcus Toxin 50 Tests

6505-160-9510
Sponge Absorbable Gelatin, USP

6505-160-9500
Sponge Absorbable Gelatin, USP, 20 x 60 x 70mm, 4's

6505-160-9510
Sponge Absorbable, Gelatin, USP, 80 x 125 x 10mm

6505-161-0600
Oxytetracycline Hydrochloride for Injection

6505-161-2950
Thrombin, Topical, Bovine, 5000 Units

6505-162-1520
Yellow Fever Vaccine, USP, 20 doses

6505-195-8674
Sodium Polyanethol Sulfonate, Reagent, 10 Gm

6505-200-6984
Oatmeal, Colloidal Concentrate, 18 oz.

6505-201-1261
Diphenhydramine Hydrochloride, USP, 1/2 oz.

6505-225-7499
Prednisolone Teritary Butylacetate Susp., 20 mg, 1 cc

6505-225-9220
Methylglucamine Diatrizoate - Sod Diartrizeate Inj.

FSN & NOMENCLATURE

6505-226-1202
Sodium Oxacillin Capsules, 48s (48 Months Potency)

6505-226-1203
Test Strips and Color Chart

6505-261-7240
Lidocaine Hydrochloride with Epinephrine Inj. Cartridges, 2%, 1.8cc, 50s

6505-261-7245
Benzethonium Chloride Tablets, 0.25 Gm (4 gr) 80s

6505-261-7251
Propylhexedrine Inhalant, NF, 0.25 Gm

6505-281-2056
O-Tolidine Dihydrochloride Tabs, 0.6 mg, 150/BTL

6505-285-2038
Acetyl Sulfisoxazole Oral Susp.

6505-286-9867
Meralluride Injection, USP, 1 cc, 12's

6505-286-9868
Mucolytic Detergent Solution, 500 cc

6505-290-6031
Bilirubin Test Kit

6505-298-2870
Corticotropin Inj., Repository, USP, 40 Units/cc, 5 cc

6505-299-8013
Insulin Isophane Suspension

6505-299-8014
Chloroquine Hydrochloride Inj., 5 cc, 10s

6505-299-8126
Hyaluronidase for Injection

6505-299-8149
Primaquine Phosphate Tablets

6505-299-8172
Lactic Acid, USP

6505-299-8274
Oxytetracycline for Susp., Oral 1.5 Gm

FSN & NOMENCLATURE

6505-299-8280
Iopanoic Acid Tablets, 0.5 Gm, 6s

6505-299-8285
Rabies Vaccine, Veterinary

6505-299-8354
Histoplasmin, 0.01 cc

6505-299-8600
Coccidioidin, 1 cc, 10 Tests

6505-299-8608
Oxytetracycline-Ophthalmic Ointment

6505-299-8614
Procainamide Hydrochloride Inj.

6505-299-8671
Selenium Sulfide Detergent Susp.

6505-299-8739
Chlortetracycline Hydrochloride Ophthalmic, Ointment, 1%, 1/8 oz. (3.5 Gm)

6505-299-8747
Chlortetracycline Hydrochloride Ointment, 3%, 1/2 oz.

6505-299-9496
Levarterenol Bitartrate Injection, 0.2%, 4cc, 10s

6505-299-9516
Methimazole Tablets, USP, 5 mg, (1/12 gr), 100s

6505-299-9663
Procaine Hydrochloride Injection, USP, 1%, 0.5 cc, 50s

6505-299-9666
Cyclopentolate Hydrochloride Ophthalmic Solution, 1%, 15cc

6505-299-9667
Protamine Sulfate Injection, NF, 10 mg, per cc, 5 cc, 6's

6505-299-9669
Phentolamine Methanesulfonate for Injection, USP, 5 mg, (1/12 gr), 6s

6505-299-9672
Silver Nitrate Applicators, 6 inch, 100s

FSN & NOMENCLATURE

6505-299-9675
Insulin Injection, Isophane, U-40, 10 cc, Potency 18 Months

6505-515-1577
Propantheline Bromide Tablets, USP, 15 mg, 100s

6505-526-0394
Dextroamphetamine Sulfate & Amobarbital Capsules

6505-527-2056
Chlorpromazine Hydrochloride Tablets, USP, 100 mg (1-1/2 gr) 500s

6505-527-6885
Probenecid Tablets, USP, 0.5 Gm (7-1/2 gr) 100s

6505-543-6541
Erythromycin Ethylcarbonate for Oral Susp.

6505-543-7914
Chlorothiazide Tablets, NF, 0.5 Gm, 1000s

6505-551-8682
Promazine Hydrochloride Tablets, 50 mg, (5/6 gr), 500s

6505-551-8683
Promazine Hydrochloride Inj. 50 mg, (5/6 gr) per cc, 2 cc, 25s

6505-576-8842
Lidocaine Hydrochloride with Epinephrine Injection, Cartridges, 2%, 1.8 cc, 50s

6505-579-9293
Hemoglobin Diluent, Dehydrated, 12s

6505-579-9294
Penicillinase for Injection, 800,000 units

6505-579-9715
Hydroxyzine Hydrochloride Tablets, 10 mg, 500s

6505-579-9717
Hydroxyzine Hydrochloride Tablets, NF, 25 mg, 500s

6505-582-2020
Methylergonovine Maleate Injection, 0.2 mg (1/300 gr) 1 cc, 12s

6505-582-4209
Sodium Diatrizoate Injection, USP, 50%, 30 cc, 25s

FSN & NOMENCLATURE

6505-582-4590
Chlorpromazine Hydrochloride Tablets, 25 mg, 500s

6505-582-4604
Hexylcaine Hydrochloride Injection, 1%, 30 cc

6505-582-4868
Diphenhydramine Hydrochloride Capsules, USP, 50 mg, 1000s

6505-582-5342
Chlorhydroxyquinolene Ointment, 1 lb jar

6505-582-5370
Procainamide Hydrochloride Capsules, 0.25 gm, 100s

6505-582-5434
Fluorescein Sodium Applicators, 50s

6505-584-0398
Propantheline Bromide Tablets, USP, 15 mg, 1000s

6505-584-2894
Sulfamethoxypyridazine Tablets, 0.5 Gm (7-1/2 gr), 1000s

6505-584-2895
Hydralazine Hydrochloride Tablets, 100s

6505-584-3131
Lidocaine Hydrochloride Jelly, 2%, 30 cc

6505-584-3179
Methylphenidote, Hydrochloride Tablets, 10 mg (1/6 gr), 100s

6505-584-3277
Promethazine Hydrochloride Tablets, USP, 25 mg, (3/8 gr), 1000s

6505-584-3280
Promethazine Hydrochloride Inj., USP, 25 mg (3/8 gr), per cc, 10 cc

6505-584-3669
Perphenazine Tablets, 4 mg, 500s, (1/16 gr)

6505-597-5841
Streptokinase, 125,000 Units

6505-597-5843
Chlorpromazine Hydrochloride Inj. USP, 25 mg (3/8 gr) per cc, 2 cc, 6s

FSN & NOMENCLATURE

6505-598-6115
Lidocaine Hydrochloride Inj., NF, 0.5%, 50 cc

6505-598-6116
Lidocaine Hydrochloride Inj., USP, 1%, 50 cc

6505-598-6117
Lidocaine Hydrochloride, USP, 2%, 20 cc

6505-606-3409
Mucolytic Detergent Solution, 60 cc

6505-616-7856
Bethanechol Chloride Tablets, USP, 10 mg, 100s

6505-616-7861
Acetone Test Tablets, 100s

6505-616-9068
Glutethimide Tablets, 0.5 Gm, (7-1/2 gr) 500s

6505-616-9128
Nystatin Tablets, Vaginal

6505-616-9129
Nystatin Tablets, USP, Oral, 500,000 Units, 100s

6505-616-9517
Prednisolone Sodium Phosphate Ophthalmic Solution, USP, 5 cc

6505-616-9518
Prednisolone 21-Phosphate Ophthalmic Ointment, 0.25 %, 3.5 gm (1/8 oz)

6505-619-8388
Chlorpromazine Hydrochloride Capsules, 75 mg, 250s

6505-619-8620
Glyceryl Trinitrate Tablets, USP, 0.6 mg (1/100 gr), 100s

6505-656-0483
Erythromycin for Injection, USP, 1 gm, 5s

6505-656-1022
Hydroxyprogesterone Caproate Injection, 1.25 mg per cc, 10 cc

6505-656-1345
Prochlorperazine Maleate Capsules 15 mg (1/4 gr), 250s

FSN & NOMENCLATURE

6505-656-1346
Prochlorperazine Maleate Capsules 15 mg (1/4 gr), 1500s

6505-656-1347
Prochlorperazine Maleate Tablets, 5 mg (1/12 gr), 500s

6505-656-1468
Senna Pod Extract Tablets, 100s

6505-656-1610
Prochlorperazine Edisylate Injection, 5 mg per cc, 2 cc, 100s

6505-660-0083
Norethandrolone Tablets, 10 mg (1/6 gr), 500s

6505-660-0132
Chloramphenicol for Ophthalmic Solution, USP

6505-660-0466
Dienestrol Cream Vaginal, 0.1%, 2-3/4 oz (78 gm)

6505-660-1601
Methocarbamol Tablets, 0.5 gm (7-1/2 gr), 500s

6505-660-1676
Kanamycin Sulfate Injection, 3 cc

6505-660-1720
Propoxyphene Hydrochloride Capsules, USP, 32 mg (1/2 gr), 100s

6505-660-1743
Chlorzoxazone Tablets, 250 mg, 1000s

6505-660-1765
Iron Dextran Complex Injection, 10 cc

6505-660-1798
Benzonatate Capsules, 100 mg (1-1/2 gr), 100s

6505-663-2636
Sodium Chloride-Sodium Bicarbonate Mixture

6505-663-2701
Chloramphenicol Palmitate, Oral Suspension, USP, 60 cc

6505-664-0857
Acetazolamide Tablets, 250 mg (4 gr), 100s

FSN & NOMENCLATURE

6505-664-4814
Undecylenic Acid Ointment, Compound, NF, 1 oz

6505-680-1908
Primidone Tablets, USP, 0.25 gm (4 gr), 100s

6505-680-2326
Pentaerythritol Tetranitrate Tablets, 80 mg, 500s

6505-680-2787
Antivenin Kit, Polyvalent, 1 Dose

6505-682-6536
Procaine Penicillin G Suspension, USP, 600,000 Units in Aqueous Suspension, Cartridge-Needle Unit, 1 cc, 20s

6505-682-6538
Benzathine Penicillin G and Procaine Penicillin G Suspension, Sterile, 600,000 Units, 2 cc, Cartridge-Needle Unit, 1-1/4 inch, 20s

6505-682-8194
Triamcinolone Acetonide Cream, Topical

6505-684-8625
Vasopressin Injection, USP, 1 cc, 10s

6505-685-5190
Oxytetracycline-Polymixin B Powder (Ear-drops)

6505-685-5335
Norethylnodrel with Mestranol Tablets, 10 mg, 500s

6505-685-5512
Benadryl Ampoules, 50 mg per 1 cc, 10s

6505-686-1029
Estrogenic Substances

6505-687-3662
Nitroglycerin Tablets, USP, 0.3 mg (1/200 gr), 100s

6505-687-4417
Atropine Injection 2 mg, 1 cc, 72s

6505-687-7901
Aspirin / Ethoheptazine Tablets, 1000s

FSN & NOMENCLATURE

6505-687-8047
Benzathine Penicillin G Suspension, Sterile, USP, 1,200,000 units in Aqueous Suspension, Cartridge-Needle Unit, 2 cc, 20s

6505-687-8075
Furazolidone & Nifuroxime Suppository, NF, Vaginal, 24s

6505-687-8205
Cetylpyridinium Chloride Lozenges, 1.5 mg, 400s

6505-687-8458
Benzathine Penicillin G Suspension, Sterile, USP, 600,000 Units in Aqueous Suspension, Cartridge-Needle Unit, 1 cc, 20s

6505-687-8459
Procaine Penicillin G and Potassium Penicillin G in Oil

6505-687-8470
Pancreatic Dornase, 100,000 Units

6505-687-8486
Diphenylhydantoin Tablets, 100s

6505-689-9245
Thiordazine Hydrochloride Tablets

6505-689-9253
Norethynodrel w/Mestranol Tablets, 100s

6505-720-9680
Succinylcholine Chloride, 1 gm

6505-721-8899
Hydroxyzine Hydrochloride Syrup

6505-723-5015
Hemorrhoidal Suppositories w/Hydrocortisone Acetate, 12s

6505-725-6992
Darvon Pulvules, 500

6505-728-2624
Flurandrenolone Cream

6505-735-3559
Chlopromazine Hydrochloride Tablets, 100s

FSN & NOMENCLATURE

6505-753-4702
Phenelzine Sulfate Tablets, 100s

6505-753-4956
Streptomycin Sulfate Injection, USP, 20 gage, 1-1/4 inch, Sterile Hypodermic Needles attached to Cartridges, w/one Plastic Cartridge Syringe, 2.5 cc, 20s

6505-753-5043
Chloroquine and Primaquine Phosphate

6505-753-9518
Insulin, Zinc Suspension

6505-753-9594
Sodium Acetrizoate 7, Polyvinyl Pyrrolidone

6505-753-9609
Hydrocortisone Sodium Succinate for Injection, 100 mg

6505-753-9611
Hexachlorophene Salicylic Acid and Sulfur Ointment

6505-753-9612
Triprolidine Hydrochloride & Pseudo Ephedrine Hydrochloride Syrup

6505-753-9615
Triprolidine Hydrochloride & Pseudo Ephedrine Hydrochloride Tablets

6505-753-9860
Allantoin Sulfanilamide and Aminoacridine Hydrochloride Ointment

6505-754-0076
Mepivacaine Hydrochloride Injection

6505-754-0080
Mepivacaine Hydrochloride Injection

6505-754-0085
Mepivicaine Hydrochloride Injection

6505-754-0086
Dicyclomine Hydrochloride, Doxylamine Succinate & Pyridoxine Hydrochloride

6505-754-0280
Chloramphenicol Sodium Succinate for Injection, USP, Equiv. to 1 gm Chloramphenicol, USP, 10s

FSN & NOMENCLATURE

6505-754-0395
Methocarbamol Injection

6505-754-2437
Triethanol Polypepticle Oleate Condensate Ear Drops

6505-754-2486
Dextroamphetamine Sulfate and Amobarbital Capsules, 250s

6505-754-2507
Dextroamphetamine Sulfate and Amobarbital Capsules, 250s

6505-754-2580
Insulin, Zinc Suspension

6505-754-2654
Tetrahydrozoline Hydrochloride Solution, 0.1%, 1 Pt

6505-754-2655
Tetrahydrozoline Hydrochloride Solution

6505-754-2656
Tetrahydrozoline Hydrochloride Solution

6505-754-2724
Aspirin Amphetamine Sulfate & Phenacetin Tablets, 500s

6505-754-2727
Rabies Vaccine, USP, Duck Embryo, 7 Doses

6505-754-2797
Salicylazosulfapyridine Tablets, 0.5 gm, 500s

6505-754-2804
Urease Test Tablets

6505-764-3313
Chlorzoxazone & Acetominophen Tablets, 500s

6505-764-3542
Penthizane

6505-764-9014
Dipyridamole Tablets

6505-765-0582
Cantanol Tablets, 0.5 gm, 500s

FSN & NOMENCLATURE

6505-765-0824
Hydroxyzine Pamoate Capsules

6505-770-8345
Nalidixic Acid Tablets

6505-773-6545
Mandelamine Suspension Forte, 8 Fl oz

6505-781-3111
Isosarbide Dinitrate Tablets, 40 mg, 100's

6505-782-2650
Poliovirus Vaccine, Live, Oral Types 1, 2 & 3, 10 Dose

6505-782-2651
Poliovirus Vaccine, Live, Oral, Types 1, 2 & 3, 100 Dose

6505-782-2688
Acetyleysteine Solution, 20%, 30 cc, 3s

6505-782-3901
Sodium Sulfacetamide & Prednisolone Acetate Ophthalmic Suspension, 5 cc

6505-782-6427
Undecylenic Acid Ointment Compound, NF, 1 cc, 160s

6505-782-6483
Triamcinalone Acetonide Solution, .0066%, 150 gm, In Aerosal Dispenser (Kenalog spray)

6505-782-6485
Demethylchlortetracycline Hydrochloride Tablets

6505-782-6506
Cedilanid-D Ampuls, 0.2 mg per cc, 4 cc, 12s

6505-782-6761
Tripolidone Hydrochloride Pseudoephedrine Hydrochloride Syrup

6505-782-6762
Zarontin Capsules, 0.25 gm, 100s

6505-783-7218
Valiom Tablets, 5 mg, 500s

6505-784-4976
Propoxyphene Hydrochloride, Aspirin, Caffeine & Phenacetin Capsules, 500s

FSN & NOMENCLATURE

6505-784-4977
Sodium Iothalamate Injection

6505-785-4357
Lidocaine Ointment, 5%, 35 gm

6505-786-8747
Oxyphenbutazone Tablets, 100 mgm, 1000s

6505-817-0360
Trimeprozine Tablets, 2.5 mgm (1/25 gr), 500s

6505-817-2215
Trifluoperazine Hydrochloride Tablets, 1 mgm (1/60 gr), 500s

6505-817-2227
Oxytetracycline Oral Suspension, 1 Pint each cc

6505-817-2228
Phenylbutazone Tablets, 100 mgm (1-1/2 gr), 100s

6505-817-2279
Chlorpropamide Tablets, 250s

6505-817-2630
Quinacrine Hydrochloride Tablets, USP, 0.1 Gm (1-1/2 gr), 500s

6505-823-7903
Testosterone Enanthate & Estradiol Valerate Inj, 2 cc

6505-823-7924
Nitrofurazone Vaginal Suppositories, 12s

6505-823-7956
Dexamethasone 21-Phosphate Neomycin 0.5% Ophthalmic Ointment 3.5 Gm, 6s

6505-823-7957
Dexamethasone Phosphate-Neomycin Ophthalmic Solution, 5 cc

6505-823-7985
Diphenylhydantoin Sodium, USP, 0.25 Gm

6505-823-8041
Atropine Injection, 2 mg (1/32 gr)

6505-853-4792
Epinephrine Injection, USP, (1/1000) Cartridge-Needle, Unit, 1 cc, 20s

FSN & NOMENCLATURE

6505-853-4799
Imipramine Hydrochloride Tablets, 25 mgm (3/8 gr) 100s

6505-853-6915
Levallorphan Tartrate Injection, USP, 1 mg/cc 1 cc, 6s

6505-853-6916
Phenmetrazine Hcl Tablets, N.F., 25 mg, 1000s

6505-853-8109
Trifluoperazine Hydrochloride Tablets, 2 mgm (1/30 gr) 500s

6505-853-8114
Antigen, VDRL, 0.5cc, 10s

6505-854-2239
Chloroquine & Primaquine Phosphate Tablets, 6s

6505-854-2242
Guanethidine Sulfate Tablets, 10 mgm (1/6 gr) 100s

6505-854-2499
Phytonadione Inj. 10 mg. 1 cc 6s

6505-854-2504
Halothane, 125 cc

6505-857-8238
Camphorated Parachlorophenol, NF, 1 oz, (28.35 Gm)

6505-864-5221
Hydroxyprogesterone, Caproate Inj. 0.25 Gm per cc, 5 cc

6505-864-7618
Morphine Inj. USP, 15 mgm Cartridge Needle Unit, 1 cc, 20s

6505-864-7619
Morphine Inj. USP, 10 mgm, Cartridge Needle Unit, 1 cc, 20s

6505-864-8091
Codeine Phosphate Injection, USP, 60 mgm Cartridge Needle Unit, 1 cc, 20s

6505-864-8092
Codeine Phosphate Inj. USP, 30 mgm Cartridge Needle Unit, 1 cc, 20s

6505-864-8094
Meperidine Hydrochloride Inj. USP, 50 mg Cartridge Needle Unit, 1 cc

FSN & NOMENCLATURE

6505-864-8095
Meperidine Hydrochloride Inj. USP, 100 mgm Cartridge Needle Unit, 20 s

6505-864-8096
Meperidine Hydrochloride Inj. USP, 50 mgm. Cartridge Needle Unit, 1 cc, 20s

6505-889-5794
Nystatin Ointment, USP, 30 Gm.

6505-889-9033
Bisacodyl Suppositories, 10 mg, 50s

6505-889-9034
Bisacodyl Tablets, 5 mgm, 1000s

6505-890-1092
Phosphatabs (Alkaline) 48s Test Kit

6505-890-1093
Pyrvinium Pamoate Oral Susp 2 fl oz.

6505-890-1110
Diphenylhydantoin Oral Suspension, NF, 1/2 pt. (237 cc)

6505-890-1112
Brompheniramine Maleate Tablets, 12 mgm

6505-890-1186
Methylprednisolone Acetate Susp., 40 mg, per cc, 5 cc

6505-890-1208
Prochlorperazine and Isopropamide Capsules, 250s

6505-890-1247
Danthron & Calcium Bis. (Dioctyl Sulfosuccinate Capsules, 1000s)

6505-890-1321
Isoxuprine Hydrochloride Tablets

6505-890-1333
Sodium Sulfacetamine & Prednisolone Acetate Ophthalmic Suspension, 5 cc

6505-890-1355
Medroxyprogesterone Acetate Tablets, 10 mgm, 100s

6505-890-1373
Methylpolysilcxane Tablets, 40 mgm, 500s

6505-890-1381
Pyrvinium Pamoate Tablets, USP, 50 mg, 25s

FSN & NOMENCLATURE

6505-890-1383
Methamphetamine & Phenobarbital Tablets, 500s, Type II

6505-890-1388
Erythromycin Estolate Capsules, 250 mg, 100s

6505-890-1420
Chlorpheniramine Maleate 250s (Ornade)

6505-890-1428
Bio-Sorb-Cream

6505-890-1479
Methylglucamine Diatrizoate (Hypaque)

6505-890-1485
Methylphenidate Hydrochloride for Injection, 10 mg

6505-890-1486
Fungizone Lotion, 3%, 30 cc (24 months potency)

6505-890-1496
Prednisolone Sodium Phosphate Inj.

6505-890-1534
Tuberculin Tine Test

6505-890-1537
Thioridazine Hcl Tabs

6505-890-1538
Thioridazine Hcl Tabs, 1000s

6505-890-1550
Trifluoperazine Hcl. Tabs (Stelazine)

6505-890-1551
Phenistix Reagent Strips (phenistix)

6505-890-1554
Fluorandrenolone Cream, 0.05%, 15 Gm tube

6505-890-1558
Sodium Phosphate - Sodium Citrate Solution

FSN & NOMENCLATURE

6505-890-1561
Methicillin Sodium for Injection, Buffered, 1 Gm

6505-890-1568
Polymyxin B. Bacitracin

6505-890-1582
Colistimethate Sodium for Injection

6505-890-1573
Estrogenic Substances, Conjugated, Cream, Vaginal, 0.625%, 1 ½ oz.

6505-890-1599
Benzathine Penicillin G, Procaine Penicillin G & Potassium Penicillin G for Injection

6505-890-1562
Oaphenadrine Citrate Tablets, 100 mg,

6505-890-1627
Dioctyl Calcium Sulfoccinate Capsules 1000's

6505-890-1633
Aluminum Acetate Solution Tablets, Effervescent, 100s

6505-890-1634
Hexachlorophene Salacylic Acid and Sulphur Cake, 3-3/4 oz.

6505-890-1657
Kaolin and Pectin Mixture

6505-890-1763
Declomycin Syrup

6505-890-1775
Methysergide Maleate Tablets

6505-890-1788
Thiopental Anesthesia Kit.

6505-890-1819
Trimethobenzamide Hcl and Benzocaine Suppositories, NF

6505-890-1840
Metronidazole Tabs, 0.25 Gm, 250's

6505-890-1856
Methyldopa Tablets, 0.25 Gm, 100's

FSN & NOMENCLATURE

6505-890-1884
Cyproheptadine Hcl, Tabs

6505-890-1891
Brompheniramine Maleate Tabs

6505-890-1892
Brompheniramine Maleate, Phenylephrine Hcl

6505-890-1898
Meglumine Iothalamite Inj.

6505-890-1901
Test Strips & Color Chart, Urinary Blood, Glucose, Protein & pH, 100's

6505-890-1902
Cyclopentamine Hydro

6505-890-1911
Cyclopentamine-Hydroxy

6505-890-1913
Dihydrostreptomycin-Polymyxin w/Activated Attapulgite Aluminum Hydroxide & Pectin

6505-890-2008
Ananase Tablets, 100s (24 Months Potency)

6505-890-2010
Bromethazine Hydro Chlor, 1 Gal.

6505-890-2012
Chlorphentiramine Maleate

6505-890-2013
Mycostatin Cream

6505-890-2015
Belladonna Alkaloids, Ergotamine Tartrate & Phenobarbital Tablets, 100s

6505-890-2024
Propoxyphine Hydrochloride, Aspirin and Phen. Capsules

6505-890-2027
Mineral Oil, Lanolated, Water Dispersible, 8 fl. oz.

FSN & NOMENCLATURE

6505-890-2081
Declomicin Tablets

6505-890-2193
Povidone-Iodine Oint., 10%, 1cc, 120's (In Plastic Tubes)

6505-890-2217
Sulfanilamide, Allantoin and Aminacrine Hydrochloride Cream, Vaginal 4 oz. (113.4 Gm)

6505-891-9994
Dextroamphetamine Sulfate and Prochlorperazine Maleate Capsules

6505-900-2146
Sodium Cephalothin for Injection, 1 Gm

6505-903-8173
Smallpox Vaccine, 100 doses

6505-904-0119
Barium Sulfate, Diagnostic

6505-905-9041
Fluocinolone Acetonide Cream, 0.025%, 425 Gm: In water-washable base

6505-913-5873
Oxytetracycline-Polymyxin B Ophth. Ointment, 1/8 oz. (3.5 Gm) 50's

6505-913-7905
Chloroquine & Primaquine Phos. Tabs, 150's

6505-913-7907
Propoxyphene Hcl, Aspirin & Phenacetin Caps, 100's

6505-913-8557
Measles, Virus Vaccine

6505-914-0246
Meplvacaine Hcl Inj, (Carbocaine Hcl)

6505-914-0252
Dihydrostreptomycin-Polymyxin Tabs (Polymagma Tabs)

6505-914-1742
Carbocaine Hcl Inj

FSN & NOMENCLATURE

6505-914-3593
Povidone-Iodine Sol, NF, 10%, ½ oz. (15 cc) 50s

6505-926-2062
Meglumine Diatrizoate Inj (Reno-Grafin-60)

6505-926-2102
Nitrofurazone & Diperodon Hcl Suppositories 12s (Furacin Urethral Inserts)

6505-926-2111
Meclizine Hydro Tablets, USP, 25 mg, 100s

6505-664-5582
Meclizine Hydro Tablets, USP, 25 mg, 100s

6505-926-2112
Meclizine Hcl Tabs. 6s (Bonine Chewable Tabs)

6505-926-2154
Indomethacin Capsules 100s

6505-926-2159
Neomycin Sulfate, Polymyxin B Sulfate & Gramicidin Cream Topical, 15 Gm

6505-926-2160
Test Kit, Syphillis Detection

6505-985-7224
Test Kit, Syphillis 100-tests

6505-926-2166
Test Kit, Pregnancy Determination, 20 tests

6505-926-2206
Test Strips & Color Chart, Urinary blood

6505-926-2239
Plumice - modified

6505-926-2241
Tolnaftate Solution

6505-926-2246
Thytropar, Injection

6505-926-2247
Procaine Penicillin

FSN & NOMENCLATURE

6505-926-4763
Zinc Bacitracin, Neomycin Sulfate (Neo-Polycin Ointment)

6505-926-4764
Smallpox Vaccine - freeze dried

6505-926-4765
Pyrimethamine Tablets (Daraprim)

6505-926-4768
Lincomycin Hydrochloride Inj. (Lincocin)

6505-926-4769
Lincomycin Hydrochloride Monohydrate Capsules (Lincocin)

6505-926-4773
Nortriptyline Hydrochloride Capsules, Equiv. to 25 mg of Nortriptyline Base, 100s

6505-926-4847
Mannitol Injection (Osmitrol)

6505-926-4884
Aluminum Aspirin Tablets Chewable 25's

6505-926-4885
Echothiophate Iodide for Ophthalmic Solution

6505-926-8844
Dioctyl Sulfosuccinate Capsules (Surfak)

6505-926-8926
Chlorpheniramine Maleate, Chlorform, Codeine Phos, Glyceryl, Guaiacolate, Methol & Phenylephrine Hydro Syrup

6505-926-8929
Chloral-Betaine Tablets (Beta-Chlor Tablets)

6505-926-8985
Dextromethorphan-Hydrobromide (Robitussin-DM)

6505-952-0267
Methylprednisolone Acetate

6505-957-9531
Reserpine Inj

6505-965-8583
Prochlorperazine Suppositories (Compazine Suppositories)

FSN & NOMENCLATURE

6505-967-8736
Prochlorperazine Suppositories, (Compazine Suppositories)

6505-969-8617
Sodium Lactate Inj

6505-982-4228
Warfarin Sodium Tabs

6505-982-4229
Warfarin Sodium Tabs

6505-982-5492
Cetylpyridinium Chloride Sol. Alcoholic 0.025%, 5 oz.

6505-982-5557
Erythromycin Estolate for Oral Suspension

6505-982-9594
Chlorpheniramine Maleate & Phenylphizine Hydro Tablets

6505-985-7079
Chlordantaed & Benzalkon Chloride Vaginal Cream

6505-985-7110
Fluocinolone Acetonide Cream, 0.025%, 15 Gm

6505-965-2476
Theophylline Ephedrine Tabs

6505-967-8735
Propoxyphrene Hcl, Aspirin, Caffeine Tabs (Darvon)

6505-958-1719
Calcium Chloride Injection

6505-958-2364
Propoxyphene Hcl Caps, USP, 65 mg, 500's

6505-961-5504
Nystatin-Neomycin Sulfate, Cream

6505-962-4375
Allybarb APC Tablets

6505-962-4376
Tetrahydrozoline Hcl Ophth Solution

FSN & NOMENCLATURE

6505-963-5355
Denamethasone Phosphate Inj (Decadron)

6505-965-2319
Trimelhobenzamide Hydro Cap

6505-965-2435
Phenmetrazine Hydro Tablets, NF, 75 mg, 1000s

EXHIBIT 7

DRUG BIDDERS LIST

DPSC, DSA

THIS LIST REPRESENTS THOSE ORGANIZATIONS WHICH ARE PRESENTLY LISTED AS BIDDERS FOR DRUG PRODUCTS. THE LIST DOES NOT PURPORT TO INDICATE THE CAPABILITY OF THE BIDDER, NOR IS IT A LISTING OF SUPPLIERS OF DRUGS TO DPSC.

THE LISTING IS VALID AS OF JULY, 1970. DPSC HISTORICAL RECORDS DO NOT ALLOW RECONSTRUCTION OF THE BIDDERS LIST AS OF 27 JANUARY 1969, WHEN EXHIBIT 6 WAS DISTRIBUTED, BUT IS REPRESENTATIVE OF THAT LIST.

EL WORKS INC
190 9TH STREET
BROOKLYN NEW YORK 10015

ABIC LIMITED CHEM & PHAR IND
P O BOX 2115
AUSTIN TEXAS 78767

ABBOTT LABORATORIES
14TH STREET & SHERIDAN ROAD
NORTH CHICAGO ILLINOIS 60064

ALBERT ACAN X-RAY INC
18800 HAWTHORNE
DETROIT 3 MICHIGAN 48203

ACETOCHEMICAL CO INC
126 02 NORTHERN BLVD
FLUSHING N Y 11368

SCHENLEY AFFIL BRANDS CORP
1290 AVE OF THE AMER
NEW YORK N Y 10019

AIR PROD & CHEMICALS INC
P O BOX 538
ALLENTOWN PA 18105

ALCON LAB INC
PO BOX 1959
FORT WORTH TEXAS 76101

ALFA INORGANICS INC
8 CONGRESS ST
BEVERLY MASS 01915

ALLEN PHARMACAL CO INC
175 PEARL ST
BROOKLYN N Y 11201

ALLERGAN PHARMACEUTICALS INC
1000 SOUTH GRAND AVE
SANTA ANA CALIF 92705

ALLIED CHEM CORP
SPECIALTY CHEMS DIV
P O BOX 70
MORRISTOWN N J 07960
ATTN BGA SALES

ALTA PHARMACAL CORP
4441 NORTH BALDWIN AVE
EL MONTE CALIFORNIA 91731

AMBUR DISTILLED PROD INC
3200 W AVER AVE
MILWAUKEE WISC 53216

AMEND DRUG-CHEMICAL CO
117-119 EAST 24 STREET
NEW YORK N Y 10010

AMERICAN ASSOC OF BLOOD BANKS
AA BB NATL CLEARINGHOUSE OFF
270 MASONIC AVE
SAN FRANCISCO CALIF 94118

AMERICAN CHEMICAL DRUG CO
DIV OF AMER TRANSPACIFIC CORP
P O BOX 3169 RINCON ANNEX
SAN FRANCISCO CALIF 94119

AMERICAN CONTINENTAL LABS
5600 BEACH BOULEVARD
BUENA PARK CALIF 90620

AMERICAN CYANAMID CO
AGRICULTURAL DIVISION
P O BOX 400
PRINCETON NEW JERSEY 08540

AMERICAN CYANAMID CO
FINE CHEMICAL
BERDAN AVENUE
WAYNE N J 07470

MCGAW LAB INC
DIV OF AMER HOSP SUPPLY CORP
P O BOX K
MILLEDGEVILLE GA 31061
ATTN MR J TAPLEY

AMERICAN HOSP SUPPLY CORP
130 SHAW RD
SAN FRANCISCO CALIF 94080

AMERICAN HOSPITAL SUP CORP
120 RARITAN CENTER PKWY
EDISON N J 08817

AMERICAN LABORATORIES INC
R D 6
GAINES VILLE GEORGIA 30501

AMERICAN LANOLIN CORP
13 RAILROAD S P O BOX 1078
LAURENCE MASS 01842

AMERICAN NATIONAL RED CROSS
18&D STREETS NW
WASHINGTON DC 20006
GENERAL SUPPLY OFCR

AMERICAN PEROXIDE CO
437 CARLTON AVENUE
BROOKLYN N Y 11238

AMERICAN PHARM COMPANY
120 BRUCKNER BLVD
NEW YORK N Y 10454

AMERICAN QUININE CO
10 FAIRCHILD COURT
PLAINVIEW N Y

AMES CO
DIV MILES LAB
1127 MYRTLE ST
ELKHART INDIANA 46514

AMALE INC
2425 W DOROTHY LANE
DAYTON OHIO 45439

AMSCO LABORATORIES
2424 WEST 23RD ST
ERIE PA 16506

ANABOLIC INC
514 RIVERDALE DRIVE
GLENDALE CALIF 91204

ANCHOR CHEMICAL
2000 SOUTH BELTLINE BLVD
COLUMBIA SOUTH CAROLINA 29205

ANDERSON-KEITH
854 CLINTON AVE
NEWARK N J 07108

ANDERSON LABS INC
P O BOX 1957
FORT WORTH TEXAS 76101

ANDOR LABS INC
6144 RUSH-LIMA RD
RUSH N Y 14543

ANKERFARM SP A
VIA CASELLA 17
20156 MILAN ITALY

APPLIED BIOLOGICALSCIENCE LAB
6320 SAN FERNANDO ROAD
GLENDALE CALIF 91201

ARBROOK
SOMERSET COUNTY
SOMERVILLE N J

ARCHER-TAYLOR DRUG CO
P O BOX 636
WICHITA KANSAS 67201

ARLIN CHEMICAL INC
P O BOX 137
CARLSTADT NEW JERSEY 07072

ARMOUR-DIAL INC
P O BOX 4309
CHICAGO ILLINOIS 60680

METRIX CLIN & DIAGNOSTICS DIV
ARMOUR PHARMACEUTICAL CO
510 EAST 41ST ST
CHICAGO ILLINOIS 60616

ABBEL PROD CO
2101 AVE Z
P O BOX 159 BAY STA
BROOKLYN N Y 11235

ASSOCIATED LABS
DBA THE DALLAS LAB
1323 WALL STREET
DALLAS 15 TEXAS 75215

ASTRA PHARMACEUTICAL PROD INC
NEPONSET ST
WORCHESTER MASS 01606

ATLAS CHEMICAL & MFG CO
P O BOX 2322
SAN DIEGO CALIF 92112

AVON PROD INC
30 ROCKFEELLER PLAZA
NEW YORK NY 10020

AYERST LABORATORIES
AMERICAN HOME PRODUCTS
685 3RD AVE.
NEW YORK N Y 10017

BADGER LABORATORIES INC
JACKSON
WISCONSIN 53037

BAIRD & MCGUIRE INC
SOUTH STREET
HOLBROOK MASS 02343

J T BAKER CHEMICAL CO
222 RED SCHOOL LANE
PHILLIPSBURG N J 08865
WARREN COUNTY

BALTIMORE BIOLOGICAL LAB
DIV BIO QUEST
DIV OF BECTON DICKINSON&CO INC
P O BOX 175
COCKEYSVILLE MD 21030

BANNER GELATIN PROD CORP
20730 DEARBORN ST P O BOX 157
CHATSWORTH CALIF 91311

BARD PHARMACALS INC
99-101 SAW MILL RIVER ROAD
YONKERS N Y 10701

BARIUM & CHEMICALS INC
PO BOX 230
STATE ROUTE 7 NORTH
N STEUBENVILLE OHIO 43952

BARNES-HIND PHAR INC
895 KIFER RD
SUNNYVALE CALIF 94086
ATTN MR KRULEVITCH DIR OF Q C

BARROWS CHEMICAL CO INC
300 PROSPECT ST
INWOOD L I N Y 11696

BARRY LABS INC
9100 KERCHEVAL AVE
DETROIT MICH 48214

BARTON DISTILLING CO
200 S MICHIGAN AVE
CHICAGO ILLINOIS 60604

BAXTER LABS
6301 LINCOLN AVE
MORTON GROVE ILLINOIS 60053

MCGAW LAB
DIV OF AMER HOSP SUP CORP
1015 GRANDVIEW AVE
GLENDALE CALIF 91201

BECTON DICKINSON-COMPANY
RUTHERFORD NEW JERSEY 07070

BEECHAM PHARMACEUTICALS
DIV OF BEECHAM INC
65 INDUSTRIAL SOUTH
CLIFTON N J 07012

BEL & ART PRODUCTS
INDUSTRIAL RD
PEQUANNOCK N J 07440

BELLEVUE LABS INC
14-21 122ND STREET
COLLEGE POINT N Y 10056

BENALEN CORP
2333 1/2 COTNER AVE
LOS ANGELES CALIF 90064

JOHN BENE & SONS INC.
437-45 CARLTON AVE.
BROOKLYN, N.Y. 11238

J & H BERGE INC
4111 SO CLINTON AVE
SO PLAINFIELD N J 07080

BETHLEHEM APPARATUS CO INC
FRONT & DEPOT STREETS
HELLERTOWN PENNSYLVANIA 18055

BIBER PHARMACAL CO INC
713 SOUTH 14TH ST
NEWARK N J 07103

BIO-CHEM PRODUCTS CO
6308 SAN FERNANDO ROAD
GLENDALE CALIF 91201

BIOCRAFT LABORATORIES INC
92 ROUTE 46
EAST PATERSON N J 07407

BIO PROD RESEARCH LAB
2330 S INDUSTRIAL PK DR
TEMPE ARIZ 85281

THE BLUE LINE CHEMICAL CO
302 S BROADWAY
ST LOUIS MISSOURI 63102

BOLAR PHARMACEUTICAL CO INC
130 LINOH ST
COPIAGUE N Y 11726

THE BORDEN CHEMICAL COMPANY
THE BORDON COMPANY
5000 LANGDON STREET
PHILADELPHIA PA 19124

BOWEN & COMPANY INC
1800 CHAPMAN AVENUE
ROCKVILLE MARYLAND 20852

BOWMAN BRAUN PHARM INC
119 SCHROYER AVE S W
CANTON OHIO 44702

BOWMAN-BRAUN PHARMACEUTICALS
119 SCHROYER AVENUE S W
CANTON OHIO 44702

BOYLE & CO
6330 CHALET DRIVE
LOS ANGELES 90022

BREON LABORATORIES
90 PARK AVE
NEW YORK N Y 10016

BRISTOL LAB
BRISTOL MYERS CO.
PO BOX 657
SYRACUSE N Y 13201
ATTN T OCONNELLY

BROEMMEL PHARM
1235 SUTTER STREET
SAN FRANCISCO CALIFORNIA 94108

DR B S PETRULIS
AMUROL PRODUCTS CO
P O BOX 300
NAPERVILLE ILL 60540

BRYANT LABORATORIES INC
880 JONES ST
BERKELEY CALIF 94710

BUFFALO DENTAL MFG CO
2911-23 ATLANTIC AVE
BROOKLYN 7 N Y 11207

BURROUGHS WELLCOME & CO
1 SCHUYLKILL AVE
NORRISTOWN PA 19404

BURROUGH BROS PHARM INC
714 E PRATT ST
BALTIMORE MD 21202

BURROUGHS WELLCOME-CO INC
1 SCARSDALE RD
TUCKAHOE N Y 10707

BURTON PARSONS & CO INC
7351 86TH AVENUE
WASHINGTON D C 20027

JOHN G BUTLER CO
540 N LAKE SHORE DR
CHICAGO ILL 60611

C & M PHARMACAL INC
1519 E 8 NILE RD
HAZEL PARK MICH 48030

CALBIOCHEM
P O BOX 54282
LOS ANGELES CALIF 90054

CAMBRIDGE CHEMICAL PROD INC
9182 GREENFIELD ROAD
DETROIT MICHIGAN 48228

CAMERON MFG CO
EAST SECOND STREET
P O BOX 391
EMPORIUM PENNA 15834

CAN-TITE RUBBER CORP
33-REDFERN AVENUE
INWOOD L I N Y 11696

CAPITOL SCIENTIFIC CO
2501 PAXTON STREET
HARRISBURG PA 17105

R P CARGILLE LABS INC
55 COMMERCE ROAD
CEDAR GROVE N J 07009

CENTURY LABORATORIES INC
4936 VETERANS MEMORIAL HGW.
METAIRIE LOUISIANA
JEFFERSON PARISH 70004

CASE LABORATORIES INC
1407 NORTH DAYTON ST
CHICAGO ILLINOIS 60622

THE L D CAULK CO
DIV OF DENTSPLY INTER INC
P O BOX 359
MILFORD DELAWARE 19963

CENTER CHEM INC
300 E 42ND ST
NEW YORK N Y 10017

THE CENTRAL PHARMACAL CO
116-128 E THIRD ST
SEYMOUR INDIANA 47274

CERTIFIED LABS INC
400 VALLEY RD
WARRINGTON PA 18976

CHASE CHEMICAL CO
280 CHESTNUT ST
NEWARK N J 07105

CHATTEM DRUG & CHEMICAL CO
1715 W 38TH ST
CHATTANOOGA TENN 37409

CHEMICAL COMPOUNDING CORP
532 JOHNSTON AVENUE
JERSEY CITY N J 07304

CHESEBROUGH-PONDS INC
485 LEXINGTON AVE
NEW YORK N Y 10017

CHEM PHARMACEUTICALS INC
5547 NORTH RAVENSWOOD AVE
CHICAGO ILL 60640

CONSOLIDATED PRODUCTS CORP
7 LIBERTY SQUARE
LYNN MASS 01901

CHICAGO SANITARY PRODUCTS CO
3100 SOUTH THROOP STREET
CHICAGO ILLINOIS 60608

CONTINENTAL CHEMICAL CO INC
2000 S BELTLINE BLVD
COLUMBIA S C 29205

CIBA PHARMACEUTICAL CO
556 MORRIS AVE
SUMMIT N J 07901

CONTINENTAL CHEMICAL CORP
1439 ASH STREET
TERRE HAUTE IND 47808

CITY CHEMICAL CORPORATION
132 WEST 22ND STREET
NEW YORK N Y 10011

COOK WAITE LABS INC
90 PARK AVE
NEW YORK N Y 10016

CLIFFORD CHEMICAL CORP
852 CLINTON AVENUE
NEWARK NEW JERSEY 07108

COOPER CHEMICAL CO
20 PARKER RD
LONG VALLEY NJ 07853

COLAB LAB INC
3 SCIENCE RD
GLENWOOD ILL 60425

COOPER LAB INC
6 ROOSEVELT AVE
PO BOX 190
MYSTIC CT 06355

COLLEGE OF AMER PATHOLOGISTS
230 NORTH MICHIGAN AVE
CHICAGO ILLINOIS 60601

CORD LABORATORIES INC
19191 FILER AVE
DETROIT 34 MICH 48234

COLUMBIA PHARMACEUTICAL CORP
530 RAY ST
FREEPORT N Y 11520

COURTLANDT LABORATORIES
5555 VALLEY BOULEVARD
LOS ANGELES CALIFORNIA 90032

COMFORT MFG CO
1056 W VAN BUREN ST
CHICAGO 7 ILL 60607

COWLEY PHARMACEUTICALS INC
65 SOUTHBRIDGE ST
AUBURN MASS 01501

P N CONDIT
MAIN STREET P O BOX 91
MAYNARD MASS 01754

AMERICAN CRYOGENICS INC
DBA COYNE CYLINDER CO
224 RYAN WAY
SAN FRANCISCO CALIF 94080

CONSOLIDATED LABORATORIES INC
3 SCIENCE RD
GLENWOOD ILL 60425

CROWL CHEMICAL CO
BOX 424
SHAMOKIN PA 17872

CRYSTAL SOAP & CHEMICAL CO INC
P O BOX 550
LANSDALE PA 19446

CURTIN SCIEN CO
2218 UNIVERSITY AVE S E
MINNEAPOLIS MINN 55414

CUSTOM PACKAGING INC
136 TICHENOR STREET
NEWARK 5 N J 07105

CUTTER LABORATORIES
15 JUST ROAD
FAIRFIELD N J 07006

DADE PHARMACEUTICALS INC
420 S W 11TH ST
HALLANDALE FLA 33009

DADE REAGENTS INC
1851 DELAWARE PARK
P O BOX 672
MIAMI FLA 33152

DAVIES ROSE HOYT KENDALL COMPANY
633 HIGHLAND AVE
NEEDHAM MASS 02194

DAVIS-EDWARDS PHARMACAL CORP
5845 NORTHERN BLVD
WOODSIDE N Y 11377

DAVIS EMERGENCY EQUIPMENT CO
45 HALLECK ST
NEWARK N J 07104

DAVIES-YOUNG CO
705 ALBANY ST
DAYTON OHIO 45401

DAY-BALDWIN INC
1460 CHESTNUT AVE
HILLSIDE N J 07205

DELMAR PHARMACAL CORP
333 COLUMBIA ST
RENSSELEAR N Y 12144

J H DELAMAR-SON INC
4507-11 NORTH KEDZIE AVENUE
CHICAGO ILLINOIS 60625

DELMAR SCIENTIFIC LABS
317 MADISON ST
MAYWOOD ILL 60153

DELTA BIOCHEMICAL INC
350 KENDALIA
SAN ANTONIO TEXAS 78214

THE DENVER CHEMICAL MFG CO
WAMPOLE LABS
35 COMMERCE ROAD
STAMFORD CONN 06904

DE PUY MFG CO
P O BOX 988
WARSAW IND 46580

DERMIK LABORATORIES INC
150 EILEEN WAY
SYOSSET LI NY 11791

DERRICK SOAP PRODUCTS
100-02 NORTH FIRST ST
ST LOUIS MO 63102

DERRY PRODUCTS INC
87-113 WISNER AVE
MIDDLETOWN NY 10940

DEWEY PRODUCTS CO
532 COTTAGE GROVE S E
GRAND RAPIDS MICH 49502

DIECO LABORATORIES
920 HENRY STREET
DETROIT MICHIGAN 48201

DOAK PHARMACAL CO I
2000 SHAMES DRIVE
WESTBURY N Y 11590

DODGE & OLCOTT INC
75 9TH AVE
N Y N Y 10011

DOME LABORATORIES
125 WEST END AVE
NEW YORK N Y 10023

DONELAIN PHARM INC
90 OAK STREET
NORWOOD N J 07648

DORSEY LAB
DIV OF WANDER CO
N E U S 66 IS 80
LINCOLN NEBR 68501

J A DOUGHERTYS SONS INC
MAIN ST
LINFIELD PA 19468

DOUGLAS CHEMICAL DIV
1 LEXINGTON AVE P O BOX 37
BETHPAGE N Y 11714

THE DOW CHEMICAL CO
U S GOVT MARKETING
2030 BUILDING
MIDLAND MICHIGAN 48640

THE DOW CHEMICAL CO
RX PHARMACEUTICALS
1200 MADISON AVE
INDIANAPOLIS INDIANA 46225

DRAKE LAB INC
9965 NORTHLAWN
DETROIT MICHIGAN 48204

DRUG PURCHASE INC
221 W 41ST ST
NY NY 10036

DUKE LABORATORIES INC
DUKE PLACE
SOUTH NORWALK CONN 06856

DUMONT PHARMACAL COMPANY
2048-2056 ABIGAIL ST
PHILADELPHIA PA 19125

DUNHALL INC
PO BOX 100
GRAVETTE ARKANSAS 72736

DUREL PHARMACEUTICAL INC
541 E THIRD ST
MT VERNON N Y 10553

S E DURST CO INC
5317 N THIRD STREET
PHILA PA 19120

DUVEEN SOAP CORP
154 MORGAN AVE
BROOKLYN N Y 11237

DYN MFG & PACKAGING CORP
285 PALISADE AVE
CLIFFSIDE PARK N J 07010

E Z EM CO INC
111 SWALM ST
WESTBURY N Y 11590

EASTERN LABORATORIES INC
1483 WASHINGTON AVE
VINELAND N J 08360

EAST SMELTING & REFINING CORP
37-39 RUBTER STREET
LYNN MASSACHUSETTS 01901

EASTERN WINE CORP
BRONX TERMINAL MARKET
NEW YORK N Y 10451

EASTMAN KODAK CO
GOVERNMENT MARKET SERVICES
343 STATE STREET
ROCHESTER N Y 14650

E B A PHARMACEUTICAL INC
425 PARK AVE
NEW YORK NEW YORK 10022

EATON LABS INC
17 EATON AVE
NORWICH N Y 13815

FARADAY LABS INC
223 HIGH ST
NEWARK NJ 07102

EDWARDS COUNCILOR CO INC
121 COLLEY AVENUE
NORFOLK VA 23510

FELLOWS MEDICAL MFG CO INC
12741 CAPITAL AVENUE
OAK PARK MICHIGAN 48237

ELANCO PRODUCTS CO
DIV ELI LILLY & CO
P O BOX 1750
INDIANAPOLIS IND 46206

FERMCO LABORATORIES
G D SEARLE & CO
P O BOX 5110
CHICAGO ILLINOIS 60680

ELBON LABORATORIES INC
10 PINE STREET
MORRISTOWN NEW JERSEY 07960

FINE ORGANICS INC
205 MAIN STREET
LODI N J 07644

ELKINS-SINN INC
22 CHERRY HILL INDUST CENTER
CHERRY HILL N J 08034

FISHER SCIENTIFIC CO
P O BOX 375 1 REAGENT LA
FAIR LAWN N J 07410

EMPIRE LABORATORIES LTD
301 LANSDOWNE AVE
TORONTO 3 ONTARIO

FISHER SCIEN CO
191 S GULPH RD
KING OF PRUSSIA PA 19406

ENDO LABS
1000 STEWART AVE
GARDEN CITY N Y 11533

C B FLEET CO INC
BOX 1100
LYNCHBURG VIRGINIA 24505

CARLO ERBA S P A
MAGGIN-SWAN
509 MADISON AVENUE
NEW YORK N Y 10022

FOREGGER CO INC
SUB OF HILLMAN
COAL & COKE CO
680 OLD WILLETS PATH
SMITHTOWN NY 11787

ETHICON INCORPORATED
SOMERVILLE N J 08876

FORT DODGE LABORATORIES DIV
AMERICAN HOME PRODUCTS CORP
800-5TH ST N W
FORT DODGE IOWA 50501

EVANS CHEMETICS INC
250 EAST 43RD STREET
NEW YORK N Y 10017

FOSTER MILBURN INC
468 DEWITT ST
BUFFALO N Y 14213

E FOUGERA-CO INC
CANTIAGUE ROAD
HICKSVILLE L I N Y 11802

FOUR PENNY PRODUCTS INC
339 NO PULASKI RD
CHICAGO ILL 60624

JOSEPH E FRANKLE COMPANY
4309-11 RISING SUN AVENUE
PHILA PA 19140

I FREIBERG-SON INC
149 MADISON AVE
NEW YORK N Y 10016

FRITZSHE DODGE & OLCOTT INC
76 9TH AVE
NEW YORK N Y 10011

FROMM LAB INC
703 LAKE SHORE RD RR1
GRAFTON WIS 53024

FROMM LABORATORIES INC
GRAFTON WISCONSIN 53024
GRAFTON WISCONSIN 53024

G - W LABORATORIES INC
20 MARKLEY ST
PORT READING N J 07604

INDUSTRIA GALENICA ITALIANA
VIA A GRAMSCI 156
PADERNO DUGNANO MILANO ITALY

GARFIELD-CO
TALMADGE ROAD
EDISON NEW JERSEY 08817

THE GARRITY CO
896 DENNISON
OAKLAND CALIF

GERAUER CHEMICAL CO
9410 ST CATHERINE AVENUE
CLEVELAND OHIO 44104

GEIGY CHEMICAL CORP
GEIGY PHARMACEUTICALS
SAW MILL RIVER RD
ARDSLEY N Y 10502

GENERAL BIOCHEMICALS DIV
LABORATORY PARK
CHARGIN FALLS OHIO 44022

GENERIC PHARMACEUTICAL CORP
ATTN STAN TEINER
P O BOX 230
WILLOW GROVE PA 19090

GLENBROOK LABORATORIES
STERLING DRUG INC
90 PARK AVENUE
NEW YORK N Y 10016

GOLD CREST CHEMICAL CORP INC
KENNETT PIKE CHESTER COUNTY
MENDENHALL PA 19357

GOLD LEAF PHARMACAL CO INC
223 SOUTH DEAN ST
ENGLEWOOD NEW JERSEY 07631

GOLDSMITH BROS DIVISION
NATIONAL LEAD COMPANY
900 W 18TH STREET
CHICAGO ILLINOIS 60608

D E GOLDSMITH CHEMICAL
909 PITNER AVENUE
EVANSTON ILL 60602

JAMES GOOD CO
2107-2115 E SUSQUEHANNA AV
PHILADELPHIA PA 19125

GOODMAN CHEMICAL N Y CORP
129 47TH STREET
BROOKLYN N Y 11232

GREENSTONE-WRIGHT INC
5511 REDFIELD DRIVE
DALLAS TEXAS 75235

A F HALPERIN CO INC
716 COLUMBUS AVE
BOSTON MASS 02120

GOTHAM PHARM CO INC
1840 MCDONALD AVE
BROOKLYN N Y 11223

HALSEY DRUG CO INC
1827 PACIFIC STREET
BROOKLYN N Y 11233

W R GRACE COMPANY
DEWEY-ALMY CHEMICAL DIV
62 WHITTEMORE AVE
CAMBRIDGE MASS 02140

UNITED STATES RADIUM CORP
MED PROD DIVISION
1425-37TH ST
BROOKLYN N Y 11218

GRAND ISLAND BIOLOGICAL CO
3175 STALEY RD
GRAND ISLAND N Y 14072

HANCE BROS - WHITE CO
12TH - HAMILTON STS
PHILADELPHIA PA 19123

GRAYS PHARMACAL CO

P O BOX 9517
NORTH HOLLYWOOD CALIF 91609

HARLEY CHEMICAL INC

17TH & FEDERAL STS
CAMDEN NEW JERSEY 08105

GREAT WESTERN CHEM CO
860 WHARF STREET
RICHMOND CALIF 94804

HARRISBURG STEEL CO
DIV OF HARSCO CORPORATION
10TH & HERR STREETS
HARRISBURG PA 17105

GRYPHON LABORATORIES LTD
20 ADVANCE ROAD
TORONTO 18 ONTARIO

HART LABORATORIES DIV
NUTRION CORPORATION
STATION SQUARE ONE
PAOLI PENNA 19301

GYMA LABORATORIES OF AMERICA
139-58 QUEENS BLVD
JAMAICA N Y 11435

HARLECO
AMERICAN HOSPITAL SUPPLY CORP
60TH & WOODLAND AVE
PHILA PA 19143

HAACK LABORATORIES INC
P O BOX 3286
3217 N W YEON AVENUE
PORTLAND OREGON 97208

HARVEY LABORATORIES INC
5109 GERMANTOWN AVE
PHILADELPHIA PENNA 19144

HALL SCIENTIFIC CORP
200 EXPRESS ST
PLAINVIEW N Y 11803

HAVER LOCKHART LABS
PO BOX 676
KANSAS CITY MISSOURI 64141

HALOCARBON LABS INC
82 BURLEWS COURT
HACKENSACK NEW JERSEY 07601

GEORGE M HAYWARD
601 WESTOVER RD
KANSAS CITY MO 64113

REED LT
DELAWARE WATE GAP
PA 18327

HOUSE OF HOLLYWOOD
777 EAST GAGE AVE
LOS ANGELES CALIF 90001

HELLIGE INC
877 STEWART AVE
GARDEN CITY N Y 11534

HU-FRIEDY INCLINOIS
3118 N ROCKWELL ST
CHICAGO ILLINOIS 60618

THE HEWITT SOAP CO
47 WEST 34TH ST
NEW YORK N Y 10001

HUNTINGTON LABS INC
P O BOX 1193
FORT WAYNE INDIANA 46801

HEXAGON LABORATORIES INC
3536 PEARTREE AVENUE
BRONX N Y 10469

D W HUTCHINSON & CO INC
700 SOUTH COLUMBUS STREET
MT VERNON N Y 10550

HEYDEN NEWPORT CHEMICAL CORP
300 EAST 42ND STREET
NEW YORK N Y 10017

HYCEL INC
PO BOX 36329
HOUSTON TEXAS 77036

S P HITE CO INC
320 LOUDON AVE N W
ROANOKE VA 24016

HYLAND DIV TRAVENOL LAB INC
4501 COLORADO BLVD
LOS ANGELES CALIF 90039

HOCKWALD/CENTER CHEMICAL CO
P O BOX 227
BRISBANE CALIF 94005

HYNSON WESTCOTT & DUNNING
CHARLES & CHASE ST
BALTIMORE MARYLAND 21201

HOLLAND RANTOS CO INC
P O BOX 5
PISCATAWAY N J 08854

INDUSTRIAL CHEMICAL DYE CO INC
641 LEXINGTON AVE
NEW YORK N Y 10022

HONIBERG MED - SURG SUPPLY CO
1001 ALBANY AVENUE
HARTFORD CONN 06112

INSTRUMENTATION LAB
113 HARTWELL AVE
LEXINGTON MASS 02173

HOOSIER VETERINARY LABS INC
THORNTON
INDIANA

APSYNCO INC
P O BOX 8
CARLSTADT N J 07072

HOPPERS LABORATORIES INC
P O BOX 82
FREDERICKSBURG TEXAS 78624

INTERNATIONAL CHEMICAL CORP
720 FIFTH AVE
NEW YORK N Y 10036

IDEAL PHARMACEUTICALS
2176 PALOU AVE
SAN FRANCISCO CALIF

K-D ENTERPRISES INC
P O BOX 345
3454 DEMPSTER ST
SKOKIE ILL 60076

IVES LABS CAMERON
DIV OF AMER HOME PROD CORP
685 3RD AVE
N Y N Y 10017

KALLESTAD LABS INC
4005 VERNON AVE
MINNEAPOLIS MINN 55416

J W IVORY INC
308 NORTH 16TH STREET
PHILADELPHIA PA 19102

KAPCO INC
2222 GLENDENING ST
P O BOX 2001
KALAMAZOO MICH 49001

JAMCO COMPANY
158 CARROLL STREET
BROOKLYN NEW YORK 11231
ATTN ANGELO PALERMO

KASAR LABORATORIES
7313 N HARLEM AVE
NILES ILLINOIS 60648

JAYMAR SCIENTIFIC CO
P O BOX 25
KENILWORTH N J 07033

KELEKET CGR CORP
1603 TRAPELO RD
WALTHAM MASS 02154

JED X RAY CORP
106 SOUTH LONG BEACH ROAD
ROCKVILLE CENTRE N Y 11570

ED JOHNSON
% THE KENDALL CO
FIBER PRODUCTS DIV
WALPOLE MASS 02081

JENSEN SALSBERY LABS
RICHARDSON MERRELL INC
520 WEST 21ST ST
KANSAS CITY MISSOURI 64141

KEY PHARMACEUTICALS INC
50 N W 176 ST
MIAMI FLORIDA 33169

THE JOHNSON DRUG CO
1116 TAMPA ST P O BOX 3091
TAMPA FLORIDA
ATTN MR W S SHEPHARD JR 33602

KINGS SPECIALTY CO
P O BOX 240
FORT WAYNE IND 46801

JOHNSON & JOHNSON
CONTRACT DIVISION
NEW BRUNSWICK NEW JERSEY 08903

C F KIRK LABORATORIES INC
201 ROUTE 22
HILLSIDE N J 07205

F JONAS CORP
50 WEST 44TH ST
NEW YORK N Y 10036

MOORE KIRK LABORATORIES INC
201 ROUTE 22
HILLSIDE N J 07205

JONCO LABORATORIES INC
3615 CARNEGIE AVE
CLEVELAND OHIO 44115

KIRKMAN LABS INC
P O BOX 3929
PORTLAND OREGON 97208

KENT PHARMACEUTICAL COMPANY
377 CRANE STREET
ORANGE NEW JERSEY 07051

THE LAMBERT COMPANY INC
9000 STATE ROAD
PHILADELPHIA PA 19136

KOSTER KEUNEN INC
SAYVILLE L I 11782

LAWRENCE PHARMACEUTICALS INC
P O BOX 5394
JACKSONVILLE FLA 32207

KREMERS URBAN CO
P O BOX 2038
5600 W COUNTY LINE RD
MILWAUKEE WISCONSIN 53201

LEDERLE LAB
DIV OF AMERICAN CYANAMID CO
PRICES & QUOTATIONS DEPT
PEARL RIVER N Y 10965

LABORATORY DIAGNOSTICS CO
1116 WALNUT STREET
ROSELLE N J 07203

LEE LABS INC
RT 1 BOX 37
GRAYSON GA 30221

LABORATORY SERVICES LIMITED
P O BOX 6562 AUCKLAND 1
NEW ZEALAND

LEEDS & DIXON LABORATORIES INC
MOONACHIE AVE
MOONACHIE N J 07074

LAB TEK PRODUCTS
MILES LABORATORIES INC
39 E BURLINGTON ST
WESTMONT ILL 60559

THOS LEEMING & CO PACQUIN
CHAS PFIZER & CO INC
235 E 42ND ST
N Y N Y 10017

LAFAYETTE PHARMACAL INC
522 N EARL AVE
LAFAYETTE IND 47902

LEHIGH CHEMICAL CO
R D #4
EASTON PA 18042

LAKESIDE LABORATORIES
1707 E NORTH AVE
MILWAUKEE WISC 53201

B LEMKE & CO
199 MAIN ST
LODI NEW JERSEY 07644

LAMBERT-HUDNUT
WARNER-LAMBERT
201 TABOR ROAD
MORRIS PLAINS N J 07950

LEMMON PHARMACAL CO
BOX 30
SELLERSVILLE PA
FORMERLY PHARMICH LABS 18960

LAMEX INC
NORCROSS GEORGIA
30071

LEVER BROTHERS COMPANY
ARMED FORCES-EXPORT DIVISION
390 PARK AVE
NEW YORK N Y 10022

LA PINE SCIENTIFIC
375 CHESTNUT ST
NORWOOD N J 07648

LIF-O-GEN INC
PO BOX 302 TRIANGLE INDUST PK
LUMBERTON NEW JERSEY 08048

[illegible]
PHILIP MORRIS INC
100 PARK AVENUE
NEW YORK NEW YORK 10017

[illegible] CHEMICAL WORKS
P O BOX 5439
ST LOUIS MO 63160

ELI LILLY & CO
307 EAST MCCARTY ST
INDIANAPOLIS IND 46206

MANOLA CO
4200 LACLEDE AVE
ST LOUIS MO 63108

LILY WHITE SALES CO INC
SUBSIDARY CHESEBROUGH-PONDS IN
10TH FLOOR-485 LEXINGTON AVE
NEW YORK N Y 10017

M P L INC
1820 W ROSCOE ST
CHICAGO ILL 60657

LINCOLN LABORATORIES INC
P O BOX 1139
DECATUR ILLINOIS 62525

MARINE PROD CO
333 WEST FIRST ST
BOSTON MASS 02127

LEO LINDEN LABORATORIES
8454 STELLER DRIVE
CULBER CITY CALIF 90230

THE MARISON CO
BOX 178
SO ELGIN ILL 60122

LIQUID CARBONIC CORP
FRONT & PORTER STS
PHILA PA 19148

MARKHAM LABORATORIES
9246 SO VICENNES AVE
CHICAGO ILL 60620

HOECHST PHARMACEUTICALS
1385 TENNESSEE AVE
CINCINNATI OHIO 45229

SE MASSENGILL CO
501 551 FIFTH ST
BRISTOL TENN 37620

THE LORVIC CORP
8810 FROST AVE
ST LOUIS MISSOURI 63134

PAUL MASSON VINEYARDS
7 BALA AVE
BALA-CYNWYD PA 19004

LUKE PHARMACEUTICAL INC
ROUTE 40
FAIR WINDS DELAWARE 19701

MATHESON COLEMAN & BELL DIV
THE MATHESON COMPANY INC
2909 HIGHLAND AVENUE
NORWOOD OHIO 45212

MACALLISTER LABORATORIES INC
9213 WADE PARK AVENUE
CLEVELAND OHIO 44106

MAYER AND MYLES LABORATORIES
BOX 167
COOPERSBURG PA 18036

GENTRY CORP
17-01 NEVINS RD
FAIR LAWN N J 07410

MAYO PHARMACEUTICAL CO
4839 LANCASTER AVE
PHILA PA 19131

EC LEWIS - CO
WINONA MINN 55987

MELROSE CHEMICAL CO INC
P O BOX 7204
OAKLAND CALIF 94601

MC KESSON LABORATORIES
P O BOX 548
BRIDGEPORT CONN 06602

MERK & CO INC
QUINTON CO DIV
RAHWAY N J 07065

MCKESSON-ROBBINS INC
90-30 METROPOLITAN AVE
REGO PARK N Y 11374
ATTN E FERRIS

MERCK-SHARPE & DOHME
DIV OF MERCK CO
SUMNEYTOWN PIKE
WEST POINT PA 19486

MCNEIL LABS INC
CAMPHILL ROAD
FORT WASHINGTON PA 19034
ATTN HOSPITAL SALES

WM S MERRELL CO
DIV OF RICHARDSON-MERRELL
CINCINNATI OHIO 45215

MEAD JOHNSON LAB
MEAD JOHNSON - CO
2404 PENNSYLVANIA ST
EVANSVILLE INDIANA 47715

METABOLIC RESEARCH FOUND INC
4520 YOAKUM BLVD
HARRIS COUNTY
HOUSTON TEXAS 77006

MEDICAL CHEMICALS CORPORATION
2137 N 15TH AVE
MELROSE PARK ILL

MICHEL & PELTON CO
5743 LANDREGAN ST
EMERYVILLE CALIF 94608

MEDICAL CHEM CORP
1713 20TH ST
SANTA MONICA CALIF 90404

MICROBIOLOGICAL ASSOC INC
4813 BETHESDA AVE
BETHESDA MARYLAND 20014

MEDICALS CHEM CORP
4122 W GRAND AVE
CHICAGO ILL 60651

MICROBIOLOGICAL SCIENCES INC
163 SAW MILL RIVER RD
YONKERS WESTCHESTER NY 10701

MEDICAL GASES INC
1088 UTICA AVENUE
BROOKLYN NEW YORK 11203

MILAN PHARMACEUTICALS INC
P O BOX 4293
MORGANTOWN WEST VIRGINIA 26505

MEDICAL SUPPLY CO
1027 WEST STATE ST
ROCKFORD ILL 61101

MILES CHEMICAL CO
DIV OF MILES LAB INC
1127 MYRTLE ST
ELKHART IND 46514

MEER CORPORATION
318 WEST 46 ST
NEW YORK N Y 10036

MILLIPORE FILTER CORP
ASHBY ROAD
BEDFORD MASS 01730

MINE SAFETY APPLIANCES COMPANY
201 NORTH BRADDOCK AVENUE
PITTSBURGH PA 15208

MISSION PHARMACAL CO
P O BOX 1676
SAN ANTONIO TEXAS 78206

MODERN MATERIALS MFG CO
1021 SOUTH TENTH ST
ST LOUIS MO 63104

MOHAWK CHEMICAL COMPANY INC
93 MAIN STREET
FRANKLIN NEW JERSEY 07416

MONSANTO COMPANY
1101-17TH STREET N W
WASHINGTON D C 20036

MOREBA LAB
DIV STIEFEL LAB INC
420 LEXINGTON AVE
N Y N Y 10017

MORTON CHEMICAL COMPANY
110 NORTH WACKOR DRIVE
CHICAGO ILLINOIS 60606

THE J BIRD MOYER CO INC
21ST & CLEARFIELD STS
PHILA PA 19132

MURRO CHEMICAL CO INC
P O BOX 7182
PORTSMOUTH VIRGINIA 23707

MUTCHLER CHEMICAL CO INC
258 BROADWAY
NEW YORK N Y 10007

MYERS LABORATORIES INC
BOX 947
WARREN PA 16365

MYERS-CARTER LABORATORIES INC
5160 W BETHANY HOME ROAD
GLENDALE ARIZONA 85301

MYNOL CHEMICAL CO
P O BOX 233
BROOMALL PA 19008

NAARDEN-FLAVOREX INC
320 S CENTRAL AVE
BALTIMORE MD 21202

NAPP CHEMICALS INC
289 ALLWOOD RD
CLIFTON N J 07012

NA-SPRA INC
9728 REAVIS PARK DRIVE
ST LOUIS MO 63123

NATCON CHEMICAL CO INC
ONE FAIRCHILD COURT
PLAINVIEW NEW YORK 11803

NATIONAL BIO SERUMS INC
40 MARKLEY ST
PORT READING NJ 07064

NATIONAL BIOLOGICAL LABS INC
P O BOX 511
VIENNA VIRGINIA 22180

NATIONAL CHEMICAL LABS PENNA
825-827 LOMBARD ST
PHILA PA 19147

NATIONAL CYLINDER GAS
DIV OF CHEMETRON CORP
840 N MICHIGAN AVE
CHICAGO ILL 60611
ATTN MED SEC

NATIONAL DRUG CO
DIV OF RICHARDSON-MERRELL
4663-85 STENTON AVE
PHILADELPHIA PA 19144

[illegible]
4128 HAYWARD AVE
BALTIMORE MD 21245

NEOCO CORPORATION
1000 N HIGHLAND AVE
LOS ANGELES CALIF 90038

NEPHRON COMPANY
P O BOX 1585
3319 PACIFIC AVE
TACOMA WASH 98408

N-Y-Q CHEMICAL
DIV OF S B PENICK CO
100 CHURCH STREET
NEW YORK N Y 10008

NEWPORT PRODUCTS CO
DIV OF SAFEWAY STORES
1501 MARIPOSA STREET
SAN FRANCISCO CALIF 94107

NITINE INC
SUBS OF SHULTON INC
697 ROUTE 46
CLIFTON N J 07015

NORDEN LABS INC
601 WEST CORNHUSKER HIGHWAY
LINCOLN NEBRASKA 68521

NORTON PROD CO
DIV OF NORTON CHEM CO INC
680 S MYERS ST
LOS ANGELES CALIF 90023

NORWICH PHARMACAL CO
17 EATON AVENUE
NORWICH NEW YORK 13815

NOVOCOL CHEMICAL MFG CO INC
2911-23 ATLANTIC AVE
BROOKLYN N Y 11207

NUTRILITE PRODUCTS INC
5600 BEACH BOULEVARD
BUENA PARK CALIF 90620

NUTRITIONAL BIOCHEMICALS CORP
26201 MILES AVE
CLEVELAND OHIO 44128

OCTAGON PROCESS INC
596 RIVER ROAD
EDGEWATER N J 07020

OHIO MEDICAL PRODUCTS CO
AIR REDUCTION CO INC
1400 E WASHINGTON AVE
MADISON WISCONSIN 53701

OMEGA CHEMICAL CORP
3 CORPORATE PARK DRIVE
WHITE PLAINS NEW YORK 10604

OMNI TECH INC
P O BOX 5399
SANTA MONICA CALIF 90405

ORGANON INC
375 MT PLEASANT AVE
WEST ORANGE N J 07052

ORTHO PHARMACEUTICAL CORP
RT 202
RARITAN NEW JERSEY 08869

ORTHOPEDIC EQUIPMENT CO
BOURBON INDIANA 46504

OWEN LABORATORIES INC
P O BOX 34630
DALLAS TEXAS 75234

PKS RESEARCH INC DBA
INTERNATIONAL PHARM MFG CO
374 W 8TH STREET
SAN PEDRO CALIF 90731

PACKAGING CORP OF AMERICA
4633 DOWNEY RD
LOS ANGELES CALIF 90058

PAULSEN DIV
ORMONT DRUG CO
520 SOUTH DEAN ST
ENGELWOOD NJ

PAYNE INCORPORATED
P O BOX 272
KANKAKEE ILLINOIS 60901

PARAMED INC
570 SOUTH DEAN ST
ENGLEWOOD N J 07631

PEROXIDE - SPECIALTIES CO
1400 CARROLL AVENUE
SAN FRANCISCO CALIF 94124

PARKE DAVIS & COMPANY
P O BOX 118 G P O
DETROIT MICHIGAN 48232

L PERRIGO CO
100 BRADY ST
ALLEGAN MICH 49010

PARKE DAVIS-COMPANY
SURGICAL DRESSING DIVISION
P O BOX 368
GREENWOOD S CAROLINA 29646

PETRI WINE COMPANY
655 FOURTH STREET
SAN FRANCISCO 7 CALIF 94107

E M PARKER CO

646 BROOKLINE AVE
BROOKLINE MASS 02146

PFANSTIEHL LABS INC

1219 GLEN ROCK AVE
WAUKEGAN ILL 60086

PASADENA RESEARCH LABS INC
2107 EAST VILLA
PASADENA CALIF 91107

PFEIFFER GLASS INC
140 BENNINGTON DRIVE
ROCHESTER N Y 14616

PENDERGRAST CHEMICAL CO
3423 BRIARCLIFF RD NE
ATLANTA GEORGIA 30329

PFIZER DIAGNOSTICS
DEPT CHDS PFIZER & CO INC
300 W 43 ST
NEW YORK N Y 10036

THE PENETONE CO
74 HUDSON AVENUE
TENAFLY NEW JERSEY 07670

PFIZER LABORATORIES
DIV OF CHARLES PFIZER CO
235 EAST 42ND STREET
NEW YORK N Y 10017

S B PENICK & CO
100 CHURCH ST
NEW YORK N Y 10008

PHARMACHEM CORP
BROAD & WOODS ST
BETHLEHEM PA 18015

PENNCO DISTILLERS INC OF PA
226 S 16TH ST SUITE 1002
PHILA PA 19102

PHARMACIA LABS
800 CENTENNIAL AVE
PISCATAWAY NEW JERSEY 08854

PENNEX PRODUCTS CO INC
EASTERN AVE AT PENNEX DRIVE
VERONA PA 15147

PHARMETICS CORP

1010 WORCESTER ST
BALTIMORE MD 21210

PHARBUSA CORPORATION
NYLOS TRADING CO
26 BROADWAY
NEW YORK N Y 10004

PHIPPS PRODUCTS CORP
18 OLIVER ST
BOSTON MASS 02110

PHYSICIANS & HOSP SUPPLY CO
1400 HARMAN PLACE
MINNEAPOLIS MINNESOTA 55403

PICKER X-RAY
GOVT SALES DIV
5009 LEE HIGHWAY
ARLINGTON VA 22207

PIONEER CHEMICAL CO INC
36-41 VERNON BOULEVARD
LONG ISLAND CITY N Y 11106

PIONEER LABORATORIES
P O BOX 368 BLACK HORSE PIKE
PLEASANTVILLE N J 08232

PITMAN MOORE INC
CAMP HILL RD
FT WASHINGTON PA 19034

PLOUGH INC
P O BOX 377
MEMPHIS TENN 38101

POLAKS FRUTAL WORKS
MIDDLETOWN N Y 10940

POLICHIMICA SAP
1 PIAZZALE AGRIPPA
MILAN ITALY

POLYSCIENCES INC
PAUL VALLEY INDUSTRIAL PARK
WARRINGTON PENNA 18976

[illegible] PHARMACEUTICAL LABS INC
111 LEUNING ST
SOUTH HACKENSACK N J 07606

PRESSED STEEL TANK CO
1490 S 66TH STREET
MILWAUKEE WISCONSIN 53214

PRIVATE FORMULAE INC
P O BOX 5334 NAGEL STATION
ST LOUIS MISSOURI 63115

PROCTER & GAMBLE DIST CO
P O BOX 599
CINCINNATI OHIO 45201

PROFESSIONAL PHARMACAL CO INC
300 W JOSEPHINE PO BOX 230
SAN ANTONIO TEXAS 78206

PROFEXRAY DIV
LITTON MEDICAL PROD INC
2235 ORTHODOX ST
PHILA PA 19137

PROGRESS LABORATORIES INC
4156 SOUTH MAIN ST
LOS ANGELES CALIFORNIA 90037

PUBLIKER IND INC
1429 WALNUT ST
PHILA PA

PULMOSAN SAFETY EQUIPMENT CRP
30-48 LINDEN PL
FLUSHING N Y 11354

THE PURDUE FREDERICK COMPANY
99-101 SAW MILL RIVER ROAD
YONKERS NEW YORK 10701

PUREX CORP LTD
WILMINGTON
CALIF 90744

PORTER BENNETT CORP
OAK AT 13TH ST
KANSAS CITY MO 64106

QUICKSILVER PRODUCTS INC
556 CLAY STREET
SAN FRANCISCO CALIF 94111

RABIN-WINTERS
DIV OF BRUNSWIG DRUG CO
700 SO SEPULVEDA BLVD
EL SEGUNDO CALIF 90245

RACHELLE LABS
P O BOX 2029
700 HENRY FORD AVE
LONG BEACH CALIF 90801

RARISPHERE CORP
1328 BROADWAY
N Y N Y 1001

THE W T RAWLEIGH CO
223-225 E MAIN ST
FREEPORT ILL 61032

REED-CARNICK
30 BORIGHT AVE
KENILWORTH NJ 07033

REED PRODUCTS COMPANY
4438N 20TH STREET
ST LOUIS MISSOURI 63107

MICHAEL REESE RESEARCH
FOUDATION
530 E. 31ST ST.
CHICAGO, ILL. 60616

REINE PHARMACEUTICAL CORP
300 NASSAU RD
ROOSEVELT L I N Y

REQUA MFG CO
4510 BULLARD AVE
BRONX N.Y. 10470

REXALL DRUG COMPANY
3901 KINGSHIGHWAY BLVD
ST LOUIS MO 63115

RHODIA INC
600 MADISON AVE
NEW YORK N Y 10022

RICHLYN LABORATORIES
CASTOR AVE AT KENSINGTON AVE
PHILA PA 19124

RIES BIOLOGICALS INC
7640 S LA CIENEGA BLVD
LOS ANGELES CALIF 90034

RIKER LABORATORIES
DIV OF DART IND
19901 NORDHOFF ST
NORTHRIDGE CALIF 91326

RIVERTON LABORATORIES INC
852 CLINTON AVE
NEWARK 8 N J 07108

A H ROBINS COMPANY INC
1407 CUMMINGS DRIVE
RICHMOND VIRGINIA 23220

ROBINSON LABORATORY INC
355 BRANNAN ST
SAN FRANCISCO CALIF 94107

ROBOZ SURGICAL INSTR CO
810 18TH ST NW
WASHINGTON 6 D C 20006

ROCHE LABORATORIES
DIV OF HOFFMANN-LA ROCHE INC
340 KINGSLAND STREET
NUTLEY NEW JERSEY 07110
ATTN M N STAMATOS

ROCKLAND DENTAL CO INC
S E CORNER 21ST & CLEARFIELD
PHILA PA 19132

ROMACO RESEARCH CORPORATION
7801 WOODMONT AVENUE
BETHESDA MARYLAND 20014

SAN REL LABS INC
106 GREEN ST
BROOKLYN N Y 11222

J B ROERIG & CO
DIV CHAS PFIZER CO INC
235 EAST 42ND ST
NEW YORK N Y 10017

SAV A LIFE OXYGEN CO
1017 BARCLAY BLDG
BALA CYNWYD PA 19004

ROMAR LABS
P O BOX 390
BOONTONN N J 07005

SAVOY DRUG-CHEMICAL
16 SO PEORIA ST
CHICAGO ILL 60607

WM H RORER INC
500 VIRGINIA DR
FT WASHINGTON PENN 19034

SCHAEFER DIV STUDEBAKER CORP
801 WASHINGTON AVE NO
MINNEAPOLIS MINN 55401

ROSELAWN LABORATORIES INC
P O BOX 130 LITTLE RIVER STA
MIAMI FLORIDA 33138

R P SCHERER S P A
APRILIA/LATINA ITALY

ROWELL LABORTORIES
BAUDETTE MINN 56623

SCHERING DIAGNOSTICS
DIV SCHERING CORP
40 MARKLEY ST
PORT READING N J 07063

PHILIPS ROXANE
PHILIPS ELECTRONICS
330 OAK ST
COLUMBUS OHIO 43216

SCHERING CORP
1011 MORRIS AVE
UNION N J 07083

T M RYAN
908 MASSACHUSETTS AVE N E
WASHINGTON D C 20002

SCHIEFFELIN & COMPANY
APEX NORTH CAROLINA 27502

RYSTAN COMPANY
117 MOUNT VERNON AV
MOUNT VERNON N Y 10550

SCHIMMEL CO INC
475 TENTH AVE
NY NY

ELIAS SALZMAN
520 5TH AVE
NEW YORK N Y 10036

A R SCHMIDT CO INC
DIV OF THE MONGUL CORP
2826 LATHAM DRIVE
MADISON WISCONSIN 53713

SANDOZ INC
PHARMACEUTICAL DIV
HANOVER N J 07936

SCHOLL MFG CO
211-213 WEST SCHILL
CHICAGO ILL 60610

SEARLE CHEMICAL CO
200 N NORTH AVENUE
NORTHLAKE ILLINOIS 60164

SEABOARD MFG LABS INC
400 N 5TH ST
PHILA PA 19123

THE SEAMLESS RUBBER CO
THE REXALL DRUG&CHEM CO
253 HALLOCK AVE
NEW HAVEN CONN 06503

G D SEARLE
P O BOX 5110
CHICAGO ILL 60680

SEAWAY PHARMACAL CORP
332 WEST DELANO AVE
MUSKEGON HEIGHTS MICH 49444

GEORGE SENN INC
2200 E WESTMORELAND ST
PHILA PA 19134

SERUMS & VACCINES OF AMER ASS
DIV OF MURA LABS INC
269 GIRALDA
CORAL GABLES F/A 33134

SHEFFIELD CHEMICAL
DIV NATIONAL DAIRY PRODS CORP
NORWICH N Y 13815

SHELDON LABS INC
542 S ALEXANDRIA AVE
LOS ANGELES CALIF 90005

SHELL CHEMICAL CORP
DIV OF SHELL OIL CO
110 WEST 51 STREET
NEW YORK N Y 10020
ATTN INDUSTRIAL CHEMICALS DIV

SHUPTRINE CO
PO BOX 644
SAVANNAH GA 31402

SMITH KLINE & FRANCH
1500 SPRING GARDEN ST
PHILA PA 19101

SMITH KLINE & FRENCH LAB
ROUTE 130 & HILTON ROAD
PENNSAUKEN N J 08810

SMITH KLINE & FRENCH LABS LMTD
BOXES 89-90 P O BROOKVALE
NEW SOUTH WALES 2100 AUSTRALIA

SMITH MILLER & PATCH INC
902 BROADWAY
NEW YORK NEW YORK 10010

SALVENTAL CHEMICAL PROD INC
13177 HURON RIVER DRIVE
ROMULUS MICH 48174

SONNEBORN CHEM & REFINING CO
277 PARK AVE
NY NY 10017

SONOROL LABS
1910 WEBSTER AVE
N Y N Y 10457

SOUTHERN DRUG & MFG CO INC
P O BOX 2506
KNOXVILLE TENN 37901

SPECIFIC SERUMS INC
20 HUDSON PLACE
HOBOKEN N J 07030

SPECTRA BIOLOGICALS INC
172 SUMMERHILL ROAD
EAST BRUNSWICK N J 08816

SPECTRONICS CORP
20 NEW YORK AVENUE
WESTBURY N Y 11590

[illegible] CO INC
17 COTTAGE PLACE
WATERBURY CONN 06720

JOHN T STANLEY
642 W 30TH ST
NEW YORK N Y 10001

E R SQUIBB & SONS
909 THIRD AVE
N Y N Y 10022
ATTN C E RICHARDSON

STAR DENTAL MFG CO
58TH-MARKET ST
PHILADELPHIA PENNA 19139

STAHL SOAP CO
17 FORREST ST
BROOKLYN N Y 11206

STAYNE LABORATORIES LIMITED
HILLBOTTOM RD SANDS
HIGH WYCOMBE BURCKINGHAMSHIRE
HIGH WYCOMBE ENGLAND 25721

STANDARD AIR CO OF N J
P O BOX 271
335 PATERSON PLANK RD
CARLSTADT NEW JERSEY 07072

STAYNER CORP
2531 NINTH ST
BERKELSY CALIF 94710

STANDARD PHARMACAL COMPANY
1300 ABBOTT DRIVE
ELGIN ILLINOIS 60120

STEIN HALL CO INC
605 THIRD AVE
NEW YORK N Y 10016

STANDARD SAFETY EQUIPMENT CO
431 NORTH QUENTIN ROAD
PALATINE ILLINOIS 60067

STERLING DRUG INC
PLANNED PRODUCER
90 PARK AVENUE
NEW YORK N Y 10016

STANSE SCIENTIFIC CO
1231 NORTH HONORE ST
CHICAGO ILLINOIS 60622

STIEFEL LABS INC
OAK HILL NEW YORK 12460

STANDARD SCIENTIFIC
65 COMMERCE RD
CARLSTADT N J 07072

STOCK SPANIER INC
74 ELMWOOD AVE
MOUNT VERNON N Y 10552

STANDARD X-RAY CO
CENCO MEDICAL
HEALTH SUPPLY CORP
4401 WEST 26TH ST
CHICAGO ILL 60623

STRASENBURGH LABORATORIES
DIV WALLACE TIERMAN INC
P O BOX 1710
ROCHESTER N Y 14603

STANLABS INC
P O BOX 3108 232 E OAK ST
PORTLAND OREGON 97208

STRASENBURGH PRESCR PRODUCTS
P O BOX 1766
ROCHESTER NEW YORK 14603

STANLEY DRUG PRODS INC

P O BOX 3109
PORTLAND OREGON 97208

STRONG COBB ARNER INC
11700 SHAKER BLVD
CLEVELAND OHIO 44120
ATTN MR ROBERT H SMITH

STUART DIVISION
ATLAS CHEMICAL IND INC
3360 E FOOTHILL BLVD
PASADENA CALIF 91109

STUART CHASE CORP
POND STREET
RANDOLPH MASS 02368

KETCHUM LABORATORIES INC
26 EDISON ST
AMITYVILLE N Y 11701

SUMMERS LABS INC
MORRIS ROAD
FORT WASHINGTON PA 19034

SUN CHEMICAL CORP
750 THIRD AVE
N Y 17, N Y 10017
ATTN MR. P C HERELD

SUNKIST GROWERS
720 E SUNKIST ST
ONTARIO CALIF 91764

SUNLIGHT CHEM CORP
55 PAWTUCHET AVE
RUMFORD R I 02916

SWIFT&CO
LTL CONTRACT SALES
PO BOX 1338
UNION NJ 07083

THE SYLVANA CO
22 E WILLOW ST
MILL BURN N J 07041

SYNTEX LABS
STANFORD IND PARK
3401 HILLVIEW AVE
PALO ALTO CALIF 94304

W A TAYLOR-CO
2 WEST 46 STREET
NEW YORK 19 N Y

TAYLOR PHARMACAL CO
122 W GRAND
DECATUR ILL 62525

TENANT DEVELOPMENT CORP
100 PARK AVENUE
NEW YORK N Y 10017

TERA PHARMACEUTICALS INC
6920 STANTON AVE
BUENA PARK CALIF 90620

TEXAS PHARMACAL CO
P O BOX 1659
SAN ANTONIO TEXAS 78206

TILDEN-YATES LABS INC
FAIRFIELD RD
WAYNE N J 07470

TORCH LABORATORIES INC
542 INDUSTRIAL PARK DR
YEADON PA 19050

TORIGAN LABS INC
218-20 98TH AVE
QUEENS VILLAGE N Y 11429

TOWNE PAULSEN&CO INC
140 E DUARTE RD
MONROVIA CAL 91016

TRAPELO DIV
LEE CORP
1601 TRAPELO RD
WALTHAM MASS 02154
JJ INCATASCIATO

TRANSTRADE USA LIMITED
515 MADISON AVE
NEW YORK 10022

TRAVENAL LABORATORIES INC
200 WILMOT ROAD
DEERFIELD ILL 60015

TRID CHEMICAL WORKS INC
341 SCHOLES STREET
BROOKLYN N Y 11206

TUMBLER LABS INC
DIV IMOCO GATEWAY CORP
PLUM & WEST STS
BALT MD 21230

TURCO PRODUCTS
PUREX CORP LTD
WILMINGTON CALIF 90744

LABORATORIES ATRAL S A R L
TUTEUR BIO-CHEMICAL INC
777 THIRD AVE
NEW YORK N Y 10017

TWENTY ONE BRANDS INC
23 WEST 52ND STREET
NEW YORK N Y 10019

GEORGE UHE CO INC
76 NINTH AVE
NEW YORK N Y 10011

UNION BROACH CO
45-18 COURT SQ
L I C N Y 11101

UNION CARBIDE CORPORATION
CHEMICALS DIVISION
270 PARK AVENUE
NEW YORK N Y 10017

U S INDUSTRIAL CHEMICALS CO
DIV NAT DISTILLERS-CHEM CORP
99 PARK AVE
NEW YORK N Y 10016

UNITED STATES SAFETY SERV CO
1535 WALNUT ST
KANSAS CITY MO 64108

USV PHARMACEUTICAL CORP
800 SECOND AVE
NEW YORK N Y 10017

UPJOHN CO
7000 PORTAGE RD
KALAMAZOO MICH 49001

VAN WATERS & ROGERS INC
BRAUN DIV
1363 S BONNIE BEACH PLACE
LOS ANGELES CALIF 90023

VAPONEFRIN CO
DIV OF U S VITAMIN & PHARM COR
800 SECOND AVE
NEW YORK NEW YORK 10017

VAUGHN INC
2176 DUNN RD
MEMPHIS TENNESSEE 38114

BEN VENUE LABS INC
270 NORTHFIELD ROAD
BEDFORD OHIO 44014

VESTAL LABORATORIES
DIV OF W R GRACE & CO
4963 MANCHESTER AVENUE
ST LOUIS MISSOURI 63110

VI-JON LABS INC
6300 ETZEL AVE
ST LOUIS MO 63133

VINELAND LABS INC
E LANDIS AVE
VINELAND N J 08360

VITA NEEDLE COMPANY
919 GREAT PLAIN AVENUE
NEEDHAM MASS 02192

VITAMINS INC
809 WEST 58 STREET
CHICAGO ILL 60621

THE VITARINE CO INC
227-15 NORTH CONDUIT AVENUE
SPRINGFIELD GARDENS N Y 11413

PENNWALT DIV
PENNWALT CORP
P O BOX 1212
ROCHESTER NY 14603

L F WERTHEIMER INC
FIRST NATIONAL BANK BLDG
CINCINNATI OHIO 45202

WALLACE PHARMACEUTICALS
DIV OF CARTER PRODS INC
HALF ACRE RD
CRANBURY NJ 08512

WEST CHEMICAL PRODUCTS INC
42-16 WEST STREET
LONG ISLAND CITY N Y 11101
ATTN MR DAVID R PECK

WALLACE & TIERNAN DIV
PENNWALK CORP
25 MAIN ST
BELLEVILLE N J 07109

WEST WHOLESALE DRUG CO
231 EAST LUZERNE ST
PHILA PENNA 19124

THE DENVER CHEMICAL MFG CO
WAMPOLE LABS
35 COMMERCE RD
STAMFORD CONN 06902

WESTINGHOUSE ELECTRIC CORP
SUITE 901
2001 JEFFERSON DAVIS HWY
ARLINGTON VA 22202

WARNER-CHILCOTT LAB DIV
WARNER LAMBERT PHARM CO
201 TABOR ROAD
MORRIS PLAINS NJ 07950
ATTN WC GOV SALES & SERVICES

WEST-WARD INC
745 EAGLE AVE
BRONX NEW YORK 10456

WARRENTEED PHARM INC
582 W GOODALE ST
COLUMBUS OHIO 43215

WESTWOOD PHARMACEUTICALS
DIV OF FOSTER MILBURN
468 DEWITT ST
BUFFALO N Y 14213

WASHINE CHEMICAL CORP
165 MAIN ST
LODI N J 07644

SCHERING CORPORATION
GALLOPING HILL ROAD
KENELWORTH N J 07033

WAYS & MEANS INC
70 WOODLAND AVE
SAN RAFAEL CALIF 94901

WHITEHALL LABORATORIES
DIV OF AMERICAN HOME PRODUCTS
685 THIRD AVENUE
NEW YORK N Y 10017

WEBSTER DRUG PROD INC
139 WEBSTER AVE
PROVIDENCE R I 02909

WHORTON PHARMACAL CO INC
4202 GARY AVENUE
FAIRFIELD ALA 35064

THE WILLIAM A WEBSTER CO
PO BOX 18358
3580 AIR PARK STREET
MEMPHIS TENN 38118

WILL SCIENTIFIC INC
5 NO HAVEN ST
BALTIMORE MD 21203

WEEKS & LEO CO INC
4000 N W 100TH ST PO BOX 3570
DES MOINES IOWA

WILLIAMS BROWN EARLE INC
904-06 CHESTNUT STREET
PHILADELPHIA PA 19107

WILSON LABORATORIES
DIV OF WILSON CO
4221 S WESTERN BLVD
CHICAGO ILLINOIS 60609

WINTHROP LABORATORIES
DIV STERLING DRUG INC
90 PARK AVE
NEW YORK N Y 10016

WITCO CHEMICAL CORP
277 PARK AVE
NEW YORK N Y 10017

WOLFF GAS PRODS INC
555 JULIE ANN WAY
OAKLAND CALIF 94621

WOOD RIDGE CHEMICAL CORPORATIO
PARK PLACE EAST
WOOD-RIDGE NEW JERSEY 07075

WYETH LABORATORIES DIVISION OF
AMERICAN HOME PRODUCTS CORP
P O BOX 8299
PHILADELPHIA PENN 19101

XTTRIUM LABORATORIES INC
415W PERSHING RD
CHICAGO ILL 60609

YARON LABORATORIES INC
P O BOX 3169
SAN FRANCISCO CALIF 94119

YATES MFG CO
1615 WEST 15TH ST
CHICAGO ILL 60608

YADOKIN INC
82 BEAVER ST
NEW YORK 5 N Y 10005

THE J S YOUNG CO
2701 BOSTON ST
BALTIMORE MARYLAND 21224

YORK SERVICE CO
30 E 42ND ST
NEW YORK N Y 10017

THE ZEMMER CO INC
231 HULTON ROAD
OAKMOUNT PA 15139

ZENITH LABORATORIES INC
140 LE GRAND AVE
NORTHVALE NJ 07642

EXHIBIT 8

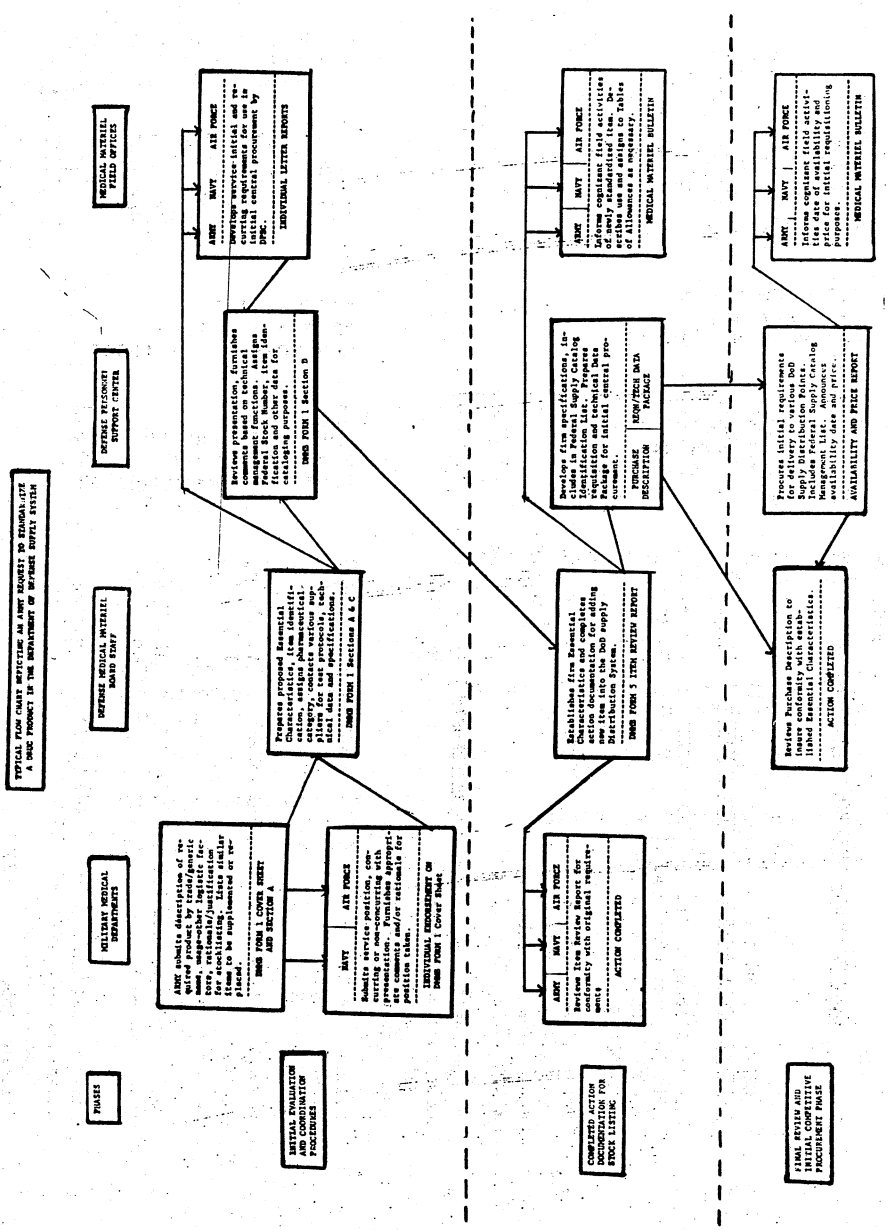
TYPICAL FLOW CHART DEPICTING AN ARMY REQUEST TO STANDARDIZE A DRUG PRODUCT IN THE DEPARTMENT OF DEFENSE SUPPLY SYSTEM
PHASES
MILITARY MEDICAL DEPARTMENTS
DEFENSE MEDICAL MATERIEL BOARD STAFF
DEFENSE PERSONNEL SUPPORT CENTER
MEDICAL MATERIEL FIELD OFFICES
INITIAL EVALUATION AND COORDINATION PROCEDURES
ARMY submits description of required product by trade/generic name, usage other logistic factors, and specific reasons for stocklisting. Lists similar items to be supplemented or replaced.
DMRS FORM 1 COVER SHEET AND SECTION A
ARMY | NAVY | AIR FORCE
Submits service position, comments or recommendations for presentation. Furnishes appropriate comments and/or rationale for position taken.
INDIVIDUAL ENDORSEMENT ON DMRS FORM 1 Cover Sheet
Prepares proposed Essential Characteristics, item identification, assigns pharmaceutical category, contacts various suppliers for samples and technical data and specifications.
DMRS FORM 1 Sections A & C
Reviews presentation, furnishes comments based on technical management functions. Assigns federal stock number, item identification and other data for cataloging purposes.
DMRS FORM 1 Section D
ARMY | NAVY | AIR FORCE
DEVELOPS service initial and recurring requirements for use in initial central procurement by DPSC.
INDIVIDUAL LETTER REPORTS
COMPLETED ACTION DOCUMENTATION FOR STOCK LISTING
Establishes firm Essential Characteristics and completes action documentation for adding item to Army and DoD supply Distribution System.
DMRS FORM 3 ITEM REVIEW REPORT
ARMY | NAVY | AIR FORCE
Reviews Item Review Report for conformity with original requirements
ACTION COMPLETED
Develops firm specifications, item identification, Supporting Identification Line, Proposed requisition and technical Data Package for initial central procurement.
PURCHASE DESCRIPTION
MIDC/TECH DATA PACKAGE
ARMY | NAVY | AIR FORCE
Informs cognizant field activities of newly standardized item. Describes use and assigns to tables of allowances as necessary.
MEDICAL MATERIEL BULLETIN
FINAL REVIEW AND INITIAL COMPETITIVE PROCUREMENT PHASE
Reviews Purchase Description to insure conformity with established Essential Characteristics.
ACTION COMPLETED
Procures initial requirements for delivery to various DoD Supply Distribution Points. Establishes Depot Supply Catalog Management Line, source, availability date and price.
AVAILABILITY AND PRICE REPORT
ARMY | NAVY | AIR FORCE
Informs cognizant field activities date of availability and price for initial requisitioning purposes.
MEDICAL MATERIEL BULLETIN

EXHIBIT-9

LIST OF DRUGS DESIGNATED LIMITED (SOLE) SOURCE BY DEFENSE MEDICAL MATERIEL BOARD

ITEM NO.	GENERIC NAME AND FEDERAL STOCK NUMBER	TRADE NAME	SUPPLIER	DATE DESIGNATED LIMITED (SOLE) SOURCE	DATES RE-EVALUATED BY BOARD
1	Sodium Diphenylhydantoin Capsules USP 100s/1000s (6505-116-9325 6505-584-2338)	"DILANTIN"	Parke-Davis & Co.	2-24-60	8-14-67 8-13-69
2	Tetracaine Hydrochloride Injection USP (for spinal anesthesia) (6505-147-1850)	"PONTOCAINE"	Winthrop Labs	4-27-60	8-14-67 8-13-69
3	Neomycin Sulfate, Hydrocortisone and Polymyxin B Sulfate Suspension (Otic) (6505-754-2436)	"CORTISPORIN"	Burroughs Wellcome & Co.	11-30-60	8-14-67 8-13-69
4	Polymyxin B Sulfate Solution (Otic) (6505-754-0001)	"AEROSPORIN"	Burroughs Wellcome & Co.	1-25-61	8-14-67 8-13-69
5	Detergent, Surgical liquid - 5 oz/gal (6505-116-1740/1750)	"pHisoHex"	Winthrop Labs	4-5-61	8-14-67 1-22-69 8-13-69 4-29-70
6	Tolbutamide Tablets USP (6505-982-9069)	"ORINASE"	The Upjohn Co.	11-15-62	8-14-67 8-13-69
7	Neomycin Sulfate, Gramicidin and Polymyxin B Sulfate Ophthalmic Solution (6505-890-1299)	"NEOSPORIN"	Burroughs Wellcome & Co.	4-30-63	8-14-67 8-13-69

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LIST OF DRUGS DESIGNATED LIMITED (SOLE) SOURCE BY DEFENSE MEDICAL MATERIEL BOARD

ITEM NO.	GENERIC NAME AND FEDERAL STOCK NUMBER	TRADE NAME	SUPPLIER	DATE DESIGNATED LIMITED (SOLE) SOURCE	DATES RE-EVALUATED BY BOARD
8	Norethindrone Acetate and Ethinyl Estradiol Tablets (6505-445-9957)	"NORLESTRIN 21"	Parke-Davis & Co.	12-9-66	1-24-68 8-14-67 8-13-69
9	Norethynodrel with Mestranol Tablets (6505-937-1760)	"ENOVID E"	G. D. Searle & Co	12-9-66	8-14-67 3-20-69 8-13-69
10	Ethinyl Estradiol Tablets and Dimethisterone with Ethinyl Estradiol Tablets (6505-937-1758)	"ORACON"	Mead Johnson Labs.	12-9-66	8-14-67 1-24-68 8-13-69
11	Ethynodiol Diacetate with Mestranol Tablets (6505-935-5836)	"OVULEN"	G. D. Searle & Co.	12-9-66	8-14-67 1-24-68 8-13-69
12	Sodium Warfarin Tablets USP (2/5/10 mg) (6505-982-4228/4229/4230)	"COUMADIN"	Endo Labs.	4-18-69	8-13-69

EXHIBIT-10

ITEMS REMOVED FROM SOLE SOURCE

1. CALCIUM PROPIONATE-SODIUM PROPIONATE JELLY (FY 1967)

2. SODIUM PARA-AMINO BENZOATE, SODIUM SALICYLATE AND ASCORBIC ACID TABS (FY 1964)

3. SENNA POD EXTRACT TABS (FY 1964)

4. ALUMINUM HYDROXIDE GEL AND MAGNESIUM TRISILICATE TABS (FY 1970)

5. PROPARACAINE HCL OPHTHALMIC SOLUTION (FY 1970)

6. NORETHYNODREL WITH MESTRANOL TABS

   ONLY 6505-685-5335 WAS REMOVED FROM SOLE SOURCE IN FY 1967.

   FSN 6505-689-9253 WAS NEVER DESIGNATED SOLE SOURCE, AND FSN 6505-937-1760 WAS REINSTATED AS SOLE SOURCE.

7. THYROID TABS, U.S.P. (FY 1964)

8. PSYLLIUM HYDROPHILC MUCILLOID WITH DEXTROSE (FY 1964)

EXHIBIT-11

ITEMS WHERE E/CS WERE REVISED AND SINGLE SOURCE BROKEN

1. HYDROCORTISONE CREAM
2. HYDROCORTISONE AND IODOCHLORHYDROXYQUIN CREAM
3. GLYCERYL GUAIACOLATE SYRUP
4. MINERAL OIL, LANOLATED
5. DEXTROMETHORPHAN HYDROBROMIDE AND GLYCERYL GUAIACOLATE SYRUP

EXHIBIT-12

ITEMS NOW BEING PROCURED FROM MULTIPLE SOURCES AFTER BEING SINGLE SOURCE

FSN	NOMENCLATURE
6505-721-9121	BELLADONNA ALKALOIDS WITH PHENOBARBITAL TABLETS
6505-890-1658	CALCIUM CARBONATE AND AMINOACETIC ACID TABLETS
6505-926-8926	CHLORPHENIRAMINE MALEATE, CHLOROFORM, CODEINE PHOSPHATE, GLYCERYL GUAIACOLATE, MENTHOL, AND PHENYLEPHRINE HYDROCHLORIDE SYRUP
6505-926-8985	DEXTROMETHORPHAN HYDROBROMIDE AND GLYCERYL GUAIACOLATE SYRUP
6505-689-5528	IODOCHLORHYDROXYQUIN AND HYDROCORTISONE CREAM
6505-926-2101	IODOCHLORHYDROXYQUIN AND HYDROCORTISONE CREAM
6505-050-4567	PSYLLIUM HYDROPHILIC MUCILLOID WITH DEXTROSE
6505-890-1333	SODIUM SULFACETAMIDE AND PREDNISOLONE ACETATE OPHTHALMIC SUSPENSION
6505-728-2007	THEOPHYLLINE AND GLYCERYL GUAIACOLATE ELIXIR
6505-530-6469	ZINC BACITRACIN, NEOMYCIN SULFATE, AND POLYMYXIN B SULFATE OPHTHALMIC OINTMENT
6505-770-8343	AMPICILLIN CAPSULES
6505-935-1148	AMPICILLIN CAPSULES
6505-783-0233	AMPICILLIN CAPSULES
6505-837-5710	AMPICILLIN FOR ORAL SUSPENSION
6505-926-8924	AMPICILLIN FOR ORAL SUSPENSION
6505-935-6535	AMPICILLIN FOR ORAL SUSPENSION
6505-926-2095	HYDROCORTISONE CREAM
6505-926-2096	HYDROCORTISONE CREAM
6505-926-2097	HYDROCORTISONE CREAM
6505-761-1506	ISOSORBIDE DINITRATE TABLETS
6505-890-2027	MINERAL OIL, LANOLATED, WATER-DISPERSIBLE

EXHIBIT-13

Shift from Non-Competitive to Competitive

Date	Item	Sole Source Mfgr.	New Mfgr
21 Dec 67	Inserts Optical CBR Mask FSN 6540-656-1240; 1243; 1244; 1247; 1248; 1251	Bausch & Lomb Inc.	Welsh Mfg. Co.
6 Sep 68	Methenaminl Mandelate, Oral Sus, USP, 0.5 Gm per 5 CC, 8 fl oz FSN 6505-773-6545	Warner Chilcott Labs	Reine Pharmaceutical Corp.
3 Jul 68	Glyceryl Guaicolate Syrup, 100 mg per 5 CC, 4 fl oz FSN 6505-064-8765	A. H. Robbins Co.	Dorsey Laboratories
13 Sep 68	Cup Earphone Audiometer FSN 6515-935-3990	Tracor Inc.	Aural Research
4 Oct 68	Dexpanthenol Inj 0.25 gm per CC, 2 CC FSN 6505-753-9516	Warren Teed Pharm	Vitarine Co.
17 Jan 69	Temple, Spectacle, Standard Gray Plastic FSN 6540-926-2282 thru 2284	Bausch & Lomb	Rochester Optical
3 Apr 69	Paper Filter for Fine Precipitate FSN 6640-986-1681	Tracer Laboratories	Sun Chemical Corp.
24 Feb 70	Acetaminophen Elixir FSN 6505-926-9055	McNeil Laboratory	G&W Laboratories
3 Jul 68	Glyceryl Guaicolate Syrup 100 mg per 5 cc, 1 gallon bottle FSN 6505-079-6269	A. H. Robbins Co.	Dorsey Laboratories

Date	Item	Sole Source Mfgr.	New Mfgr.
1 Oct 69	Flame Photometer FSN 6650-122-6991	Instrument Lab Co.	American Hospital Supply Corp.
Oct 69	Power Supply Unit	Electrofilm - Heater Kunz & Root - Battery Charger Zero Mfg. Co. - Case	Q-Line Instrument Co.
30 Oct 69	Refrigerator Mechanical Whole Blood FSN 4110-113-8334	Glenco Refrigerator Co.	Jewett Mfg. Co.
29 May 69	Thyroid Tablets USP 6505-153-9745	Armour Pharmaceutical	Parke Davis Co.
3 Jun 70	Tubocurarine Chloride Inj 6505-299-9475	Abbott Laboratories	Squibb
3 Dec 69	Alcohol Dehydrated 6505-105-0000	U. S. Industrial Co.	Publicker Industries
22 Jul 69	Ampicillin Capsules 6505-935-1148	Bristol Laboratories	Wyeth Laboratories
15 Aug 68	Undecylenic Acid Ointment 6505-664-4814	WTS Pharmacraft	Leeming Pacquin Co.

EXHIBIT- 14

SMALL BUSINESS ALLOCATION

	1968	1969
DPSC Total Medical Materiel Purchases	$106,782,729	$89,794,313
Small Business	$6,816,654	$7,431,230

EXHIBIT- 15

CONVERSION FROM SMALL BUSINESS TO LARGE BUSINESS

FY 70

Day Baldwin

Westwood Pharmaceuticals, Div of Foster-Milburn Co.

Endo Laboratories

Pilling Co.

Medical Chemicals Corp.

Consolidated Labs

FY 69

Baltimore Biological Labs, Div of Bio Quest, now a Div of Becton-Dickinson & Co.

Pharmusa Corp.

Strong Cobb Arner Inc.

Foster Milburn Inc.

Bloomfield Industries Inc.

Courtland Labs

Davies Young Soap Co.

FY 68

Bard Parker Co., Inc.

Breon Labs

C. R. Daniels Company

Eisele & Co. Inc.

Lakeside Labs

Nysco Labs, Inc.

Riker Labs

Rabin-Winters Corp.

FY 68 (Cont'd)

Spectra Biologicals Inc.

U. S. Vitamin & Pharmaceuticals

Wampole Labs

Medical Supply Co.

EXHIBIT-16

TEN-POINT QUALITY ASSURANCE PROGRAM

1. SPECIFICATIONS

GUIDELINES:

U.S.P. AND N.F.

PROFESSIONAL GUIDANCE FROM DMMB

TECHNICAL DATA FROM OTHER SOURCES

REASONS FOR ADDITIONAL SPECIFICATION REQUIREMENTS:

ADVANCEMENT AND MODIFICATIONS TO U.S.P. AND N.F. ARE TIME CONSUMING

SPECIAL PACKAGING

DETERIORATION OF DRUGS DUE TO CONDITIONS AND STORAGE

STABILITY TESTS

ADVANCED INSTRUMENTATION INCREASING PURITY

2. PRE-AWARD SURVEY

ESTABLISH CAPABILITY AND QUALIFICATIONS

PLANT EVALUATION

3. PRE-AWARD SAMPLES

DETERMINE FIRM'S POTENTIAL

ANALYSIS OF SAMPLES

4. PRODUCT INSPECTION

POST AWARD CONFERENCE

SURVEILLANCE OF PRODUCTION, QUALITY CONTROL, AND WAREHOUSING

ACCEPTANCE INSPECTION AND TESTING

TECHNICAL GUIDANCE BY DPSC

5. REVIEW OF INSPECTION DATA AND TEST RESULTS

6. LABORATORY ANALYSIS

DPSC AND OTHER GOVERNMENT LABORATORIES

VERIFICATION TESTING

PRE-AWARD SAMPLES

FIELD COMPLAINTS

DEPOT SAMPLES

7. DEPOT SURVEILLANCE

CYCLIC INSPECTION FOR VISUAL DEFECTS

GUIDE IS IN-STORE QUALITY CONTROL MANUAL

SUSPECT MATERIAL TESTED BY LABORATORY

8. COMPLAINT EVALUATION

ANALYZE, TEST, EVALUATE FIELD COMPLAINTS

DETERMINE COMPLIANCE WITH PRODUCT SPECIFICATIONS

9. CUSTOMER LIAISON

CONTACT WITH FIELD ACTIVITIES

CUSTOMER REACTION TO QUALITY AND SUPPORT EFFECTIVENESS

10. CLINICAL EFFECTIVENESS AND THERAPEUTIC EQUIVALENCY

FOR SEVERAL ITEMS AS DATA BECOMES AVAILABLE

MILITARY PHYSICIANS AND PATIENTS ARE CAPTIVE CONSUMERS

EQUIVALENCY ESSENTIAL TO PRACTICE OF MEDICINE

OBJECTIVE: THERAPEUTIC EQUIVALENCY OF SAME DRUG ITEM, PRODUCED BY DIFFERENT MANUFACTURERS, AND DISPENSED INTERCHANGEABLY IN A GENERIC SYSTEM.

EXHIBIT-17

Other Support

There is an Inter-Agency Agreement between the Defense Supply Agency and the Public Health Service, which provides that DPSC will render all required services for the supply support of PHS requirements of medical items through procurement sources or from stocks on hand in the depot system.

The Defense Personnel Support Center has agreed to provide procurement support to the Veterans Administration on a selected item basis upon request by them.

Effective 1 July 1970, DPSC will provide procurement support for the District of Columbia.

This Center also supports the Medical AID Programs.

EXHIBIT 18

THE DEFENSE PERSONNEL SUPPORT CENTER (DPSC)
QUALITY ASSURANCE PROGRAM

The Defense Personnel Support Center Quality Assurance Program consists of the following features:

Specifications and Purchase Descriptions: Maximum technical support is directed toward development of precise and definitive specifications for medical materiel. These specifications provide objective standards to measure and determine that quality products are procured.

Preaward Plant Surveys: The preaward facility survey is another significant feature in the Quality Assurance Program. Based upon the nature of the item and the known capabilities of the company, the Directorate of Medical Materiel of DPSC determines whether an inspection is required prior to the award of a contract. If a survey is needed, a Defense Contract Administration Service (DCAS) field inspector and/or a DPSC quality control specialist, experienced in the commodity, visit the plant to evaluate production capability, quality control procedures and housekeeping practices. Since this program was started on 1 January 1962, over 900 medical materiel manufacturers have been surveyed by government inspectors. A significant number of manufacturers have been rejected one or more times for failure to meet the DPSC quality control or sanitary standards.

Laboratory Analysis: The DPSC Medical Laboratory is equipped and staffed to accomplish chemical, physical and bacteriological tests. The laboratory tests preaward samples from prospective contractors to determine if the firm has the capabilities to produce an item which meets the applicable specification. The laboratory also analyzes samples of manufacturers' products before, during and after the production run, as well as samples submitted by hospitals and depots. The latter samples apply to stocks suspected of being unsuitable for further use and issue. Assistance is received from other Government, military and commercial laboratories when specialized testing is necessary.

Inspection Services: Inspection for medical contracts is the responsibility of DCAS. Due to the criticality of medical materiel, steps were taken to insure utilization of highly qualified personnel as medical inspectors. Qualification standards are established and two comprehensive training courses are required for all inspectors of drugs, chemical and blood grouping and typing reagents. Three instructional courses are required for inspectors of surgical and dental instruments, medical devices and equipment. The DCAS quality assurance representatives have been indoctrinated in product inspection as well as plant inspection, and they possess the capability to ensure that the materiel procured meets the specification requirements.

Depot In-Store Quality Control Program: The DPSC has an active In-Store Quality Control Program for the surveillance of depot stock. The basic objective of the program is to assure that medical materiel is "fit-for-issue". A detailed In-Store Quality Control Manuel, first published in 1958 and subsequently revised, is used as a guide for periodic inspection and surveillance of depot stocks. If materiel is suspected of being unsuitable for use after visual inspection, depot stocks are suspended and samples of the suspected materiel are submitted to DPSC for laboratory analysis. In this manner, DPSC evaluates the condition of depot stocks to assure the suspension or destruction of unsuitable materiel and accomplish repairs or modifications of medical equipment.

Field Quality Control System: The DPSC actively solicits reports from military hospitals and other military medical treatment facilities concerning the adequacy of materiel being used. These reports are submitted independently by the user or obtained as a result of a visit to the installation through participation in the DSA Quality Check Program. This system permits DPSC to evaluate the condition and quality of medical materiel through the life of the items.

DSA Quality Check Program: This program is accomplished through visits by qualified technical personnel to using activities to obtain first-hand information regarding the quality, reliability, and maintainability of DPSC furnished materiel.

EXHIBIT 19

DEPARTMENT OF DEFENSE POLICIES AND PROCEDURES FOR PREPARATION OF SPECIFICATIONS TO INSURE ACQUISITION OF QUALITY MEDICAL MATERIAL

The policy of the Department of Defense is to purchase quality drugs to meet designated delivery schedules from the lowest, responsive, responsible supplier (bidder) and in accordance with the procedures of the Armed Services Procurement Regulation. Drugs may be generic or brand name, but provision must be made for a sufficient span and latitude of high quality drugs to permit our military physicians to make a deliberate choice and not a forced decision. To carry out this function, the Department of Defense established the Defense Medical Materiel Board, composed of the Surgeons General of the three Military Medical Services and a staff of highly qualified professional personnel. The Board has the assigned responsibility to determine those chemical, physical and physiological characteristics considered as mandatory requirements of a drug or biological necessary to meet the professional needs of the physician and dentist to adequately treat diseased conditions of patients under their care. In conformance with directives issued by the Department of Defense, the Board designates pharmaceuticals by generic name, except in those instances where professional knowledge and experience has demonstrated that only the product of a specific manufacturer (brand name) can be relied upon to produce the desired consistent physiological effects.

As evidence of the above, the Defense Medical Materiel Board has used its authority to designate specific acceptable sources of supply sparingly. As of 30 December 1966, of the over 1200 items of drugs and biologicals, only 31 items have been designated by the Board for sole source procurement. These items include 10 pharmaceutical products, 8 recently adoptel oral contraceptive tablets and 13 laboratory reagents. There are 409 items which are not specifically designated by the Board as sole source, but which, although solicited competitively, are procured from a single source. Specifications are written for the generic item and the product is so solicited. Notices of impending procurements over $10,000 are published in the Department of Commerce, Commerce Business Daily and specifications and solicitations are forwarded to prospective suppliers in an attempt to broaden the base and achieve competition. However, either because of production capability, pharmaceutical know-how, the initial investment expense, patents or licensing, only one source has responded to a solicitation.

The drugs (as well as other medical items) which are to be procured by DPSC are selected or standardized by the DMMB. On standardizing a drug, the DMMB identifies the characteristics and attributes which the item must possess to satisfy the medical professional needs. Based on the guidance furnished by DMMB, DPSC must draft specifications which will permit the acquisition, by generic description, of that drug possessing the quality required for medical professional needs. Initially, the data for these specifications is obtained from the information supplied by the DMMB, from the contents of the compendia, from FDA, from any available literature, from the in-house knowledge derived from experience with the same or similar items and from those producers who have supplied the item in question to the Military Departments and whose item has been found to be acceptable by the DMMB.

The use of data from the supplier whose product has been determined to be acceptable is in many instances both necessary and desirable if a quality product is to be obtained. The Department of Defense does not have an original research program in drugs from which to draw some of the essential information. The data from the sources mentioned above selectively forms the basis for the specifications after it has been screened and evaluated to determine which is relevant to and reasonably necessary for assuring the acquisition of quality drugs. Specifications are continually reviewed and strengthened with a view toward improving the probabilities of obtaining, regardless of source, the quality product required. The program for the continuing reevaluation of specifications depends for its data not only upon the sources previously used, but also on the test reports and other information received through the DPSC con-

tract inspection system and the feed back resulting from storage and field use. Improved specifications serve to better apprise sources of supply of what the Government requires, thereby improving the opportunity of industry to compete for Government procurements. Every effort is made to prepare specifications so as to achieve maximum feasible competition between suppliers consistent with obtaining items of the quality required.

EXHIBIT 20

TOTAL DRUG EXPENDITURES AND BREAKDOWN BY MAJOR THERAPEUTIC CATEGORIES

	1968	Percent of total	Percent single source	1969	Percent of total	Percent single source
Total drug expenditures	$106,782,729			$89,794,313		
Analgesics	4,425,729	4.1	99.4	4,778,208	5.3	75
Anorexigenics	249,055	.23	100	180,544	.20	94
Antibacterials and anti-infectives	1,240,621	1.2	78	1,329,954	1.5	96.8
Antibiotics	22,773,859	21.3	76.5	18,443,675	20.5	78.3
Antidiabetics (does not include insulins)	446,376	.42	100	761,656	.84	100
Antiemetics and antinauseants	1,919,839	1.8	100	670,876	.74	100
Antifungals	1,248,136	1.2	82.6	2,585,215	2.9	86.3
Antihistamines	5,894,393	5.5	96	4,664,177	5.2	99.5
Antihypertensives	823,610	.77	99.6	1,197,639	1.3	99.6
Cardiotonics and heart preparations	179,511	.17	25.5	163,336	.18	49.5
Coronary vasodilators	454,743	.43	97.9	243,476	.27	97.3
Diuretics	986,780	.92	85.4	1,428,717	1.6	100
Hormones (includes thyroids and insulins, does not include oral contraceptives)	5,337,372	5.0	83.6	3,267,300	3.6	64.2
Macrocytic, Primary, pernicious	0	0	0	0	0	0
Oral contraceptives	2,828,301	2.6	92	1,508,571	1.7	79.4
Psychotherapeutic agents (includes antidepressants and tranquilizers)	5,298,660	4.9	96.8	4,750,312	5.3	96.1
Sedatives hypnotic	86,098	.08	54.9	165,348	.18	60.2
Skeletal muscle relaxants	1,473,539	1.4	97	208,821	.23	85.7
Sugars	5,491	.005	0	14,792	.016	0
Urinary tract	396,616	.37	56	339,242	.37	79
Vasodilators	100,486	.09	100	122,458	.14	100
Anticoagulants	204,945	.19	99	147,585	.16	73.4

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

DEFENSE SUPPLY AGENCY—DISTRIBUTION OF TOTAL PHARMACEUTICAL PURCHASES BY SOURCE OF PROCUREMENT, 1968-69

Source of procurement	Amount purchased	Percentage of total purchases
Combination drugs	$42,054,453	39.6
Single entity drugs	39,599,407	37.3
Small business awards	13,716,931	12.9
Sole source drugs	6,174,067	6.3
Foreign drugs	4,109,028	3.9
Total	106,193,886	100.0

DEFENSE SUPPLY AGENCY—COMBINATION DRUGS PROCUREMENTS: DISTRIBUTION OF SMALLER COMPANY CONTRACTS SECURED UNDER NEGOTIATION, 1968–1969

Number and drug supplier	Number of different drugs supplied [1]	Total sales	Percentage of grand total
Top six suppliers:			
1 A. H. Robins [2]	10	$2,988,463	47.6
2 Travenol (Baxter) [3]	6	717,217	11.4
3 Wm. Rorer [4]	1	363,470	5.8
4 Chase [5]	4	328,599	5.2
5 Strong Cobb Arner [6]	2	302,914	4.8
6 McGaw [7]	1	271,162	4.3
Totals		4,971,825	79.2
Remaining suppliers:			
1 Burton Parsons	1		
2 Cutter [8]	2		
3 Allergan Pharmaceuticals	4		
4 Purdue Federick	3		
5 Harleco	1		
6 National Cylinder	1		
7 Gotham	1		
8 Premo	2		
9 Massengill	2		
10 Dyn	2		
11 Vitarine	1	1,309,648	20.8
12 Knoll	1		
13 Holland Rantos	1		
14 Dorsey	2		
15 Stuart	1		
16 Lilly White Sales	1		
17 Whitehall	2		
18 G. & W. Lab	2		
19 Dermik	2		
20 Day Baldwin	1		
21 Baltimore Biologicals	1		
Totals		1,309,648	20.8
Grand totals		6,281,473	100.0

[1] Besides different drugs supplied, this figure includes differently specified dosages of the same drug (e.g., a bottle of aspirin 100's as differing from 200's).

[2] A. H. Robins' secured drugs were: Methocarbamol and aspirin (500's); Methamphetamine HCl and Phenobarbital (both 500's and type II 500's); Glycopyrrolate and Phenobarbital (500's); Belladona Alkaloids w/Phenobarbital (500's); Sodium Aminobenzoate, Ascorbic Acid and Salicylate (500's); Dextromethorphan Hydrobromide and Glyceryl Guaiacolate syrup (4 fl. oz); Brompheniramine Maleate, Phenylephrine HCl and Phenylpropanolamine HCl Elixir (500's and 4 fl. oz. and 1 gal.).

[3] Travenol (Baxter) secured drugs were: Sodium Phosphate, Sodium Citrate solution; 4.5 oz.; Dextrose and Sodium Chloride injection, 250 cc. (12's) and 1,000 (6's); Dextrose, Calcium Chloride, Magnesium Chloride, Sodium Chloride and Sodium Lactate, 1000 cc. w/airway tube (6's); Dextrose in lactated ringers injection, 1,000 cc. (6's).

[4] Wm. Rorer's only secured drug was Aluminum Hydroxide Gel w/Magnesium Hydroxide, 6 fl. oz.

[5] Chase's secured drugs were: Heptavitamin Tablets (100's), Oleovitamin A&D (100's); Thiamine HCl, Niacinamide and Riboflavin (1,000's); Calcium Carbonate and Aminocetric (500's).

[6] Strong Cobb Arner's secured drugs were: Aminophylline and Phenobarbital (1,000's); and Sodium Bicarbonate, charcoal and peppermint tablets (1,000's).

[7] McGaw's only secured drug was Dextrose and Sodium Chloride injection (1,000 cc., 6's).

[8] Cutter's secured drugs were Dextrose and Sodium Chloride injection (250 cc., 12's and 1,000 cc., 6's).

DEFENSE SUPPLY AGENCY—DISTRIBUTION OF SOLE SOURCE DRUGS PROCURED BY BRAND NAME, 1968–69

Pharmaceuticals (brand name)	Supplier	Total sales	Percentage of grand total	
pHisoHex	Winthrop	$1,773,290	26.4	26.5
Pontocaine HCL	do	8,556	0.1	
Neosporin, opthalmic solution	Burroughs-Wellcome	189,838	2.8	7.6
Aerosporin, otic solution	do	49,530	0.7	
Cortisporin, ophtalmic solution	do	272,443	4.1	
Ophthetic, ophthalmic solution	Allergan Pharmaceutical	43,128	0.6	
Dilantin Sodium	Parke-Davis	100,296	1.5	2.0
Norlestrin-21	do	35,302	0.5	
Coumadin sodium	Endo Labs (Du Pont)	39,073	0.6	
Orinase	Upjohn	436,662	6.5	
Oracon	Mead-Johnson	2,400,359	35.7	
Ovulen-21	Searle	1,365,590	20.3	
Grand totals		6,714,067	100.0	

Senator NELSON. Tomorrow's hearing will be held in room 1202.

(Whereupon, at 12:15 p.m., the committee adjourned, to reconvene at 10 a.m., Tuesday, August 18, 1970.)

COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

(Present Status of Competition in the Pharmaceutical Industry)

TUESDAY, AUGUST 18, 1970

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

The subcommittee met, pursuant to recess, at 10:10 a.m., in room 1202, New Senate Office Building, the Honorable Gaylord Nelson (chairman of the subcommittee) presiding.

Present: Senator Nelson.

Also present: Benjamin Gordon, staff economist; Elaine C. Dye, clerical assistant; and Keith A. Jones, minority counsel.

Senator NELSON. Our first witness this morning is Dr. Jesse Steinfeld, Surgeon General, Public Health Service.

Dr. Steinfeld, we are pleased to have you here today. Please identify your associates for the record. If you or anyone else wishes to comment from time to time, please identify yourself so we get the record correct.

You may present your statement however you may desire. It will be printed in full in the record. If you wish to extemporize, feel free to do so.

STATEMENT OF DR. JESSE L. STEINFELD, SURGEON GENERAL, PUBLIC HEALTH SERVICE, DEPUTY ASSISTANT SECRETARY FOR HEALTH AND SCIENTIFIC AFFAIRS, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE; ACCOMPANIED BY ALLEN J. BRANDS, PHARMACY LIAISON REPRESENTATIVE, PUBLIC HEALTH SERVICE; AND WINTON B. RANKIN, SPECIAL ASSISTANT TO ASSISTANT SECRETARY FOR HEALTH AND SCIENTIFIC AFFAIRS

Dr. STEINFELD. Thank you, Senator. With me on my left is Mr. Winton Rankin, Special Assistant to the Assistant Secretary for Health and Scientific Affairs, and on my right is Mr. Allen Brands, Chief Pharmacist Officer of the Public Health Service.

I would like to read the statement and perhaps make several comments on it.

I am pleased to appear before the Monopoly Subcommittee of the

Senate Small Business Committee to present information on the Public Health Service's policy and practices regarding the selection and procurement of drug products.

The Public Health Service is one of the smaller direct purchasers of drugs among the Federal agencies. In fiscal year 1969, we purchased approximately $6 million worth of drugs. This is less than the $48 million worth purchased by Veterans' Administration or the purchases of Department of Defense, which amounted to more than $100 million that year.

However, despite the relative size of our direct drug purchases, as the principal health agency of the Government we accept the responsibility for insuring that the PHS clinics and hospitals provide, within available funds and facilities, the very best drugs and care possible.

The Public Health Service in its direct medical care activities operates over 60 hospitals: 51 of these for American Indians, eight for merchant seamen and certain Federal employees, two for narcotic addicts, one for the mentally ill, and one for patients with leprosy. These hospitals have about 12,000 beds and over 100,000 annual admissions. In addition, there were over 3 million outpatient visits for treatment at the hospitals and clinics last year.

The Service is responsible for providing health care services to Indians, merchant seamen, certain Federal employees, Public Health Service commissioned officers, Coast and Geodetic officers, Coast Guard personnel, dependents of the members of the uniformed services, narcotics addicts, and victims of leprosy. In addition, the Service conducts clinical research at the Clinical Center, National Institutes of Health and research on narcotic addiction.

The scope of health care services provided includes prevention, early diagnosis, treatment and containment of disease and rehabilitation to enhance recovery.

The Service has accredited training programs for physicians, dentists, nurses, pharmacists, medical record librarians, practical nurses, and other health personnel.

Mr. Chairman, we have furnished the committee tables giving detailed information about the drugs purchased in fiscal years 1968 and 1969.

In fiscal year 1969, the Public Health Service purchased over $6 million worth of drug products, of which 53 percent was obtained through the Veterans' Administration, 33 percent from drug companies having contracts under the Federal supply schedule, about 6 percent from the Military Defense Personnel Support Center, 4 percent by competitive bidding, and the remaining 5 percent was purchased locally or from sources without contracts under the Federal supply schedule. The General Services Administration, which is generally responsible for nonmilitary Government procurement, has delegated the responsibility to the Veterans' Administration for drug procurement.

Our goal is to secure quality drugs for use in the PHS installations at a reasonable price. Further, we want the drugs to be employed rationally in patient treatment.

There are a number of ways in which drugs can be employed ir-

rationally, although I think a better word might be, inappropriately. The Task Force on Prescription Drugs in our Department, which reported on a number of drug matters in February of last year, listed a number of kinds of irrational prescribing as follows:

The use of drugs without demonstrated efficacy;

The use of drugs with an inherent hazard not justified by the seriousness of the illness being treated;

The use of drugs in excessive amounts, or for excessive periods of time, or inadequate amounts for inadequate periods;

The use of a costly duplicative or "me-too" product when an equally effective but less expensive drug is available;

The use of a costly combination product when equally effective but less expensive drugs are available individually;

The simultaneous use of two or more drugs without appropriate consideration of their possible interaction;

Multiple prescribing, by one or several physicians for the same patient, of drugs which may be unnecessary, cumulative, interacting, needlessly expensive, or any combination of those;

There are a number of steps being taken within our Department which are designed to improve the use we make of drugs. Among these:

We distribute to the various drug purchasing stations the results of the National Academy of Sciences-National Research Council drug efficacy studies as they are released by the Food and Drug Administration. These reports go out by mail in most cases, but where there is a hazard to health, the messages will be forwarded by telephone. For example, the Food and Drug Administration's conclusion on Panalba and earlier conclusions with regard to chloramphenicol were telephoned to the purchasing offices.

Then we rely upon the clinicians and their associates at each hospital (or group of hospitals in the case of some smaller installations) to determine what drugs are required at each installation for good medical care. Each installation has a committee called the "pharmacy and therapeutics committee," whose function, among other things, is to select the drug products to be stocked at that installation and list them in a formulary which guides the purchasing agent as well as the prescribing physicians. In this way, we believe the best therapeutic agents available are secured and we are able to avoid unnecessary purchase of duplicate drugs having essentially the same pharmacological action. I attach Guidelines for the Pharmacy and Therapeutics Committees—they have been submitted—consistent with those recommended by the American Society of Hospital Pharmacists and the American Pharmaceutical Association.[1]

Senator NELSON. May I ask a question, Doctor?

Dr. STEINFELD. Certainly.

Senator NELSON. At the bottom of page 5 is the sentence:

> In this way, we believe the best therapeutic agents available are secured and we are able to avoid unnecessary purchase of duplicate drugs having essentially the same pharmacological action.

Are you talking about that multiplicity of drugs that were produced rapidly over the past several years to duplicate the function

[1] See information beginning at p. 7690.

of well-established drugs already in the marketplace? Is that what you are referring to?

Dr. STEINFELD. Among other things, yes. The idea here is that when physicians get together and have available to them expertise from pharmacists who are not employed, let us say, by a particular drug manufacturer, and seek to determine which drug should be available for them and their confrees in a particular hospital, they are less likely to use the very latest drug, maybe the most expensive drug, which simply does the same thing that another drug which had been available for many years would do. So, I think it is a check-and-balance system.

It is a form of group practice so that—rather than each individual prescribing whatever drug he feels might be useful—a group sits together and evaluates the situation.

I should add, Senator, that in preparation for these hearings, I suddenly realized that we do not centrally review the formularies at all of our various installations and that some of these for one or another reason may locally have drugs that we would not consider very good. When I say "we," I am not speaking as if all wisdom resided in Washington at the headquarters of HEW, but rather that "we" would represent the thinking of a collective review of the formularies in all the hospitals. We found some things that seemed out of line. We might very well take appropriate action and make recommendations to that local hospital regarding its formulary.

Senator NELSON. The problem that appears clearly from the testimony of the Veterans' Administration, and yesterday the Department of Defense, is that there is a strong tendency for the hospital therapeutics committee as well as the central purchasing agent, even if they differ with the judgment of the individual physician in the particular drug that he wishes to prescribe, will nevertheless yield to his wishes. That accounts for the fact that the DOD and Veterans' Administration purchase substantial numbers of drugs which are duplicative, with no evidence that they are better than well-established drugs, but they are more expensive. They have in their formularies drugs which the Medical Letter has stated are either ineffective, or ineffective in combination, or not more effective than the established drugs, and yet more expensive.

We have gone through a long list of them and it is clear to me that the therapeutics committee is not nearly as effective at the local level as it ought to be because it defers to the demands of the prescribing physician. In fact, the Department of Defense said yesterday—I do not want to quote, the record will speak for itself—but the essence of what was testified to yesterday was that we have civilian doctors coming into the military service and some of them are young, just out of medical school. We have a hard panel of doctors who are hard to restrain and we cannot refuse to allow them to use the drugs they are used to, know of, or feel they ought to have. That accounts, therefore, for a number of these drugs being in their formulary.

My response to that was that if in a Department of Defense installation, the Defense Department could not insist upon the highest standards and practice in terms of stocking the best drugs and in terms of establishing the best guide rules for rational prescribing,

then it cannot be done any place in the United States and it will never be done. We have all this talk about a therapeutics committee composed of medical experts, but the therapeutics committee gives in to the demands of the individual physician in the hospital—physicians who have no controlled studies to demonstrate that the drugs they want to prescribe is as good as, or better or equivalent to, the drugs that are established and published in the U.S. Pharmacopeia and National Formulary, attested to for their effectiveness by the most distinguished pharmacologists and clinicians in the country. If those therapeutics committees are still going to allow these drugs to go into the formulary on demand of the individual physicians, where then in the country can we establish a good formulary and a practice that seeks to achieve the ideal of rational prescribing?

Dr. STEINFELD. I cannot speak for the Department of Defense. And I certainly agree with you that we do not have the best system available. Doctors are fiercely independent, even those who work for the Federal Government, at the VA, or DOD, or the Public Health Service.

The problem, I think, begins at the beginning, in medical school. I taught medical students for 10 years before I came to work for the Government, and they read the advertisements and they want to try new things. I think one of the criticisms of American medicine—that it has not responded to so many of its challenges—is a compliment, Senator, in the sense that physicians do not try all of the wild new things—quack remedies, bizarre tests, wild operations, and so forth.

I think, fundamentally, medicine is a very conservative art and science and that this is useful, but the problem is that we must balance the education of the physician: provide him with information about drugs, accurate, valid information about drugs, and so that he will prescribe appropriately, and will not assume an expertise which he does not possess.

We have not yet achieved this. We have not achieved the mechanism for educating physicians either in Federal employment or in the civilian community. It is something we certainly have to work on, and I think the hearings that you are conducting are a major step in the right direction of providing this information, at least getting us to move in the direction of getting some information out and developing the mechanism to get it out. But I do not have an immediate solution.

Senator NELSON. In most very good general hospitals there are clinicians who are expert in the administration and use of drugs within their specialty. If a hospital is big enough, you can cover the whole range of afflictions that may be treated rationally with drugs, and you can establish a therapeutics committee, and you can use the U.S. Pharmacopeia and the National Formulary which drafts its list of drugs consulting with the finest clinicians in the country, and the guidance of the Council on Drugs of the American Medical Association. You can also call upon distinguished men of national reputation which all of the doctors would have heard of in their schools—the Dr. Dowling's and Adriani's, for example. You can establish a formulary, and say that this is "the formulary." Why

can't you tell the doctor: "If you have cause to believe you need something for your patient that is not in the formulary, supply the therapeutics committee the rationale, such as controlled studies, something in addition to testimonials." Why can't this be done?

I do not think it is very good to say "my instinct is excellent, therefore, I will give a drug," such as happened with the fixed dose combination antibiotics, the use of which was opposed by the best practitioners in this country for 15 years. They were finally recommended for removal from the marketplace by the National Academy of Sciences-National Research Council. With all the expertise available in establishing the formulary, what is the problem?

So a doctor says, well, I have been prescribing for years X drug, and I like it and my patients get well. As every doctor knows, if you just give your patient enough rest and good food and a sense of security, 90 percent of them will get well without doing anything else. So, what is the problem in saying: "Now here is our formulary. We are not rigid about this. If you have any controlled studies, any scientific evidence that another drug that you want to use is superior for some reason or another, bring it to the therapeutics committee and we will evaluate it." Why is that so difficult to do?

Dr. STEINFELD. First, we are looking into methods for developing a formulary. I do not know that it is all that difficult to do. What it does is remove from an individual institution its determination to choose the drugs that the physicians there want to use, but in essence they are limited by the drugs that are available in the commercial market in any case. This would narrow it down further and further as experts would specify, and what you are saying is that the experts throughout the country are better than the experts at any local hospital.

Senator NELSON. No.

Dr. STEINFELD. Well, I think they are. I would agree to that.

Senator NELSON. I was not saying that, but yesterday DOD said they had plenty of experts but that they very frequently defer to the demands of the individual practitioner because, in fact, he is going to get angry if they don't.

Dr. STEINFELD. I am sure that is so.

Senator NELSON. In any event, I think any individual practitioner confronted with a list of drugs based on the best judgment of medical experts would not be inclined to battle against the practice of good medicine. If you get all the best expertise together on any particular subject matter, that represents the best scientific knowledge we now have in the country, and if somebody has some better scientific knowledge, the best of the scientists will adopt it. But we are not really following that, at least as extensively and conscienciously as we ought to in our therapeutics committees and in establishing our formularies.

Dr. STEINFELD. No, you are right. We do not have a single formulary, and I think it is something that we must give serious consideration to. I think, though, that we do have a good health system and though I do not want to get off the point, I think one of the advantages of it is that the individual must think for himself.

Now, maybe he does not think too well. Maybe he prescribes irrationally or inappropriately. Some of the things certainly are harm-

ful and should be withdrawn. But if the Government determines extensively what laboratory tests should be available, which drugs should be available, which types of operations, and so forth, and one could carry this on further. I think one must balance the value of requiring the physicians at a hospital to think for themselves, to read about drugs, to inform themselves about the value of one antibiotic versus another for a particular infection, rather than having all of the decisions more or less made for them so that they can choose from a relatively limited number.

There is a process of continuing education which I think the local pharmacy and therapeutics committees carry out by having to develop their own formularies, having to read the literature, hopefully, reviewing the original data, arguing and discussing. I was a member of one at a place called John Wesley County Hospital in Los Angeles, and we took our job seriously. So that I think there is an educational process that perhaps, but not necessarily, would be lost if we had a National Formulary. I am sure that we could balance things to improve the system and still permit or provide or encourage the doctors, pharmacists, to continue to read, inquire, and search out what they feel is the appropriate answer.

Senator NELSON. Well, I have not suggested whether there should be a National Formulary one way or the other. It may give lots of flexibility to have a good hospital in which the therapeutics committee decides on the drugs they want to use, but there ought to be some review. And if the therapeutics committee is including drugs which the review committee has not requested, and are not supported by the best of the clinicians and pharmacologists in the country, that the therapeutics committee ought to have to respond to it with evidence to support its position.

I was not suggesting that you interfere with the practice of medicine. This reinforces the practice of medicine because I think everybody—I think every doctor in this country will concede that if he is just practicing without the opportunity for conducting carefully controlled studies himself, that there is not really any way for the greatest genius in the world to decide whether when he administers a combination of tetracycline and novobiocin to his patients, that that is not better than the tetracycline alone and, in fact, as the NAS–NRC decided, worse. How does he decide this?

It is not a reflection on the physician that he is unable to decide that. It takes controlled studies which the doctor is not in a position to make himself.

What we are really doing is purchasing thousands of drugs, most of them duplicative. They do the same thing. They cost more money. Various molecular modifications are made that are totally insignificant and they end up producing a drug that is not as good as the basic drug. The modified drugs are advertised widely, great claims made for them and there sits the physician. He says, "Well, I want to help the patient. That sounds very good."

What is his basis for making a judgment? There is not any, unless he conducted or had access to carefully controlled studies. So it seems to me that in this aspect the doctor cannot conceivably, from his own experience, develop an expertise in this area unless he deals with a

very limited number of drugs for an extended period of years. He may, but it is just not within the realm of possibility for the finest of brains in the world to do that as against the collective knowledge of the expert pharmacologists and clinicians and controlled studies over a period of years. And yet as a result of the procedure we follow, we had the fixed dose antibiotic combinations in the market for 15 years, widely prescribed, despite the fact that the AMA's Council on Drugs and every distinguished pharmacologist and clinician in the country said it was irrational to prescribe them. It never got through. They had all the reason in the world to read the literature and all the literature was against the fixed dose antibiotic combinations, yet they were the biggest sellers in the country, among the 200 most frequently prescribed drugs.

Now, whatever explanation one may have, the method followed was a total failure. We have moved 15 years later through the NAS–NRC after a prolonged fight by the great and distinguished Senator Estes Kefauver, who said you have to prove effectiveness, and then after he got that law through, we finally start coming up with the formal judgments under the law by the Government which is now taking them off the market. We would have gone on prescribing them despite what the literature said.

So, in the face of this, it seems to me, there is a grave responsibility in the medical profession, the DOD, and in Public Health Service, to say these drugs are proven ineffective and we are not going to put them in our armamentarium.

I do not know how you achieve that unless there is some really vigorous leadership at all levels from the American Medical Association, DOD, Public Health Service, medical schools and everything else .

Dr. STEINFELD. And by the hospitals in the review of the various patients' records after the patient leaves the hospital, by the doctor's own peers. I agree with you that it is not right and I think our new regulations from Food and Drug Administration will require demonstrated effort to determine a basis for the synergism or a number of other factors before a new combination drug will be permitted on the market.

Senator NELSON. If we follow the rules of rational prescribing as stated by HEW's Task Force on Prescription Drugs, most of this would not happen.

Dr. STEINFELD. I think most of this has already happened. What we have got to do is get rid of the bad things and prevent any more from occurring.

Senator NELSON. There is a long article in the August 10 issue of the Journal of the American Medical Association saying what has been said by many clinicians and pharmacologists for a long time. It is entitled, "Propoxyphene Hydrochloride, A Critical Review", and it states that a review of studies shows that "propoxyphene is not superior to codeine or aspirin in terms of analgesic effect. * * * It appears that factors other than intrinsic therapeutic value are responsible for the commercial success of propoxyphene." I consider that a rather masterful understatement. In any event, it concludes as the Medical Letter has already done, that it is no better than

aspirin or codeine in terms of analgesic effect. Yet, the Defense Department and Public Health Service, continue acquiring and using the drug at a tremendous expense over and above the cost of aspirin or codeine.

The position of the Medical Letter was made known in the January 23, 1970 issue.

Propoxyphene hydrochloride is Darvon, as you know.

Dr. STEINFELD. Yes. Darvon. I thought that it did have some effectiveness. I agree with you there are other drugs that are much less expensive about which a great deal is known. However, if we have a patient who has pain and who has had a bleeding problem or a peptic ulcer, we would not want to put him on aspirin. We perhaps would not want to put him on codeine.

There is need—I do not want to get into the merits of propoxyphene—there is need for a nonaspirin analgesic. Aspirin is not the innocuous drug that we usually think of. It may cause bleeding from the stomach or even from other parts of the body, so there is need for another analgesic.

I think this one may be prescribed far out of proportion to the instances where it may be useful. But I think we should continue to search for other forms of analgesics.

Senator NELSON. If you have a reason for not prescribing aspirin, a reason for not prescribing codeine, in such cases propoxyphene hydrochloride might be the right one?

Dr. STEINFELD. There might be one of several others. There would still be several others.

Senator NELSON. The first sentence in the JAMA article says:

> More prescriptions for propoxyphene hydrochloride are dispensed in retail pharmacies in the United States than for any other drug.

Surely they are not all cases where one has an ulcer or for some reason aspirin or codeine should not be used. Darvon has become the popular drug to be used as an analgesic and it is promoted under the brand name. Yet the Medical Letter of January this year says:

> In the few studies which have been done, comparing dextropropoxyphene with aspirin or APC, dextropropoxyphene 32.5 to 65 milligrams has consistently proven inferior to aspirin or APC tablets. No evidence that has appeared since this review establishes the superiority of the 65 milligram doses of propoxyphene to two tablets of either aspirin or APC.

So you have a situation in which a drug that is very expensive, compared to APC or aspirin, becomes a large part of the purchases in not only the retail marketplace but in DOD and the Veterans' Administration. I do not know how much is bought by Public Health Service but to illustrate—DOD pays an average of $12.75 for 500 tablets versus aspirin which would cost 35 cents for 500. The Defense Department spent a total of $4,360,784 on Darvon. Comparable cost of aspirin would have been $172,380, more than $4 million less. What is more odd is that all the best expertise available says it is no better than aspirin and yet it becomes so widely prescribed.

Now, what evidence was submitted to any therapeutics committee that Darvon was, in fact, superior to the well-established analgesics in the marketplace?

Dr. STEINFELD. I have no idea, Senator Nelson. Apparently, advertising is extremely effective in this instance. I would say, though, that we did our best with the medical students to convince them to use APC. Phenacetin has been shown to cause interstitial nephritis when used for a long period of time, so aspirin by itself is probably superior to APC if the individual does not have a hemorrhagic problem, but this does happen and the question is what can we do about it.

Senator NELSON. Does not this raise the question whether or not it may be better if doctors and scientists interfered with medical practice rather than let the pharmaceutical firms, through advertising and promotion, be the ones responsible for convincing the doctor to use a drug for which there is no demonstrated therapeutic superiority over an established drug?

We have two points here. Everybody admits that advertising and promotion is what sells the drug, not proven therapeutic superiority. So every time doctors say we cannot interfere with the doctor's independent judgment, who is interfering? The advertising and promotion. And since the responsibility of the profession is to the welfare of the public, a little interference with the doctor's judgment, which may be determined by advertising and promotion, would be in the best interests of the public, would it not?

Dr. STEINFELD. Yes, I think we have to determine the appropriate amount.

Senator NELSON. I thought it was interesting, by the way, as an aside, that within the Journal of the American Medical Association, they headline the piece "Propoxyphene Hydrochloride, A Critical Review". In the article there is no mention of Darvon. If you look very carefully on the last page in fine print, and have good strong glasses, you will discover it is Darvon. I think it is interesting to note that they did not put in big parentheses up at the top, Darvon, which is the way it is promoted in the journal—in JAMA. How many doctors who are prescribing Darvon, would you guess, know what propoxyphene hydrochloride is or recognize immediately that it is Darvon?

Dr. STEINFELD. I could not guess, Senator, but I do not think in writing this article—I do not think the authors would have used the name Darvon in the title of their article. I do not think trade names are generally used.

Senator NELSON. No. This is an editorial up here. My point is that if for years a drug has been promoted in your publication, and you decide it is important to notify the profession that it should not be used, it is interesting to me to note that in the article they do not identify the drug by the brand name which is Darvon. I think it quite possible that many, many doctors who have long been prescribing Darvon as an analgesic, really do not know that it is propoxyphene hydrochloride. Incidentally, they sent this drug along with the astronauts who rode Apollo around the moon.

Dr. STEINFELD. I hope they did not check with the Public Health Service first.

Senator NELSON. Please continue.

In view of the expenses on Apollo I am sure they could afford the extra price if that is what they want.

Dr. STEINFELD. These guidelines have been distributed in our Indian Health Operating Manual to the hospitals serving the Indians and in the Division of Hospitals Operating Manual to the other hospitals.

If in a particular case, especially an emergency, a nonformulary drug is required, it is obtained on the open market. But the formulary does greatly reduce the total number of drugs that we are required to carry in stock, still providing for what we feel is the best drug therapy available.

Also, we are making a pilot study of methods of bringing more firsthand knowledge about drugs to bear at the point of prescribing. At hospitals in Baltimore, Md.; Gallup, N. Mex.; and Crow Agency, Mont.; clinical pharmacists who are particularly knowledgeable are making clinical medical rounds with physicians; in this way the latest information about drug effects, contraindications and incompatibilities is available to the physician as he decides what medication to employ for each patient. If this experimental procedure gives the expected results, it will be expanded to other hospitals.

Later there is a total utilization review, performed at each installation or group of installations during which a peer committee reviews the entire care afforded a patient during his hospital stay. Among other things, this covers the drugs that were used, and the reasons for using them. Through such "audits" we are able to detect opportunities for improved patient care and act upon them. We submitted earlier copies of the guidelines for total utilization review as issued by Indian Health Service and the Federal Health Programs Service.

When a hospital determines what drugs it requires it purchases most of them through the Veterans' Administration and the Military Defense Support Center (almost 60 percent in fiscal year 1969). Both the Veterans' Administration and the Center make inspections of drug manufacturers prior to awarding contracts for drug supplies, and have the drugs that are supplied on contract tested to be sure they meet specifications. We do not further test the drugs that we obtain from these sources.

If the drugs a hospital needs are not available from the Veterans' Administration, they are secured from the Public Health Service Supply Service Center at Perry Point, Md. The Center purchases by formal bid and from the Defense Personnel Support Center, DPSC. In some cases these drugs are repacked to provide special sizes that are needed in the Federal hospitals. Before making a direct purchase, the Perry Point installation determines that the supplier has been inspected and found acceptable either to the Veterans' Administration or to the Military Defense Support Center. If it has not been inspected by one of these groups, we make our own inspection to determine that the firm is an acceptable supplier. If the prospective supplier has been inspected and found not acceptable to one of the other agencies, then we do not purchase from that firm.

Drugs purchased directly by the Perry Point installation are tested in quality control laboratories at that point for quality and purity before being distributed to the hospitals for use.

You have also expressed an interest, Mr. Chairman, in the use we make of the combination drugs. Based on cost, over 80 percent of the

drugs purchased by the Public Health Service are single entity products. Over half the combination drugs consist of large volume injection solutions and measles vaccine combined with immune globulin. The remaining products, making up the group generally regarded as combination products accounts for less than 10 percent of the drugs purchased.

Senator NELSON. Eight or 10?

Dr. STEINFELD. I have figures varying from eight to 12 depending on how we do it, so we are picking 10. We have included vitamins in the combination drugs, triple sulpha, in such things as procaine penicillin where the procaine is added to prolong the period of action or to decrease the pain at the time depending on its objective, even though it is a single drug. We have been calling that a combination. Thus, it is apparent that while we do not issue any directives from Washington banning the combination products, the informed actions of the experts in the hospitals who decide what to put in their formularies has led over the years to a significant emphasis on single entity drugs. I think this is good, and I think we will emphasize it even more strongly in the future. There are some combination products that serve a very useful purpose and will continue to be employed. A lot of them, however, do not contribute to good medical practice.

I believe, Mr. Chairman, that our drug procurement operations have successfully contributed to our goal of making available to the Public Health Service physicians and their patients safe, effective drugs that meet recognized standards of purity and strength and that contribute to rational drug therapy.

I think we can also improve our performance. I thank you for the opportunity to present this statement.

Senator NELSON. Thank you. I realize your purchases are relatively small compared to the Veterans' Administration's at $48 million and the Defense Department's at over $100 million, and that you buy, as I understand it, over 50 percent from the DOD or VA.

Dr. STEINFELD. Yes.

Senator NELSON. Is any effort made to secure drugs from what are legally classified as small businesses?

Dr. STEINFELD. I think when the bids go out, if all things are equal, the small business would be given preference, but the primary concern relates to the other factors, safety and efficacy. But all other things being equal, it would be small business that would get the bids.

Mr. GORDON. Mr. Chairman, may I interrupt? In exhibit 1 supplied by Public Health Service which is attached to your letter of June 19, 1970, it shows that PHS purchased a total of $6,192,536 in fiscal 1969. On July 23, 1970, you presented data purporting to show purchases directly from small drug manufacturers for fiscal 1969. Now, these purchases totaled $589,901. However, of this amount, large companies accounted for $438,872. You included in small business such companies as Hoechst, Ives Laboratory, a part of the American Home Products, Organon, which is a large company, Philips-Roxanne, a subsidiary of M. V. Philips, a very large company in Holland, Rachelle, which is part of International Rectifier, and that

comes out to $438,901. So, actually, this leaves a total for small business of only $151,028.11.

Now, on the basis of total purchases of $6.2 million, the share of small business is 2.4 percent, which I think is a rather small amount.

Now, let me ask you this. How do you determine whether to purchase through VA as against direct bidders?

Mr. BRANDS. We purchase through VA those items that they stock. If our Supply Service Center at Perry Point gets a request from one of the stations to stock the item because they feel they can get it at less cost, then our Supply Service Center will survey the facilities to see what their annual usage rate will be. Then this item will be let out on bid to see if the bid is lower than either the VA or the military if the military stocks it. If it is not a certain percentage lower, I believe the figure is 15 to 20 percent, then it will not be stocked because of costs of warehousing and shipping the products again.

Mr. GORDON. Do you have any small business set-asides?

Mr. BRANDS. No, sir.

Mr. GORDON. A certain percentage of your purchases——

Mr. BRANDS. No, sir. They are given the same opportunity to bid on our products equally with other firms, with the large businesses.

Mr. GORDON. How do you determine the quality, safety, and efficacy of the drugs you buy?

Mr. BRANDS. The quality of the drug is determined through USP and NF testing procedures at our Supply Center at Perry Point.

Mr. GORDON. You do that yourselves?

Mr. BRANDS. Yes, sir.

Mr. GORDON. Have you had any complaints about the drugs you have bought directly?

Mr. BRANDS. We have had six rejects in 1968 and three in 1969, sir.

Mr. GORDON. Could you supply those for the committee?

Mr. BRANDS. Yes, sir; we will.

(The information referred to follows:)

REJECTS BY PHS SUPPLY SERVICE CENTER FOR NONCOMPLIANCE WITH SPECIFICATIONS

FISCAL YEAR 1968

1. Antipyrine and Benzocaine Solution: Certified Laboratories (from DPSC); crystalline precipitate.
2. Sodium PAS Tablets: Consolidated-Midland; two rejections. Low tablet hardness; tendency to chip.
3. Cascarasagroda Tablets: Brewer (from DPSC); failed USP disintegration test.
4. Sodium Salicylate, Enteric Coated Tablets: Davis-Edwards; failed disintegration test.
5. Atropine Sulfate Injection: Intra Products; wrong strength.

FISCAL YEAR 1969

1. Pseudoephendrine Tablets: Davis-Edwards; mislabeled, foreign odor, low assay.
2. Antipyrine and Benzocaine Solution: Certified Laboratories (from DPSC); crystalline precipitate.
3. Dextro-amphetamine Sulfate Tablets—Boler-made for American Quinine; labeling problem.

Mr. GORDON. Have you noticed any difference in quality of the products bought directly as against going through the VA or DSA or purchasing directly?

Mr. BRANDS. To my knowledge, no, sir; there is no noticeable difference in quality that could be actually documented.

Mr. GORDON. Now, the HEW Task Force Report on Prescription Drugs has made the following recommendation:

> The Department of Health, Education and Welfare should conduct a continuing survey of drug costs, average prescription prices and drug use.

What is your organization doing to keep down the cost of drugs?

Dr. STEINFELD. I think the best thing we can do to keep down the cost of drugs is to provide information on the relative efficacy and safety of some of the old established drugs which are not patented any more, and to provide the information that has been developed by the National Academy of Sciences and National Research Council on combination drugs to the prescribing physician with the hope that he will do the rational thing.

Mr. GORDON. Is this the study that you are making at present?

Dr. STEINFELD. We have a man working now for the Department in the Health Services Research and Development Center of the Health Service's Mental Health Administration, in Dr. Paul Lazarow's operation, Dr. Donald Brodie, who did a drug utilization study which was published April 1, 1970. He is now working full time with Dr. Lazarow, and, hopefully, developing mechanisms that will improve drug utilization and control.

Mr. GORDON. That is drug utilization. How about other aspects of the drug pricing?

Dr. STEINFELD. I think what we can do——

Mr. GORDON. Not what you can do. What are you doing at present?

Dr. STEINFELD. I think what we are doing at present is making available to the medical profession the results of the Task Force on Prescription Drugs and implementing the NAS–NRC findings.

Mr. GORDON. The staff has prepared a table which compares some of the prices paid by the Public Health Service, VA, and DSA, and I ask, Mr. Chairman, that this be inserted in the record at the appropriate place.

Senator NELSON. All right.

Mr. GORDON. For example, the Defense Supply Agency paid for oxytetracycline $3.96 for a hundred, whereas the PHS paid $8.63. Was it not possible to buy through the DSA?

Dr. STEINFELD. I should hope so.

Mr. GORDON. Why the difference in price?

Mr. BRANDS. I would have to check that, sir. I believe the volume we purchased on oxytetracycline was purchased locally under a Federal supply schedule contract instead of from DOD.

Mr. GORDON. The Medical Letter, as Senator Nelson has stated on several occasions, has said that there is no clinical difference between

tetracycline HCL and the rest of the tetracyclines. Now, the DSA paid 90 cents for tetracycline and the Public Health Service paid $8.63 for oxytetracycline. Would you explain this, please.

Dr. STEINFELD. I cannot explain it.

Mr. GORDON. And then also——

Dr. STEINFELD. Mr. Brands says he can.

Mr. BRANDS. Did you say the Defense Supply Service Center had the other price?

Mr. GORDON. Ninety cents for tetracycline hydrochloride in hundreds.

Mr. BRANDS. And we paid $8.63 for oxytetracycline.

Mr. GORDON. And since they are just as good, why pay the high price?

Mr. BRANDS. I am sorry. I cannot explain that. This is one of those things that gets by, I think.

Senator NELSON. Well, would that not suggest the same problem we are talking about?

Mr. BRANDS. Yes, sir.

Senator NELSON. That doctors want oxytetracycline.

Mr. GORDON. Now, there is another one, demethylchlortetracycline for which you paid $13.79 as compared to 90 cents for tetracycline paid by the Defense Supply Agency. There is quite a difference, wouldn't you say?

Senator NELSON. Same problem.

Dr. STEINFELD. Yes.

Mr. GORDON. And we have the same problem with dexamethasone for which you paid $58.35 a thousand, when prednisone is as good as any other corticosteroid, according to the Medical Letter. The Defense Supply Agency bought prednisone at $4.45 a thousand.

Senator NELSON. We will print those in the record.

(The charts, above-referred to, follow:)

PUBLIC HEALTH SERVICE PRICE COMPARISON WITH VA AND DSA

Product	DSA	VA	PHS
Meprobamate (400 mg 500's)	[1] $1.67	[2] $36.25	$2.84
Oxytetracycline (250 mg. 100's)	3.96	7.90	8.63
Peritrate (20 mg. 1,000)	[4] 18.10	18.10	9.98
Peritrate (10 mg. 1,000)		[3] 9.44	2.60
Phenobarbital (30 mg. 1,000)	[5] 1.40		.46 ($0.33 for 25)
Serax (15 mg. 500)		13.48	14.38
Dexamethosone (500 mg. 1,000)			58.35
Demethylchlortetracycline (Declomycin) (500 mg. 100's)	10.99		13.79

[1] Foreign purchase from Syntetic.
[2] Purchase price was $7.25 per 100.
[3] Purchase price was $4.72 per 500.
[4] Purchase price was $9.05 per 500.
[5] Purchase price was $0.14 per 100.

PUBLIC HEALTH SERVICE PRICE COMPARISON WITH VA AND DSA

Product	DSA	VA	PHS
Darvon compound (65 mg. 500s)	$12.89 Lilly	$12.95 Lilly	$13.37 VA
Donnatal (1,000s)	$2.48 Robins	$6.70 Robins	$7.30 VA
Tedral (1,000s)	$9.60 Warner	$9.61 Warner	$10.42 VA
Tedral-SA (500s)	$16.09 Warner	$20.40 Warner	
Gelusil (1,000s)	$6.87 Warner	$5.32 Warner [1]	$8.20 VA
Maalox (6 oz)	$0.095 Rohrer	$0.09 Rohrer	$0.11 VA
Fiorinal	$8.55 DPSC	$9.49 DPSC	$8.67 VA
Robixisal		$18.37 Robins	$20.00 VA
Ornade (250s)	$13.95 SKF		$20.52 SKF
Dimetapp (500s)	$17.70 Robins		$32.67 Robins
Coricidin (100s)	$1.06 Schering		$2.23 Schering
pHisoHex (1 gal.)	$3.51 Winthrop		$3.77 Winthrop
Cortisporin	$0.47 Burroughs-Wellcome		$1.09 Burroughs-Wellcome
Ovulen 21 (63s)	$0.42 [2] Searle	([3])	$0.69 Saerle [4]
Oracon (63s)	$0.63⅔ [5] Mead Johnson		$0.67 [6] Mead Johnson
Norinyl (60s)	$0.37⅔ [7] Syntex		$0.60⅓ [8] Syntex
Ovral (63s)	$0.60 [9] Wyeth	([10])	$0.70 [11] Wyeth
Eskatrol (250)	$17.14 SKF		$22.80 SKF

[1] Bottles of 5,000 sold for $26.59.
[2] Three cycle price was $1.26.
[3] GSA paid 17 cents per cycle.
[4] Searle's price is $2.07 per 3 cycles.
[5] Mead Johnson's price is $1.91 for 63 tablets.
[6] Mead Johnson's price is $2.01 for 63 tablets.
[7] Syntex's price was $1.13 for 60 tablets.
[8] Syntex's price was $1.81 for 60 tablets.
[9] Wyeth's price was $1.80 for 63 tabs.
[10] GSA paid 16¼ cents per cycle.
[11] Wyeth's price was $4.20 for 6 cycles.

Senator NELSON. Does minority counsel have any questions?

Thank you very much. We appreciate your taking time to come today.

(The complete prepared statement and supplemental information submitted by Dr. Steinfeld follows:)

STATEMENT BY JESSE L. STEINFELD, M.D., SURGEON GENERAL, PUBLIC HEALTH SERVICE, DEPUTY ASSISTANT SECRETARY FOR HEALTH AND SCIENTIFIC AFFAIRS, DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

I am pleased to appear before the Monopoly Subcommittee of the Senate Small Business Committee to present information on the Public Health Service's policy and practices regarding the selection and procurement of drug products.

The Public Health Service is one of the smaller direct purchasers of drugs among the Federal agencies. In fiscal year 1969, for example, we purchased approximately $6 million worth of drugs. This is much less than the $48 million purchased by Veterans' Administration or the purchases of Department of Defense which amounted to more than $100 million that year.

Despite the relative size of our direct drug purchases, as the principal health agency of the Government we accept the responsibility for insuring that the PHS hospitals and clinics provide within available funds and facilities the very best drugs and care possible.

The Public Health Service in its direct medical care activities operates over 60 hospitals; 51 for Indians, eight for merchant seamen and certain Federal employees, two for narcotic addicts, one for the mentally ill and one for patients with leprosy. These hospitals have about 12,000 beds, and over 100,000 annual admissions. In addition, there were over 3 million outpatient visits for treatment at the hospitals and clinics, and outpatient offices last year.

The Service is responsible for providing health care services to Indians, merchant seamen, certain Federal employees, Public Health Service commissioned officers, Coast and Geodetic officers, Coast Guard personnel, dependents of the members of the uniformed services, narcotic addicts and victims of

leprosy. In addition, the Service conducts clinical research at the Clinical Center, National Institutes of Health and research on narcotic addiction.

The scope of health care services provided includes prevention, early diagnosis, treatment and containment of disease and rehabilitation to enhance recovery conditions.

The Service has accredited training programs for physicians, dentists, nurses, pharmacists, medical record librarians, practical nurses and other health personnel.

Mr. Chairman, we have furnished the committee tables giving detailed information about the drugs purchased in fiscal years 1968 and 1969.

In fiscal year 1969, the Public Health Service purchased over $6 million worth of drug products of which 53 percent was obtained through the Veterans' Administration, 32.8 percent from drug companies having contracts under the Federal supply schedule, 5.6 percent from the Military Defense Personnel Support Center, 3.6 percent by competitive bidding and the remaining 5 percent was purchased locally or from sources without contracts under the Federal supply schedule. The General Services Administration which is generally responsible for nonmilitary Government procurement, has delegated the responsibility to the Veterans' Administration for drug procurement.

Our goal is to secure quality drugs for use in the PHS installations at a reasonable price. Further we want the drugs to be employed rationally in patient treatment.

There are a number of ways in which drugs can be employed irrationally. The Task Force on Prescription Drugs in our Department, which reported on a number of drug matters in February of last year listed a number of kinds of irrational prescribing as follows:

The use of drugs without demonstrated efficacy.

The use of drugs with an inherent hazard not justified by the seriousness of the illness.

The use of drugs in excessive amounts, or for excessive periods of time, or inadequate amounts for inadequate periods.

The use of a costly duplicative or "me-too" product when an equally effective but less expensive drug is available.

The use of a costly combination product when equally effective but less expensive drugs are available individually.

The simultaneous use of two or more drugs without appropriate consideration of their possible interaction.

Multiple prescribing, by one or several physicians for the same patient, of drugs which may be unnecessary, cumulative, interacting, or needlessly expensive.

There are a number of steps being taken within our Department which are designed to improve the use we make of drugs:

We distribute to the various drug purchasing stations the results of the National Academy of Sciences–National Research Council drug efficacy studies as they are released by the Food and Drug Administration. These reports go out by mail in most cases, but where there is a hazard to health, the messages will be forwarded by telephone. For example, the Food and Drug Administration's conclusions on Panalba and earlier conclusions with regard to Chloromycetin were telephoned to the purchasing offices.

Then we rely upon the clinicians and their associates at each hospital (or group of hospitals in the case of some smaller installations) to determine what drugs are required at each installation for good medical care. Each installation has a committee called the "Pharmacy and Therapeutics Committee" whose function, among other things is to select the drug products to be stocked at that installation and list them in a formulary which guides the purchasing agent as well as the prescribing physicians. In this way, we believe the best therapeutic agents available are secured and we are able to avoid unnecessary purchase of duplicate drugs having essentially the same pharmacological action. I attach guidelines for the Pharmacy and Therapeutics Committees consistent with those recommended by the American Society of Hospital Pharmacists and the American Pharmaceutical Association. These guidelines have been distributed in our Indian Health Operating Manual to the hospitals serving the Indians and in the Division of Hospitals Operating Manual to the other hospitals.

If in a particular case, especially an emergency, a nonformulary drug is required, it is obtained on the open market. But the formulary does greatly re-

duce the total number of drugs that we are required to carry in stock, still providing for the best drug therapy available.

Next, we are making a pilot study of methods of bringing more firsthand knowledge about drugs to bear at the point of prescribing. At hospitals in Baltimore, Md., Gallup, N. Mex., and Crow Agency, Mont., clinical pharmacists who are particularly knowledgeable are making clinical medical rounds with physicians; in this way the latest information about drug effects, contraindications and incompatibilities is available to the physician as he decides what medication to employ for each patient. If this experimental procedure gives the expected results, it will be expanded to other hospitals.

Later there is a total utilization review, performed at each installation or group of installation, during which a peer committee reviews the entire care afforded a patient during his hospital stay. Among other things this covers the drugs that were used, and the reasons for using them. Through such "audits" we are able to detect opportunities for improved patient care and act upon them. I submit copies of the guidelines for total utilization review as issued by the Indian Health Service and the Federal Health Programs Services.

When a hospital determines what drugs it requires it purchases most of them through the Veterans Administration and the Military Defense Support Center (almost 59% in fiscal year 1969). Both the Veterans Administration and the Center make inspections of drug manufacturers prior to awarding contracts for drug supplies and have the drugs that are supplied on contract tested to be sure they meet specifications. We do not further test the drugs obtained from these sources.

If the drugs a hospital needs are not available from the Veterans Administration they are secured from the Public Health Service Supply Service Center at Perry Point, Maryland. The Center purchases from drug companies that have contracts under the Federal Supply Schedule. In some cases these drugs are repacked to provide special sizes that are needed in the Federal hospitals. Before making a direct purchase, the Perry Point installation determines that the supplier has been inspected and found acceptable either to the Veterans Administration or to the Military Defense Support Center. If it has not been inspected by one of these groups, we make our own inspection to determine that the firm is an acceptable supplier. If the prospective supplier has been inspected and found not acceptable to one of the other agencies, then we do not purchase from that firm.

Drugs purchased directly by the Perry Point installation are tested in quality control laboratory at that point for quality and purity before being distributed to the hospitals for use.

You have also expressed an interest, Mr. Chairman, in the use we make of the combination drugs. Based on cost, over 80% of the drugs purchased by the Public Health Service are single entity products. Over half the combination drugs consist of large-volume injection solutions and measles vaccine combined with immune globulin. The remaining products, making up the group generally regarded as combination products accounts for less than 8% of the drugs purchased. Thus, it is apparent that while we do not issue any directives from Washington banning the combination products, the informed actions of the experts in the hospitals who decide what to put in their formularies has led over the years to a significant emphasis on single entity drugs. I think this is good. There are some combination products that serve a very useful purpose and will continue to be employed. But a lot of them do not contribute to good medical practice.

I believe, Mr. Chairman, that our drug procurement operations have successfully contributed to our goal of making available to the Public Health physicians and their patients safe effective drugs that meet recognized standards of purity and strength and that contribute to rational drug therapy. I thank you for the opportunity to present this statement.

NATIONAL CANCER INSTITUTE—BIOGRAPHICAL SKETCH

Name: Jesse L. Steinfeld, M.D.
Position: Surgeon General, USPHS, 1969–.
Birthplace and date: West Aliquippa, Pennsylvania; January 6, 1927.
Education: B.S., University of Pittsburgh, Pittsburgh, 1945; M.D., Western Reserve School of Medicine, Cleveland, 1949.

Experience: Deputy Director, National Cancer Institute, 1968. Associate Director for Program, National Cancer Institute, 1968. Professor of Medicine, University of Southern California, School of Medicine, 1967. Associate Professor of Medicine, USC, 1963. Assistant Professor Medicine, USC, 1959. Chief of Cancer Chemotherapy, City of Hope Medical Center, Durate, California, 1958-59. Clinical Investigator, National Cancer Institute, 1952-58. Atomic Energy Commission Post-doctoral Fellowship in the Medical Sciences, 1951-52. Cancer Coordinator, USC, 1965-68. Chairman, Interdepartmental Cancer Research Committee, USC, 1961-68. Chairman, Radioisotope Committee, USC, 1960-66. Member, State of California Governor's Advisory Cancer Council, 1960-68: Vice President 1966-68. Director, USC Cancer Chemotherapy Program and Cancer Research Training Program, 1959-68. Chairman, Western Cooperative Cancer Chemotherapy Group, 1963-68. Member, Editorial Board, *Cancer Research*, 1964-69. Member, Editorial Board, *Journal of the NCI*, 1955-57. Consultant, National Cancer Institute, 1965-68. Consultant, Veterans Administration Hospital, Long Beach, 1960-68. Consultant, City of Hope Medical Center, 1961-68.

Association Memberships: Diplomate, American Board of Internal Medicine. American College of Physicians (Fellow), American Association for Cancer Research. American College of Clinical Pharmacology (Fellow), American Society for Clinical Oncology. Society of Nuclear Medicine. American Society of Hematology. International Society of Hematology. American Medical Association. California Medical Association. Los Angeles County Medical Association. Western Society for Clinical Research. American Federation for Clinical Research.

Special awards, citations or publications: Author or co-author of more than 40 publications in cancer, cancer chemotherapy, metabolic changes in patients during cancer growth, etc, President, American Society for Clinical Oncology, 1970. Governor, American College of Physicians, 1970. Executive Council, Association of Military Surgeons, 1970.

PUBLIC HEALTH SERVICE—BIOGRAPHICAL SKETCH

Name: Allen J. Brands.

Position: Pharmacy Liaison Representative, Public Health Service.

Birthplace and date: Kansas City, Missouri; September 19, 1914.

Education: B.S., University of Southern California, 1941, Pharmacy cum laude.

Experience: Assistant Store Manager, Owl Drug Company, California, 1941-1943. U.S. Marine Corps, Battalion Radar Officer, 1943-1946. Manager Retail Pharmacy, Owl Drug Company, California, 1946-1950. Assistant Chief, Pharmacy Service, PHS Hospitals, Seattle, Washington and Baltimore, Maryland. 1950-1951. Placement Officer, Division of Commissioned Officer Personnel, Public Health Service, Washington, D. C. 1953-195. Chief, Pharmacy Branch, Indian Health Service, Public Health Service, 1955 to present. Pharmacist Advisor, Bureau of Health Services, PHS, 1965-1967. Chairman, Pharmacy Career Development Committee, PHS, 1966-present. Pharmacy Liaison Representative, Public Health Service, 1967-present. Chairman, Career Service Board for Pharmacy, DHEW, 1968-present.

Association Memberships: Rho Chi, Past President of Theta Chapter. Phi Kappa Phi (National Honor Society). American Pharmaceutical Association—Member. American Society of Hospital Pharmacists—Member. PHS Commissioned Officers Association, National Executive Committee, Member and Treasurer. American Pharmaceutical Association, City of Washington Branch, Treasurer and President. Member, Skull and Dagger, All University Honorary Society, USC. Member, Committee on Constitution & Bylaws, American Society of Hospital Pharmacists, 1968-1969. Chairman, Committee on Standards for Pharmacy Services and Pharmacy Facilities in Mental Retardation Institutions. Consultant, American Medical Association's Committee on Drugs. Member. Visiting Committee of the College of Pharmacy, Wayne State University. Member, Committee on Governmental Pharmaceutical Services, American Pharmaceutical Association, 1968-present. Member, Public Health Services Committee, National Association for Retarded Children, 1969-1970. Delegate, U.S. Pharmacopiel Convention, Decennial Meeting, 1970. Staff Member of DHEW Secretary's Task Force on Prescription Drugs.

Special awards, citations or publications: Public Health Service Surgeon General's Commendation Medal. Outstanding Alumnus, College of Pharmacy, University of Southern California, 1967. Listed in Who's Who in American Men of Science. Six publications.

DEPARTMENT OF HEALTH, EDUCATION AND WELFARE—BIOGRAPHICAL SKETCH

Name: Winton B. Rankin.

Position: Special Assistant to the Assistant Secretary for Health and Scientific Affairs 1969–.

Birthplace and date: Bessemer City, N.C.; October 26, 1916.

Education: B.S., Appalachian State Teachers College, Boone, North Carolina, 1935. B.S., Pharmacy, Ferris Institute, Big Rapids, Michigan, 1937. M.S., Chemistry, North Carolina State College, Raleigh, North Carolina, 1939.

Experience: Deputy Commissioner, Food and Drug Administration, 1966-1969. Assistant Commissioner, Food and Drug Administration, 1961-1966. Assistant to the Commissioner, Food and Drug Administration, 1954-1961. Assistant Director, Division of Field Operations, Food and Drug Administration, 1948-1954. Employee Member Civil Service Commission Board of Review for the Food and Drug Administration, 1953-1959. Food and Drug Officer, Food and Drug Administration Headquarters, 1946-1948. Chief Inspector, Boston District. Food and Drug Administration, 1944-1946. Food and Drug Inspector, Food and Drug Administration, 1940-1944. Seafood Inspector, Food and Drug Administration, 1939-1940. Retail Pharmacist, Wilson, North Carolina, 1939.

Association Memberships: American Association for the Advancement of Science. Association of Official Analytical Chemists. Association of Food and Drug Officials of the United States. American Management Association.

Special awards, citations or publications: Numerous papers on administration of the national food and drug laws. Superior Service Award, Federal Security Agency, 1952. Citation for outstanding contributions to the National Public Health and Welfare, Drug and Allied Products Guild, Inc., 1964. Honorary D.Sc. Degree, Ferris State College, 1965. Honorary member, American Pharmaceutical Association, 1967.

[Division of Hospitals Circular Memorandum No. 66–31]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
Washington, D.C., June 9, 1966.

To: Medical Officers in Charge, U.S. Public Health Service Hospitals, U.S. Public Health Service Outpatient Clinics
Subject: Utilization Program
Applies to: All Stations

1. Background and Division Policy

Recent enactment of health insurance legislation for the elderly, Public Law 89–97, "Social Security Amendments of 1965," and subsequent actions taken by the Joint Commission on Accreditation of Hospitals at its Annual Meeting of December 11, 1965, have spurred new interest in optimum utilization of hospital facilities and services.

This Circular Memorandum establishes the Division of Hospital's policy that a Utilization Program will be in effect at each Public Health Service Hospital, beginning July 1, 1966.

Although not mandatory for PHS Outpatient Clinics, it is recommended that these stations also establish formal procedures to assure efficient utilization of personnel, physical resources, and patients' time.

2. Utilization Committee

To further achievement of excellence in medical care practice and to implement changes in practices and procedures that will assure optimum efficiency, a Utilization Committee will be established by the MOC of each PHS Hospital no later than July 1, 1966.

The Medical Officer in Charge may find it desirable to integrate the functions of the Utilization Committee with an existing committee, such as the Medical

Audit Committee. However, the term "Utilization" should be included in the committee's designation to signify this function.

The Utilization Committee will be representative of the various specialties and sub-specialties present in specific hospitals, including radiology and pathology. The number of members will depend upon the size of the hospital; it should be no fewer than 3 nor more than 15 members. It will meet regularly, at least once a month. The Medical Officer in Charge or members of the medical administrative staff may attend the meetings as Ex-Officio members of the committee. Paramedical and administrative staff members shall serve as consultants, as needed.

3. Utilization Reviews

Two kinds of utilization reviews will be undertaken by the Utilization Committee. The first, studies elements of utilization retrospectively, from samples of medical records and is concerned with the medical necessity of admissions, services provided, and length of stay. The second, studies every case remaining in the hospital for an extended duration.

(a) Retrospective Review

Headquarters will select diagnostic categories to be reviewed by the Utilization Committee and will provide the sample data necessary for securing the medical records. From data stored in the computer, Headquarters will forward to the Chairman of the Utilization Committee, worksheets containing summary information on the sample of cases to be reviewed, for distribution to committee members. Other data of value in utilization review will also be provided by Headquarters in advance of committee meetings, including utilization experience of other Federal and non-Federal hospitals.

Each hospital will receive the initial set of worksheets within two weeks following issuance of this Circular Memorandum. Thereafter, stations will receive worksheets three months in advance of the review period.

Medical records, as indicated by unit record numbers on the sample worksheets, will be provided by the Medical Record Service upon request of Utilization Committee members during the month before the date of the next monthly meeting.

At each Committee meeting, a physician will discuss the disease entity to be reviewed the following month. His discussion should include guidelines covering (1) indications for admission, (2) acceptable diagnostic and therapeutic practices, (3) usual length of stay, (4) complications affecting the length of stay, (5) discharge criteria, and (6) need for follow-up. This physician may or may not be a member of the Committee, but should be knowledgeable about the disease.

The full Committee will consider all cases in which individual members feel that there has been ineffectual utilization of the hospital's resources. When necessary, the responsible physician may be requested to provide the Committee with additional data to assist in evaluating the case. If the Committee concludes that there has been poor utilization, possible solutions will be considered and recommendations made in the minutes of the Committee meeting.

Data on the worksheets will be tabulated and the following summary information submitted to the Medical Officer in Charge:

(1) Number of cases reviewed;
(2) Number of cases judged to present problems;
(3) Nature of the problems, in terms of patterns of ineffectual practices;
(4) Recommendations, representing consensus of the Committee, for improvement;
(5) Suggested disease categories for future review.

Individual worksheets need not be retained. In no case will a physician evaluate one of his own cases.

Studies will be initiated by the Committee based upon problem areas appearing in individual charts. Professional and supervisory staff will be made available to assist the Committee in carrying out further statistical studies and analyses to find possible solutions to problems of ineffectual hospital utilization.

Upon request to Headquarters staff, assistance will be given in the statistical design of Division-wide studies encompassing problem areas common to all hospitals. Through its central computer program, Headquarters will submit routinely to each station, data on length of stay for specific diagnoses, and lists of those cases not falling within commonly accepted ranges of stay as established by Headquarters for screening purposes.

(b) Quarterly Education Program

Under the direction of the Medical Officer in Charge, these studies and the recommended changes in procedures will be presented in staff meetings, and in printed form, as a part of the hospital's continuing education and in-service training programs, at least quarterly.

(c) Review of Extended Hospital Stay Cases

Reviews shall be made of each beneficiary case of extended duration. The plan may specify a different number of days for different disease categories, or may set a single time limit for all cases; for example, 30 days, following which case review must be made.

Two or more physicians or a sub-committee will review all cases of extended duration no later than one week following the period of extended duration. Chiefs of Medicine, Surgery, Pediatrics, and other services, if large enough, will be designated the responsibility of performing this function on their services. They will appoint two staff members to assist them in the reviews. No physician will review his own cases.

The group will note whether the attending physician has certified a need for care beyond the predetermined time limit, and whether they agree with his decision. Three decisions are possible:

(1) Further stay is no longer medically indicated.
(2) Further stay is medically necessary.
(3) Further stay is necessary for other reasons (specify).

A report of justifiable extended stay cases will be submitted to the Utilization Committee Chairman at each monthly meeting.

If, after opportunity for consultation is given the attending physician, and consideration is given to availability and appropriateness of out-of-hospital facilities and services, the appointed physicians decide that hospitalization is unwarranted, there shall be notification in writing to the Committee Chairman and to the attending physician within 48 hours.

Psychiatric and tuberculosis patients may be excluded from this review procedure.

4. Documentation of Utilization Review Plan

The hospital will have a currently applicable written description of its utilization review plan. Such description shall include:

(1) Organization and composition of the Committee, and sub-committees, if desired, which are responsible for the utilization review function, including term of duty and rotation of membership;
(2) Frequency of meetings (at least monthly);
(3) Types of records to be kept (worksheet summaries, Utilization Committee minutes, study reports);
(4) Method to be used in selecting cases on a sample basis. (Computer-processed sample provided by Headquarters.)
(5) Definition of what constitutes the period of extended duration requiring the case review (thirty days, or by specific disease category, if desired.)
(6) Arrangements for Committee reports and their dissemination.

A sample Utilization Review Plan, prepared at one of the PHS Hospitals, is attached for your information. A sample Utilization Review Worksheet is attached, and a table of Length of Stay for Patients 65 or Older.

5. Minutes and Recommendations Held Confidential

Minutes of the monthly Utilization Committee meetings, summary information, recommendations, and reports to the Medical Officer in Charge on extended hospital stay cases, will be held confidential. Authority for implementation of recommendations resides in the office of the Medical Officer in Charge.

6. Publications

The following publications are enclosed for your information:

(1) "Utilization Review—A Handbook for the Medical Staff," American Medical Association, 1965. (Enclosure: omitted.)
(2) "Health Insurance for the Aged—Conditions of Participation for Hospitals," DHEW, Social Security Administration, 1966. (Enclosure: omitted.)

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DIVISION OF HOSPITALS
OPERATIONS MANUAL

PHARMACY

PART: C
CHAPTER: 4
SECTION: 1.2

SUBJECT:
PHARMACY COMMITTEE

.1 The development of an effective pharmacy program, in individual hospitals and clinics and for the Division of Hospitals as a whole, requires close cooperation between the pharmacists and the other professional groups concerned. The selection at a station, from among substances which possess medicinal power, those, the utility of which is most fully established and best understood, should be handled by a group upon which the medical officer in charge can depend for recommendations concerning the types and amounts of drugs to be available in the pharmacy and drug therapeutic practices in general. This group is referred to as the Pharmacy Committee. PURPOSE

The Pharmacy Committee is an advisory group and serves as the organizational line of communication or liaison between the medical staff and the Pharmacy Department. The committee is responsible to the medical staff as a whole and its recommendations are subject to medical staff and administrative approval.

.2 It is essential that the Pharmacy Committee consist of chiefs or deputy chiefs of medical, dental, and pharmacy services with the Clinical Director or Chief of Medicine serving as chairman and the Chief Pharmacist as recording secretary. Membership should be limited to ten persons. If necessary, in order to allow all chiefs to serve, a semi-rotating system may be instituted. COMMITTEE MEMBERSHIP

Junior staff members may attend meetings as observers but should not serve on this committee. Nursing and administrative personnel (purchasing in particular), if represented, should serve as non-voting members in order that only clinicians and pharmacists evaluate pharmacological agents.

.3 The responsibilities of each individual member of the Pharmacy Committee are described in detail in Attachment C4.1.2a. Each member should read that section to better understand the duties he will be expected to perform. The medical officer in charge of each station is requested to call this material to the staff's attention to help insure the continuing implementation of the selective drug therapy program. INDIVIDUAL COMMITTEE MEMBER RESPONSIBILITIES

.4 The following list of Committee functions, which is not necessarily all-inclusive, is offered as a guide: COMMITTEE FUNCTIONS

A. To serve as an advisory group to: (1) the medical staff and hospital administration in formulating broad professional policies regarding the evaluation, selection, procurement, storage, control, nomenclature, distribution, use, safety practices and other matters relevant to drug usage: and (2) the pharmacist for the choice of drugs to be stocked.

.4 Continued

B. To prepare and make available to the professional staff complete, unbiased, current information on matters relative to drugs and drug therapy.

C. To develop a formulary or basic drug list of accepted drugs for use in the hospital based on the generic, non-proprietary, or official name concept.

D. To evaluate objectively and continuously clinical data, literature reports, reported adverse reactions, and medical records for the purpose of: (1) making additions to or deletions from the formulary or (2) modifying the usage or administration of a drug.

E. To recommend policies for the safe use of drugs in hospitals including a study of such matters as investigational drugs, radiopharmaceuticals, hazardous drugs, side effects, and contraindications.

F. To make recommendations concerning drugs to be stocked at nursing station medication centers and in the specialty clinics.

G. To study problems relating to the proper distribution and labeling of medications for in- and out-patients and nursing medication centers.

H. To review periodically the stock status of all drugs, with special reference to the pharmaceutical specialties; to prevent unnecessary duplication of the same basic drug or its combinations and to avoid surplus stocks of usable drugs.

I. To plan and establish suitable educational programs for the professional staff on pertinent matters related to drugs and their use such as the Dental Pharmacology Reviews prescribed by the American Dental Association for Dental Internships.

MEETINGS .5 Meetings should be held regularly at least six times a year, and preferably monthly.

MINUTES AND RECORDS .6 Agendas and minutes of the Pharmacy Committee meetings will be prepared by the Committee's secretary and copies of each will be circulated among the staff as soon as possible after each meeting.

One copy of the minutes will be transmitted, as issued, to the PHS Medical Supply Service Center, Perry Point, Maryland, and one copy to the Chief, Division of Hospitals, Attention: Chief, Pharmacy Branch.

Copies of meeting agendas and minutes will be kept on file in the pharmacy for five years.

The Joint Commission on Accreditation of Hospitals, in evaluating a pharmaceutical service, checks, among other things, on the composition and activities of the Pharmacy Committee. The surveyor may request the minutes of the meetings for this purpose.

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RESPONSIBILITIES OF INDIVIDUAL PHARMACY COMMITTEE MEMBERS ATTACHMENT C4.1.2a

"Responsibilities and Functions of the Individual Pharmacy Committee Member." Relatively little has appeared in print on this subject, although much has been written upon the functions and responsibilities of a pharmacy committee acting as a whole. The functions, responsibilities, and qualifications of the individual committee member have been subjects to which considerable thought has been given in the development of its total pharmacy program in the Division of Hospitals of the Public Health Service. This section is developed to serve as a guide in formulating a plan of instruction for newly appointed pharmacy committee members in discharging their important duties. It is important that any plan of instruction should emphasize that the pharmacy committee is the forum for medical staff self-government in drug evaluation and utilization, a program we refer to as Rationale Drug Therapy and Quality Control of Medications. This approach will give prestige to the venture and be most likely to effect acceptance by medical staffs, residents, and interns.

Pharmacy and drug therapeutic committees do not represent a new procedure to many hospital administrators, hospital pharmacists, and clinicians. However, there are probably some hospitals and hospital staffs that are only vaguely familiar with their place and function in the administration of the modern hospital. It seems appropriate, therefore, to mention briefly at this point, events considered as the four landmarks of the development of the pharmacy committee in the rapidly growing field of hospital pharmacy administration:
(1) the 1937 "Report of the Committee on Pharmacy" of the American Hospital Association. This report contained the following statements concerning the proposed standards of operation of a pharmacy committee, "The hospital shall appoint a pharmacy committee which shall meet at regular intervals. The members of the committee shall be chosen from the several divisions of the medical staff. The pharmacist shall be a member of the committee and shall serve as its secretary. He shall keep a transcript of proceedings and forward a copy to the proper governing body of the hospital. The purposes of the pharmacy committee shall be:

(a) To determine the policy of operation of the pharmacy, and to deal with such matters of a pharmaceutical nature as may from time to time arise.
(b) To add or delete from the drugs used.
(c) To supervise the purchase and issuance of drugs, chemicals, pharmaceutical preparations, biologicals, and professional supplies within the hospital."

(2) The Manual of Hospital Standardization, published in 1946, by The American College of Surgeons. This manual repeated in essence what has already been stated above, in its section dealing with "Minimum Standards for Pharmacies in Hospitals."
(3) The 1950 revision of the "Minimum Standards for Hospital Pharmacies." This manual again reaffirmed what has already been stated. The American Society of Hospital Pharmacists released these same standards at that time. In this same year they were approved with minor changes by The American Hospital Association's Council on Professional Practice.

They were also accepted in principle by The Catholic Hospital Association's Committee on Pharmacy Practice, and endorsed by The American Medical Association, and
(4) The Joint Committee on Accreditation of Hospitals requires, among other things, for the full approval and credit of a pharmaceutical service in a hospital:

(a) An active pharmacy committee
(b) An up-to-date hospital formulary

These actions by national organizations certainly establish beyond question the necessity and legitimacy of the pharmacy committee in the administrative and clinical organization of the modern hospital.

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ATTACHMENT C4.1.2a Page 2

The following people are eligible to membership on the pharmacy committee:
(1) The hospital administrator (if a physician and a qualified clinician)
(2) Chiefs of major clinical services, including dentistry
(3) The clinical director or clinical coordinator in large hospital that have such a position
(4) The chief pharmacist.

The director of nursing services, and the purchase and supply officer might be considered as associate members without voting privileges. They do not participate in committee actions. They attend on call to receive and give information. Also, interns and residents should be invited to attend as observers for the educational value of the committee discussion in pharmacology.

THE HOSPITAL ADMINISTRATOR

Whether the hospital administrator is an active and participating member of the pharmacy committee or a member ex-officio should depend upon his knowledge of modern drug therapy. Unless the administrator is a physician familiar with present-day concepts of clinical pharmacology, biochemistry, and microbiology and is so recognized by the medical staff, he should disqualify himself for active membership on the committee. Whether an active member of the committee or an ex-officio member, he has certain responsibilities as administrator of the hospital in the functioning of the committee. These responsibilities are:
(1) Establish the policy as to the existence, purpose, scope, and duties of the committee.
(2) Determine the term of office of its members.
(3) Appoint a chairman annually.
(4) Provide means for implementing the committee's actions and recommendations through prompt channels of communications to the various departments of the hospi...

The policy statement of the administrator should define in general terms the functions of the committee. As a concrete example of what is meant here, we give the policy statement for the functions of pharmacy committees in Public Health Service hospitals:
"(1) Prepare and formulate current information on drug therapy for the guidance of the staff. This includes the adoption of a station formulary consisting of the A.S.H.P. Formulary Service, and the station supplement to it, usually termed a "Drug List."
(2) Review periodically the stock status of drugs with special reference to the pharmaceutical specialties in order to avoid the development of surplus stock of usable drugs.
(3) Consider periodically the additions and deletions of items from New Drugs, Accepted Dental Remedies, U.S. Pharmacopoeia and National Formulary.

(4) Serve as an advisory group to the pharmacist regarding the therapeutic agents to be stocked in the pharmacy.
(5) Serve as an advisory group to the pharmacy department regarding therapeutic agents to be stocked as ward, and prepackaged, medications.
(a) The committee will review requests for items not routinely stocked, including drugs not yet available in interstate commerce, upon written request of a medical or dental officer and approval of his chief of service. These requests should contain a justification of the item requested, and a statement of the amount needed, on the basis of a specific patient or service need. (See Form PHS-1689 "Request for Purchase of Non-Basic Drug")
(b) Requests should not ordinarily be made for items by trade names, especially when such items are also official in the U. S. Pharmacopoeia or National Formulary.
(6) Consider other pharmaceutical or related matters referred by the medical officer in charge."

It is advisable that the appointment system for committee members be of a "staggered nature." Such a system provides for continuity of committee action. The appointment of an entirely new and different committee at one time leads to obvious difficulties. It is imperative that committee members hold positions of responsibility. They should be at the level of chiefs, deputy chiefs, or assistant chiefs of service.

If a hospital has a clinical director or coordinator, either he or the administrator (if a physician and clinically qualified) is probably most suitable for the position of chairman. In the event it is not feasible for either of these to act as chairman, the policy of appointment should be clear that either by direct appointment by the administrator, or election by the staff, a chairman well versed in clinical pharmacology and biochemistry will be selected.

The minimum number of meetings to be held each year should be definitely stated. A method of disseminating the decisions and recommendations of the pharmacy committee to the professional staff must be provided. This could be done either through a "House Publication" if such is in effect, or through a pharmacy bulletin. The distribution of the decisions and conclusions of the pharmacy committee in printed form is of greatest importance.

THE CHAIRMAN

The success of a given pharmacy committee depends to a large measure upon the effort the chairman puts into planning the committee's meetings. His responsibilities are to:

(1) Insure that the proper "working tools" for the committee are readily and easily available; and that each committee member is fully informed as to where these "tools" are kept. Some of the more important "tools" are the latest additions and revisions of the U.S. Pharmacopoeia, The National Formulary, New Drugs, Accepted Dental Remedies, Facts and Comparisons, and the A.S.H.P. Formulary Service. The latest texts in pharmacology, biochemistry, microbiology, and clinical toxicology must be readily available as well as a representative number of current medical and pharmacy journals, and manufacturer's package-label inserts.

(2) Instruct each committee member in the responsibilities he expects them to assume. He should inform them as to the principles he wishes them to follow in evaluating drug therapy problems. He should indoctrinate them with the importance of communicating to their respective departments, the importance of the committee's actions and the benefit of communicating drug therapeutics' problems to the committee for action.
(3) Prepare an agenda for each meeting and circulate it in sufficient time to allow all members of the committee to study it and formulate proposals and opinions of considered value.
(4) Assign one or two committee members to the task of fully preparing themselves to discuss any new drug therapy problem to be presented before the committee and offer their advice on the subject.
(5) Insure that communication channels are kept open between the pharmacy committee and chiefs of services and departments of the hospital affected by actions of the committee. He should make certain that the minutes of pharmacy committee meetings are reaching chiefs of services promptly and being discussed with members of the respective services.
(6) Insure that the presentation of a summary of important actions of the pharmacy committee is made at staff meetings of the hospital.
(7) Insure that the pharmacy committee and the hospital pharmacy are meeting the minimum standards of the Joint Committee on Accreditation of Hospitals on such matters as hospital formulary, drug inventory, number of committee meetings, minutes, etc.

THE RECORDER OR SECRETARY

As has already been pointed out, this individual should be the chief pharmacist of the hospital. Among his important duties are:
(1) The maintenance of an adequate up-to-date library and drug therapy reference file for the use of the committee and the staff.
(2) The interviewing and screening of professional medical representatives (detail men) of pharmaceutical firms, and arranging for departmental interviews with them when indicated. This is an important function of the secretary inasmuch as it keeps him informed of the latest drug therapy agents being detailed by the pharmaceutical firms to physicians on the staff. This function is administratively valuable to the hospital in that it conserves time of staff members without loss of valuable information that the detail representatives have for members of the various services.

The secretary also arranges with the detail representative for the presentation of exhibits to the staff at optimum times. At such meetings the detail representative of a pharmaceutical firm has the opportunity to discuss the pharmacology, biochemistry, and pharmacy of his product with all interested staff members.

(3) The prompt preparation, dissemination, and custody of accurate minutes of committee activities. This responsibility cannot be emphasized too strongly. The issuance of the minutes promptly in printed form after each meeting has already been stressed. The proper custody of the minutes is equally important. The inspector for the Joint Commission on Accreditation of Hospitals may ask to inspect the record of pharmacy committee meetings. It will be remembered that this inspector in evaluating the hospital pharmacy will consider the recorded activities of the pharmacy committee as well as the presence of a hospital formulary.

The minutes of the committee and the format of the formulary must obviously be more than a recording of decisions and a list of drugs. The minutes must contain the pharmacological basis for drug selection or rejection.

The formulary must contain a format on each drug containing its generic or official name, its identifying characteristics, actions, contraindications, side effects, toxicology, posology, and if significant, size and strengths available. We consider the following a good example of reporting in the minutes:

"Methantheline Bromide (Banthine) ampuls, 50 mg. - Service requiring it: Medical Service (requested by Dr. _____).
Pharmacological Action Needed: "For suppression of pancreatic secretion in acute pancreatitis and treatment of patients with peptic ulcer complicated by vomiting."
Is There a Similar-Acting Drug Stocked in the Pharmacy Which May be Used? (Atropine and Belladonna):

"Methantheline Bromide is more effective in the relief of pain and in the suppression of pancreatic secretion."

Remarks by Dr. _____: "Oral Methantheline Bromide often cannot be used in pancreatitis because of vomiting. In some patients with peptic ulcer Methantheline Bromide is more effective than Atropine."

Action Taken: It was agreed to stock the preparation.

(4) The preparation of the agenda approved by the chairman and its release to committee members sufficiently in advance of the meeting to allow time for intelligent preparation.
(5) Editing the formulary (after review by all pharmacy committee members and final review and approval by medical and dental staff) as well as custody and issuance of formulary and supplements to medical staff members, residents, interns, and other authorized personnel such as nurses and medical record librarians.
(6) The encouragement of individual staff members to present requests to the committee, and the assistance to staff members in collecting proper and adequate information to cover the request.
(7) Serving as a drug therapy consultant to the staff, especially the residents, interns, and nurses. These services are usually given in private conferences, but there is much value also to be obtained from formal lectures to medical and dental interns and the nursing staff.

THE NON-OFFICE HOLDING PHARMACY COMMITTEE MEMBER

Members of the committee should consist of chiefs, deputy chiefs, or assistant chiefs of clinical services. Where committees are composed of junior staff men and residents, experience has been that such committees' decisions and recommendations have been ineffective. Medical staffs under these conditions invariably treat the committee decisions with little concern.

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The individual committee member should assume the following responsibilities:
(1) Prepare himself by sufficient study to intelligently discuss and participate in making decisions on the subjects placed on the agenda for consideration.
(2) Attend all meetings regularly and promptly.
(3) Place the medical needs of the patients and the hospital above his personal scientific interests and desires in making recommendations and decisions.
(4) Disseminate the committee's thinking and aims among his colleagues on his service, as well as bringing his colleagues' problems and thinking to the attention of the committee.
(5) Stress the use of generic, non-proprietary and official names when working with the staff or teaching residents, interns, nurses and medical record librarians.

There is a fine point in ethics involved in this responsibility. It is generally accepted as an unethical procedure for a physician to refer his patients to one pharmacist in a community for prescription service. When faced with the request for a recommendation, ethics require that he name several reputable pharmacists and allow the patient to make his choice. The same ethical question can be raised when several reputable pharmaceutical houses are manufacturing the same item and meeting the drug specifications of the U. S. P. and N. F. This is particularly true when a hospital is operating on public funds, or monies derived from charitable foundations.

There are other sound arguments for the use of generic or "official" names. For example, there is always the danger that a hospital may leave itself open to charges of "substitution" if it employs a trade or brand name for a preparation and later uses an identical preparation of another trade or brand name or an identical preparation that has only an "official" or generic name. Further, the use of generic and official names insures the fact that the medical staff, residents, interns, nurses and medical record librarians, are speaking a common language. Also such a system gives an institution a recognized standard terminology for drugs. It is a responsibility of all teaching hospitals to use the official and generic names for drugs.

Brand name products of well known reputable firms meet the official standards and are, of course, preferred to similar items of unknown manufacturers. Hospital pharmacists properly performing their functions select products of reputable pharmaceutical manufacturers in meeting their drug needs; products of manufacturers, who usually have built their reputation on quality brand name items. The point we stress is the need for adopting scientific medical nomenclature in drug terminology.
(6) Favor the policy of using "Blind Tests" in controversial areas. In other words, drugs to be studied should be so labeled that only the chairman and secretary of the committee know the exact identity of a drug until the committee has had time to evaluate all the clinical and pharmacological evidence presented to it.
(7) Keep himself appraised not only with the pharmacological merits of drugs but also with their comparative costs in relation to their efficacy.
(8) Weigh his decisions not only in the light of providing the best drug therapy for patients, but also in preventing needless and wasteful duplication in the same class of drugs.
(9) Advocate the practice among his colleagues of having new drug requests from his service reviewed by the representative members of the service before submitting the requests to the pharmacy committee. This practice insures agreement on need, and assures presentation of adequate information for the committee to act upon.
(10) Work for the establishment of meaningful drug terminology. Discourage the unsafe practices in drug identification such as the use of synonyms, numbers, and trade names without knowledge of the generic, non-proprietary or official name; also promote and advocate the use of the metric system in prescribing, ward medication labels, and formularies.
(11) Advocate and work for the establishment of "Restricted Drug Lists." Many modern-day drugs, because of their complex action, potency, and toxicity, should, in the interest of better patient care, be restricted to use by those staff members with special competency in their administration. A typical example of a restricted drug list policy is presented for your consideration.

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RESTRICTED DRUG LIST POLICY U.S.P.H.S. HOSPITAL - BALTIMORE, MD.

Drugs "accepted" by the pharmacy committee are placed in the most appropriate of the five (5) groups listed. Drugs are removed from restrictive groups as soon as the committee has sufficient evidence to indicate that there is no longer need for the control. Requests for drugs in Group One (A) are presented on the usual floor requisition form. The signature of the charge nurse is required. Requests for drugs controlled by regulations (Group One (B)) (Liquor, Ethyl Alcohol, Hypnotics and Narcotics) require the signature of the charge nurse also. Requests for drugs in Groups II, III, IV, and V must be on a physician's prescription order blank. The name of patient, name of the drug, the dose and signature of prescriber is required.

Restricted Drug Groups

Groups

I (A) Drugs for nursing units (may be ordered by the charge nurse).
(B) Drugs controlled by regulations (must be ordered by charge nurse).
(Narcotics, Hypnotics, Ethyl Alcohol and Spirituous Liquors.)

II Drugs requiring special prescription for patient signed by a medical officer.

III Drugs requiring special prescription for patient signed by chief, deputy chief, assistant chief or resident.

IV Drugs requiring special prescription for patient signed by chief, deputy chief, or assistant chief.

V Drugs requiring special prescription for patient signed by chief or deputy chief of service.

Drug Restricted List Policy

Signature of any one individual indicated is required to obtain a medication in a particular group.

Groups		Chiefs	Deputy Chiefs	Ass't Chief	Staff Physician	Resident	Intern	Nurse
I	(A)	x	x	x	x	x	x	x
	(B)	x	x	x	x	x	x	
II		x	x	x	x	x	x	
III		x	x	x	x	x		
IV		x	x	x				
V		x	x					

(12) Develop a methodical procedure by which he can arrive at a sensible and logical evaluation of a drug.

The following approach is currently being used in U. S. Public Health Service hospitals and clinics in indoctrinating pharmacy committee members and clinical staff on the philosophy and method of drug evaluation.

(1) The index to Sollman's Manual of Pharmacology (7th edition) shows about 2400 items.
(2) The introduction to The Merck Index (6th edition) states that the text covers 8,000 drugs and chemicals.
(3) The National Formulary (9th edition) lists about 500 drugs.
(4) The U. S. Pharmacopoeia (14th edition) lists approximately 500 drugs.
(5) New and Non-Official Remedies (1952) mentions in the neighborhood of 1,000 items.

There is of course, considerable over-lapping in these listings. However, taking this fact into consideration, there are undoubtedly more than 2500 different drugs available at any one time when allowance is made for the continual introduction of new preparations. We do not believe it is an overstatement to say that there are many more drugs available than are necessary to practice good medicine. All of us are aware of the confusion that this abundance causes in the field of drug therapy. There are too many drugs to choose from; there is a tremendous amount of over-lapping; there are too many compounded prescriptions available; and new agents are added at a greater rate than older ones are discarded or declared obsolete. This situation is not new, but the point of concern is that it is allowed to remain with us and grow. The problem of any one physician in keeping abreast of the developments and learning to distinguish between the good, the better, and the best, always becomes progressively more difficult.

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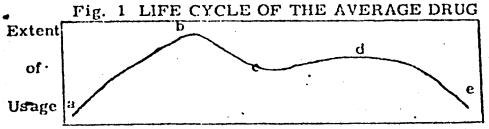
The Council on Pharmacy and Chemistry of the American Medical Association has stated this situation so clearly we would like to quote from one of their writings 1/on the subject, "A fundamental requirement to successful treatment is that the physician have the clearest possible understanding of the remedial agents that he prescribes. This is difficult at best, and is rendered increasingly more difficult with multiplication of agents that are nearly, but not quite equivalent. Each may show minor differences, which may or may not be important, but which are difficult to learn if he spreads his experience too widely, and, therefore, too thinly. It were much, much better for medical practice if modifications which do not offer substantial advantages were shunted into the discard before they see publicity and add to the confusion of the practitioners."

The Public Health Service firmly believes that a better job of successfully treating the sick can be done if our therapeutic armamentaria are reduced to carefully selected, indispensable, tried and true drugs which we learn to use well. The fact that our hospital pharmacy committees have developed formularies, we believe indicates the existence of a felt need for bringing order out of a chaotic situation. In preface to specific comments on criteria and methods of selection of drugs, we believe that it might be helpful to first try and visualize the life cycle of the average drug. We attempt to portray this diagrammatically in Figure 1.

Fig. 1 LIFE CYCLE OF THE AVERAGE DRUG



The drug is introduced at "a." It becomes quite popular and reaches a peak of usage at "b." Some of its deficiencies become apparent and physicians become overly cautious, dropping its use to an abnormally low level at "c." With further experience the drug's use later rises to an optimal level at "d." Finally, as better agents are developed, it proceeds to obsolescence at "c." This cycle is quite rapid with some drugs and very slow with others. It took quinine 323 years to approach "c." On the other hand, sulfanilamide ran its course in a decade. Although some fundamental agents, like sodium chloride and dextrose, may never become truly obsolete in the practice of medicine, this diagram does serve to help one visualize the usual dynamics in the field of drug therapy.

Fig. 2 DISTRIBUTION OF AVAILABLE DRUGS

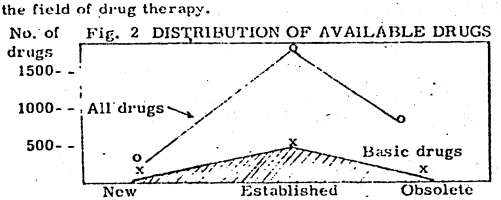


Figure 2 is presented in an effort to visualize another important aspect of clinical pharmacology. In this we attempt to illustrate the current status of all drugs available at one particular time by classifying them arbitrarily into three groups; "New," "Established," and "Obsolete." A random sample of items listed in N.N.D., U.S.P., N.F., A.D.R., and the Blue Book suggested that a reasonable distribution might be 5% "New," 63% "Established," and 32% "Obsolete." Applying these percentages to our guess of 2500 as the number of drugs now available, the points shown in Figure 2 are established. In view of the sources we used in presenting this diagram, the value shown as "New" is probably too low and that for "Obsolete" too high. For example, it was reported some years ago that 88 firms placed a total of 170 new single chemicals on the market in five years. To visualize the abundance of "Established" and "Obsolete" items available, we show the distribution of the 263 drugs we consider basic 2/ as worked out by Pharmacy Committees in U. S. Public Health Service Hospitals and Clinics in 1953. The ratio changes little over the years.

1/ Journal of the American Medical Association Vol. 139, No. 6, February 5, 1949.

2/ The term basic is used as a synonym for fundamental, essential, point of departure, foundation, indispensable.

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METHOD FOR SOLUTION

To reduce the large number of drugs currently available to a compact and effective therapeutic armamentarium, there has to be developed sound methods for discriminating in an objective fashion. The first step should be to list and then categorize the therapeutic needs to be met.

The broad therapeutic categories in "New and Non-Official Remedies" are most useful for this purpose.

With this as a structure of the broad therapeutic needs to be met, the next step is to develop appropriate criteria to use in selection of the actual agents to be included in each category and the necessary sub-categories. These criteria for selection of basic drugs within each of the therapeutic categories may be stated in many ways.

We suggest the following approach as an example:

(a) Be sure the drug's therapeutic efficacy is well established.
(b) Give preference to United States Pharmacopoeia, National Formulary, New Drugs and Accepted Dental Remedies Drugs.
(c) Avoid unnecessary duplication of action.
(d) Avoid consideration of drugs of secret composition.
(e) Avoid mixtures of drugs unless they provide a real advantage in combination.

The motto of the Pharmacy Committee might well be: "Prove all things; hold fast to that which is good." (For the patient.)

SUPPLEMENTS TO FORMULARY

New developments are constantly with us in this rapidly moving age in drug therapy. It is, therefore, essential that a pharmacy committee not only develop but also maintain a supplement to its formulary. Clinicians wishing to introduce the use of a non-formulary drug should propose the use of the drug to the pharmacy committee. The pharmacy committee should consider the proposed drug in the light of the evidence presented by the proposer, their collective knowledge of the drug, and the adequacy of drugs already listed in their formulary and the supplement to meet the need alleged. The pharmacy committee would add those new items which it accepts to the supplement of their formulary. Such new items added should be described in the same manner as used in the format of their formulary. The date of the addition to the supplement should be recorded. The committee should review the staff experience with drugs in the supplement to their formulary after an adequate trial period (six to twelve months) and on this basis decide whether to:

(a) Drop the drug,
(b) Retain it for further evaluation,
(c) Propose it be moved from the supplement to the formulary.

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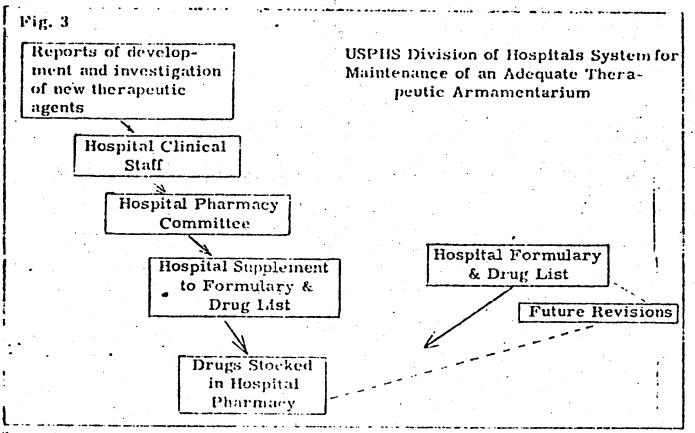
This plan, as used in the U. S. Public Health Service is depicted in Figure 3. Such a system insures the inclusion and deletion of drug therapy agents based on opinions of several clinicians, opinions formed as a result of careful studies and discriminating clinical experiences.

Fig. 3



In spelling out this program for a pharmacy committee and especially the responsibilities of its members, we recognize that many staff physicians when first hearing of it may consider it an abrogation of their rights to freedom in the practice of medicine. In fact they may claim it comes dangerously close to telling a physician what drugs he may and should use. Is this true? Certainly it is, but is not this kind of group consultation desired and sought for by all physicians and dentists truly interested in their callings? Further, we question whether the program suggested is any more limiting in scope than that placed on the indiscriminate performance of surgical operations or highly specialized medical or dental procedures. The emphasis is again placed on medical staff self-government and analysis of objective and procedure. We emphasize again that the program simply requests the staff member to submit any new drug which he desires to use for committee evaluation; to support his request by an oral and written statement of the pharmacological and therapeutic needs to be met; and to satisfy the committee that he is not being motivated by a scientific whim.

Viewed in the foregoing light we see no unreasonable restrictions being placed upon the practice of sound medicine. We believe that the physician is obtaining the advantage of a profound pharmacological consultation in a manner analogous to a radiological or pathological consultation.

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Summing up this lengthy presentation, the endeavor has been:

First: To point out the four landmarks in the field of hospital administration that establish the importance of a functioning pharmacy committee. These landmarks were established by medical, hospital, and pharmacy groups working toward a common goal of better patient care.

Second: To detail the responsibilities, functions, and duties of the individual members of the pharmacy committee. In doing this attention was focused on:

(a) 4 Responsibilities of the Administrator
(b) 7 Responsibilities of the Chairman
(c) 7 Responsibilities of the Pharmacist Recorder or secretary and,
(d) 12 Responsibilities of the individual Committee Member.

Third: To emphasize a few factors which we feel are leading to an extremely confused and complicated situation today in drug therapy; and to suggest a democratic method in medical self-government by which a physician or dentist on a hospital staff can obtain an exhaustive drug consultation from a competent and active group of clinicians - the hospital's pharmacy committee.

The pharmacy committee technique as a means of providing the best in drug therapy is a sound advance in hospital administration and clinical practice. This fact is attested to by the many clinicians who are being properly served by such committees and who are enthusiastic with the results. Obviously, the success of an individual hospital program must depend upon the perspective, interest, understanding, and industriousness of the clinicians and pharmacist who serve on the committee as voting members as well as the sincerity, interest, and support of the physicians and dentists who have the privilege of using the hospital, and last but not least, the complete support of the hospital administrator.

The foregoing is taken from a paper prepared for the Division of Hospitals in 1953 by co-authors Kenneth R. Nelson, M.D., and Clifton K. Himmelsbach, M.D.

CHAPTER 2
MEDICAL FACILITIES AND PATIENT MANAGEMENT

I. MEDICAL FACILITIES

4-2.1 UTILIZATION REVIEW COMMITTEE

A. Purpose.

(1) To establish a formal plan to maintain the highest possible quality of patient care and effective utilization of health services by routine audits of medical records to determine if medical care, and utilization of the facility are appropriate.

(2) To assure that Indian Health Service hospitals meet the standards of the Joint Commission on Accreditation of Hospitals.

B. Policy. Each IHS hospital will have in effect a plan for monthly utilization review of inpatient services to include at least:

(1) A review of the medical necessity of admissions.

(2) A review of professional services provided. (Overuse or underuse, logical substantiation of diagnoses, proper use of consultants, whether required diagnostic workups were initiated and carried out promptly, etc.)

(3) A review and evaluation of the diagnostic procedures and treatment prescribed.

(4) A review of factors relating to duration of stay (hospital staffing, assistance in discharge planning, availability of out-of-hospital facilities and services which assure continuity of care, etc.)

C. Standards.

(1) Approval and Operation of Plan

a. The Area Office is responsible for the approval of the hospital's plan.

b. The hospital's staff is responsible for its operation.

(2) Written Description of Plan

Each hospital shall have a currently applicable, written description of its utilization review plan. Such description includes:

4-2.1C(2) continued

a. The organization and composition of the committee;

b. Frequency of meetings;

c. The type of minutes to be kept;

d. The method to be used in selecting cases on a sample or other basis;

e. Arrangements for committee minutes and their dissemination.

(3) Committee Composition

The utilization review will be conducted by a staff committee or committees of the hospital composed of two or more physicians and the Director of Nursing with the inclusion of other professional personnel.

Existing staff committees may assume the review responsibility stipulated in the plan. In smaller hospitals, all of these functions may be carried out by a committe of the whole or a medical care appraisal committee.

(4) Records

a. Minutes of committee meetings are to be kept of the activities of the committee.

b. Minutes will be submitted to the Service Unit Director and the Area Director.

c. Minutes of each committee meeting will be retained as required by the Joint Committee on Hospital Accreditation.

(5) Follow-up

a. The committee will make recommendations to the Serv Unit Director for necessary action and follow-up to assure the best use of service and resources to obt the highest possible care.

b. The Service Unit Director will be responsible for necessary corrective action.

c. In the submission of the minutes to the Area Direct the Service Unit Director will advise of corrective action taken or to be accomplished.

3-7.4D continued

in general an officer can expect assignments to rotate between locations that are considered more or less isolated and those not so isolated. Each officer may also expect to receive an Alaskan assignment sometime during his career. Officers with Division experience will generally be assigned to one man stations. The senior pharmacy officer will be in charge when two or more pharmacists are on the staff of a pharmacy service.

3-7.5 PHARMACY AND THERAPEUTICS COMMITTEE

The development of an effective and comprehensive pharmacy program requires close cooperation between the pharmacy service and the other professional services. Necessary control of pharmaceutical usages is best handled by a group upon which the Indian Health Area Director and field facilities can depend for recommendations concerning types and numbers of drugs to be available in the pharmacy and therapeutic practices in general. It is recommended that an Area Pharmacy and Therapeutics Committee be formed so as to serve the entire Area. Such a committee will provide a committee having varied experience, a continuity of members, and permit the utilization of specialists assigned to the Area. In addition, transfers and resignations within the Area will have less effect on committee membership.

In addition to the Area Pharmacy and Therapeutics Committee, each Service Unit with a pharmacist shall have a Service Unit Pharmacy and Therapeutics Committee. This committee should meet at least every other month. The membership should consist of all medical, dental, and pharmacy officers (except in the larger hospitals) and the Director of Nurses. The purpose of this committee is to consider pharmacy and therapeutic matters within the narrower and more specific framework of local conditions and circumstances.

A. Membership and Meetings

(1) The Area Committee should consist of the Indian Health Area Director or his designated representative as Chairman; other medical officers as designated by the IHAD; Chief, Nursing Services Branch (as a non-voting member); Chief, Area Dental Services Branch; the Chief, Area Pharmacy Branch as Executive Secretary and possessing a vote and a Service Unit pharmacist as Recording Secretary.

(2) The Pharmacy and Therapeutics Committee should meet regularly, a minimum of twice a year.

3-7.5 continued

B. Functions and Responsibilities. It is the responsibility of the Pharmacy and Therapeutics Committee to insure that, according to the committee's judgment, the best therapeutic agents are available for the current and anticipated needs and to avoid unnecessary duplication of drug therapy agents having identical or similar pharmacological action. Drug therapy agents approved for permanent stock by the committee will be listed in the Area Formulary.

The committee's functions are to:

(1) Develop and maintain a current formulary of accepted drugs for use in the Area.

(2) Prepare and formulate current information on drug therapy for the guidance of the staff.

(3) Review periodically the current stock status of drugs with special reference to preventing unnecessary duplication of drugs having similar or identical pharmacological action and elimination of unnecessary drugs.

(4) Review periodically the additions to and deletions from New and Nonofficial Drugs and Accepted Dental Remedies.

(5) Evaluate clinical data concerning drugs requested for use and approve additions to or deletions from the Formulary. Pharmaceutical aids, needed in compounding, need not be approved by the committee.

(6) Serve as an advisory group to the Area regarding:

a. Drugs to be stocked at nursing stations, clinics, health centers, health stations, health locations, and schools, and

b. other pharmaceutical or related matters.

(7) Review the emergency purchases of drugs not in the Formulary.

(8) Ascertain compliance with Federal laws and regulations governing pharmacy activities.

(9) Review Adverse Drug Reaction Reports.

In an emergency, it is not to be construed that Service Unit Directors must have the approval of the Area Pharmacy and Therapeu Committee in order to obtain a drug not listed in the Formulary.

3-7.5B continued

However, a quantity only for the particular emergency should be purchased. The Service Unit Director or his designated representative should approve all requests for emergency drug items not regularly stocked.

C. Records. It is recommended that records be prepared by the secretary and that the permanent record of the committee's activities be kept in the office of the executive secretary. Copies of minutes and records will be prepared and forwarded to each member of the committee, the Indian Health Area Director, each facility, and the Chief, Division of Indian Health, attention: Chief, Pharmacy Branch, through the Indian Health Area Director.

3-7.6 AREA AND HOSPITAL FORMULARY

An Area Formulary containing all drugs approved by the Area Pharmacy and Therapeutics Committee will be compiled and maintained current by the Chief, Area Pharmacy Branch with the Area Pharmacy and Therapeutics Committee serving as an advisory body. The format of the Formulary will be standard throughout the Division. Generic or official names, when they exist, will be used instead of trade names. The metric system will be used and lists of package sizes will be available. Alphabetical cross references of generic-trade and trade-generic names will be included. A current copy of the Area Formulary will be maintained at each nursing station and each field facility where drugs are located.

The Chief, Division of Administrative Services, Public Health Service, shall be notified of additions and deletions to the Area Drug Formulary.

3-7.7 ADVERSE DRUG REACTION REPORTS

Each facility shall participate in the adverse drug reaction reporting program of the Food and Drug Administration. Such reports will be forwarded directly to the Food and Drug Administration with a copy of the report being filed in the pharmacy that provides services for the facility.

3-7.8 PHARMACY LIBRARY

A. A library with the latest edition of the following books shall be maintained in each pharmacy:

- United States Pharmacopeia
- National Formulary

3-7.8A continued

- New and Nonofficial Drugs 1/
- United States Dispensatory
- Facts and Comparisons
- Modern Drug Encyclopedia and Therapeutic Index with Supplements (Modern Drugs) 1/
- Accepted Dental Remedies 2/
- The Medical Letter
- The American Hospital Formulary, ASHP 3/ with annual supplements

B. At facilities with a pharmacy the latest edition of the following books, journals, and publications shall also be available:

- Remington's Practice of Pharmacy
- Clinical Toxicology of Commercial Products, Gleason, Goselin, and Hodge
- Pharmacology
- Pharmacological Basis of Therapeutics, Goodman and Gilman 1/
- Handbook of Poisoning, Dreisbach
- The Merck Index
- Bacteriology
- Biochemistry
- Medical Dictionary 1/
- Organic Chemistry
- Hospital Management

1/ These books and publications shall be available at stations without pharmacies with a full-time Medical Officer.

2/ This book shall be available at all stations with a Dental Officer on the staff.

3/ This book should be at each nursing station and outpatient clinic.

3-7.8B continued

- Blue Book or Red Book
- Federal and State laws and regulations pertaining to drugs, narcotics, hypnotics, alcohol and spirituous liquors and State and local pharmacy laws and regulations. 1/
- Current Therapy, Conn or Drugs of Choice, Modell 1/
- Drug and Cosmetic Review Magazine
- Journal of the American Pharmaceutical Association
- Journal of Pharmaceutical Sciences
- American Journal of Hospital Pharmacy
- American Professional Pharmacist

C. The pharmacy shall also maintain files containing literature on the newer therapeutic agents, and the house organs, catalogs and price list of pharmaceutical manufacturers.

3-7.9 INVESTIGATIONAL DRUGS

Investigational drugs, and drugs not available in interstate commerce, must have the approval of the Chief, Division of Indian Health, for authority to procure and use.

A. Prior to requesting approval for the clinical trial of any drug, the proposed study will be cleared by the Area Pharmacy and Therapeutics Committee, which is prescribed in Section 3-7.5 of this Chapter, and the Area Research Committee, which is prescribed in Part I Chapter 7 of this manual. It is recommended that the Committees consider such proposals in the light of current knowledge of the drug and other drugs in the same therapeutics class, and that a scientific clinical research protocol be formulated to evaluate the particular agent.

B. Research protocol should set forth the laboratory and the clinical aspects of the study, make provisions for control, assure the availability of adequate laboratory and other diagnostic and testing resources for the particular study or follow-up, and indicate the basis upon which it is planned to make comparisons with accepted pharmacological agents.

C. The principal investigator must be considered an expert qualified by scientific training and experienced to investigate the safety of drugs.

1/ These books and publications shall be available at stations without pharmacies with a full-time Medical Officer.

3-7.9 continued

D. The principal investigator and the medical officer responsible for the patient's care are reminded that even though a physician's treatment is proper and careful in the administration of a drug, he may nevertheless be held liable for the consequences of his treatment if he failed to advise the patient in advance of the nature of the treatment and its probable consequences. Also, the physician's first responsibility is to his patient and he should not prescribe a drug when the effect may be unknown.

E. In presenting a request to Headquarters, the following information will be furnished:

(1) Name of principal investigator with a listing of his training and experience.

(2) Purpose of the study.

(3) Benefits the beneficiaries may derive from such a study.

(4) A statement as to whether or not the proposed study has been explained (preferably in writing) to the tribal health committee and whether or not the committee concurs.

(5) A short statement as to how the study will be conducted, location, and subjects (age, sex, ambulatory or hospitalized).

(6) The degree of risk involved.

a. Will a recognized and accepted treatment be withheld?

b. Are the side reactions such that the patient's normal mode of living may be affected? - i.e., impaired vision, nausea, headache, vertigo, malaise, insomnia, gastro-intestinal upset.

c. Is the toxicity of the drug such that it is contra-indicated in certain pathological conditions such as cardiovascular disease or impaired renal function?

d. Is there indication of the drug causing blood dyscrasias?

e. Is it necessary for the patient to be kept under close clinical supervision and observation?

(7) Has the drug been previously used on human subjects?

(8) Names of the drug--trade, generic, chemical, etc.

3-7.9E continued

(9) Information on the drug as supplied by the manufacturer and from other sources with toxicity, undesirable side reactions as well as the desirable actions of the drug.

(10) Additional staffing, costs and/or workload on present staff.

F. When approval for the use of an investigational drug has been given by the Division Chief, the following procedures will be used:

(1) The voluntary consent of each human subject will be obtained; a signed written consent will be obtained from each one or his legal guardian and kept on file.

(2) A physical examination should be done on each subject.

(3) It shall be the responsibility of the Chief Investigator using the investigational drug to furnish the Chief, Pharmacy Service pertinent information on the drug.

(4) It shall be the responsibility of the pharmacy service to prepare and to make available to the nursing service summaries of this basic information on investigational drugs.

(5) The administration of investigational drugs by any route by members of the nursing staff is prohibited until such time as adequate information concerning the actions, uses, dosage, toxicity, and precautions of such drugs is available on the nursing unit in a form approved by the Pharmacy and Therapeutics Committee.

(6) Investigational drugs will be clearly labeled as such by the pharmacy.

-7.10 AUTOMATIC STOP ORDERS

There will be automatic stop orders on dangerous drugs used within the hospitals.

A. Narcotics - seventy-two (72) hours.

B. Sedatives, Hypnotics, Soporifics and Tranquilizers - ninety-six (96) hours.

C. Antibiotics and steroids - ninety-six (96) hours.

D. Anticoagulants, ergot preparations and derivatives, Oxytocic drugs - to be ordered specifically as to dosage and time.

E. All other drugs - seven (7) days.

3-7.11 STANDING ORDERS

A. There should be written standing orders, signed by the Service Unit Director and approved by the Indian Health Area Director upon the recommendation of the Area Pharmacy and Therapeutics Committee, for Public Health Service nurses and Bureau of Indian Affairs school employees covering emergency situations when a medical officer is not immediately available.

B. Drugs should be selected for inclusion in standing orders on the basis of their relative safety when used according to the stated directions by a nurse or school employee, stability under field conditions, established merit, and ability to fulfill the needs. The number of such drugs should be kept at a minimum. Narcotics, hypnotics, amphetamines, and tranquilizers will not be included in the standing orders. In general, with the exception of anti-infective agents, legend drugs (those requiring a prescription for dispensing) will not be included in standing orders, and the directions for these exceptions will specify clearly the limitations in use.

C. The standing orders should include an appendix containing a listing of the drugs with dosage, limitations by age, interval between dosage generally followed and any other pertinent information.

3-7.12 PRESCRIPTION WRITING AND DRUG DISPENSING

A. Prescriptions will include the name and age of the patient, date, generic or official name of drugs, strength, quantity, adequate directions and the prescribing medical or dental officer's signature (initials will not be used). The metric system should be used for weights and measures. One prescription will be written on a blank. The pharmacy officer dispensing the prescription will initial the face of the prescription.

B. Other than the dispensing of drugs by a medical or dental officer and situations covered by standing orders, drugs will be dispensed only by a pharmacy officer and in his absence, a nurse officer under the direct supervision of a medical officer and only on the order of a medical or dental officer.

C. Medical and dental officers shall not write prescriptions for narcotic or hypnotic drugs for their own or their family's use.

3-7.12 continued

D. Many drugs are used on a continuing basis over long periods of time. To avoid prescribing large quantities of drugs (over a 30 days' supply) and to avoid unnecessary visits to the physicans for additional quantities, outpatient prescriptions with the exception of narcotics and hypnotics may be filled in accordance with the following procedure:

(1) The number of refills authorized will be written on the prescription by the physician.

(2) The pharmacist will write on the original prescription each time the prescription is refilled. No more than the authorized number of refills will be permitted.

(3) The total quantity of medication may be limited to a definite period such as six months as determined by the pharmacy and therapeutics committee. After this period the patient would see the physician for a new prescription.

(4) A record of each refill must be included in the patient's record and show the number of the prescription, the name of the drug, the date of the refill, and the date of the original prescription.

(5) A record of the number and cost of refill prescriptions will be kept and reported on the quarterly report - pharmacy Form PHS 1310-1. The cost of refills will also be added to the Outpatient Costs and prescription costs in January and July; however, they are not to be added to the Outpatient Visit total.

(6) The pharmacist will exercise professional judgment in providing refills of prescriptions for outpatients.

3-7.13 A PHARMACY AND A DRUG-ROOM, DEFINITION OF

A Pharmacy is a drug compounding and dispensing area with a pharmacy officer in charge.

A Drug-room is a drug dispensing area without a pharmacy officer in charge.

3-7.14 PHARMACY MANAGEMENT

A. Records, Responsibility for Keeping. In compliance with Federal laws and regulations and Division policy, each member of the professional staff shall be responsible for maintaining appropriate records on drugs and drug stocks under his jurisdiction. The Chief, Area Pharmacy Branch shall review such records periodically and assist in their maintenance. All pharmacy records on narcotics,

3-7.14A continued

exempt narcotics, hypnotics, spirituous liquors, and ethyl alcohol and all prescriptions shall be retained for two years in accordance with the HEW Staff Manual, Records Management, PHS Appendix B-334.

B. Pharmacy Operations - Daily Record and Quarterly Summary, Form PHS-1308. The daily record and quarterly summary Form PHS-1308, shall be used to record the daily count of measurable workload items. This information is subsequently transcribed to Part I of the quarterly report of pharmacy operations, Form PHS-1310-1. The reverse side of the form provides space for quarterly summarization of the monthly records. Instructions for completing Form PHS-1308 are contained in Exhibit 3-7.14B.

C. Reports. All reports shall be forwarded through the appropriate facility, field office and/or Indian Health Area Director.

(1) Pharmacy Operations - Quarterly Report, Form PHS-1310-1. The quarterly report provides information on the workload of the pharmacy and the drug cost for inpatient and outpatient medical care. Each pharmacy shall prepare the report for submission through the Service Unit Director so as to reach the Area Office no later than the 5th of the month following the close of the quarter. Area requirements as to the due date of this report may vary from Area to Area, but in no event should the date be later than the fifth of the month. Sufficient copies shall be prepared so as to provide the following:

a. The original to be sent to the Indian Health Area Director, Attention: Chief, Area Pharmacy Branch.

b. One copy to Indian Health Area Director, Attention: Chief, Area Finance Branch.

c. Two copies for the reporting station, one for the Service Unit Director and a file copy for pharmacy.

Instructions for completing Form PHS-1310-1 are contained in Exhibit 3-7.14C(1).

(2) Pharmacy Operations - Summary, Form PHS-1310-2. At the end of each fiscal year, each pharmacy shall prepare and submit an annual summary, Form PHS-1310-2, to the same sources and through the same channels as the quarterly report, Form PHS-1310-1. The data for the summary report is obtained from the quarterly report, Form PHS-1310-1. The values of inventory and drugs received and issued shall be entered as of the nearest dollar. All items on the summary shall be completed including the "Actual Stock Turn (Annual)" section