hoped at the outset of this program to complete 250 Intensified Drug Inspections during the current fiscal year, and to cover the other 250 prescription drug manufacturers in fiscal 1970. It now appears that this schedule may have been overly ambitious, but we will move ahead as rapidly as possible. Obviously, this program will not eliminate the need for inspections in subsequent years. But I strongly believe it will achieve significantly higher standards of drug manufacturing on an industry-wide basis.

No single program, of course, can insure the American public of safe drugs that will do what they are intended to do. In addition to other enforcement and compliance activities, we plan to further expand the capabilities of our National Center for Drug Analysis at St. Louis. We are also moving ahead with the implementation of the recommendations of the National Academy of Sciences-National Research Council concerning the efficiency of pre-1962 new drugs. This will provide the prescriber, and the purchaser of the over-the-counter products, a more precise picture of what these medications will do. And we are continuing biologic availability studies to determine whether there are therapeutically significant differences between chemically equivalent drugs.

In this connection, I'm sure most of you will recall the performance differences among chloramphenicol capsules that required FDA action just about a year ago. That situation, unfortunately, became part of the socalled "generic-brandname" controversy. I say "unfortunately" because it seems to me that drug equivalency problems aren't necessarily related to the name by which a drug is sold. Just a few weeks ago, for example, Merck, Sharp & Dohme recalled from the market 15 lots of its hypertensive preparation, Aldomet tablets (or, generically speaking, methyldopa tablets). The recall was undertaken because disintegration rates were below the company's specification. The cause, apparently, was related to the particle size of a so-called inert ingredient. This is not dissimilar to the earliest problem with chloramphenicol capsules. The Merck management acted with commendable responsibility in catching the problem, confirming the deficiency through human blood level studies, and promptly initiating the recall. But it does illustrate that an equivalency problem can occur anywhere within the drug industry. We have to get at the basic causes o fthese problems; they can't be solved by comparing the names that appear on the product labels.

There is another problem area concerning drugs which also requires, I believe, renewed concentration on causes. During the last fiscal year, the FDA received 406 New Drug Applications. During the same 12 months, 59 NDAs were approved. These figures are not directly related, of course, since an application may not be acted upon in the same fiscal year that it is submitted. Nevertheless, I think it is significant that, for the year, the number of applications found incomplete, or returned as not approvable, outnumbered those approved by better than 5-to-1. More than 80 percent of the applications that were found not approvable lacked adequate information about manufacturing processes. More than half of these applications also suffered from deficiencies in clinical studies and inadequacies in efficacy data. The message, it seems to me, is clear: there is still a need for better data in industry's submissions to the Agency.

We are as interested as industry in getting to the market as swiftly as possible new drugs that can mean better health care for American citizens. But we cannot disregard our responsibility to determine that such drugs are safe and effective for their intended uses before they reach the market. By the same token, the manufacturer cannot disregard his responsibility to submit sound data that demonstrate safety and efficacy. I must tell you frankly that we have not seen the degree of improvement in the quality of clinical data from drug investigations that we would like. I intend to give this matter renewed attention in the weeks ahead, and possibly call upon experts outside the Agency as well to see if we cannot find the means to correct existing shortcomings.

As far as other priorities are concerned, the Agency as a whole will continue to give its most urgent attention to potential health hazards in every area of our responsibilities. Our concern with microbiological contamination of consumer commodities is, of course, part of this overall health-protection program.

Last September, as some of you know, a National Center for Microbiological Analysis went into operation on a pilot basis at our Minneapolis District laboratory. Samples of food products from around the Nation, starting with those classes of foods most susceptible to contamination by harmful bacteria, are being sent to the Minneapolis Center for analysis. This pilot operation should begin to give us a better grasp of the extent of the problem, and, more important, pinpoint the product classes where the hazard is greatest. The necessary next step,

of course, is to track down the sources of contamination and develop effective preventive measures. In addition to food products, we also plan to have our Districts submit samples of drugs and cosmetics to the National Center.

This pilot program in Minneapolis represents a new approach to further enlarge FDA's capabilities to monitor and control bacterial contamination. As you know, we had previously assigned bacteriologists to each of our District Offices to carry out this essential analytical work. The frequent recalls of products because of Salmonella contamination gave major impetus to the expansion of this program within FDA. And, I must add, industry has also responded to this growing awareness of the health hazard posed by microbiological contamination.

In dealing with a problem such as bacterial contamination, I think it is clear that FDA and industry are not adversaries. We have had to act together to begin to combat this threat to the public health, and I am happy to say that there has been a high degree of cooperation in this effort. I would hope that this same attitude—this mutual appreciation of the importance of the consumer interest—can prevail in other areas as well. Certainly, we will have ample opportunity to test this premise in the weeks ahead.

Very soon now, we will publish a new proposal outlining Good Manufacturing Practices in the food industry. Also ahead are proposed revisions of the Good Manufacturing Practices regulations for the drug industry. I do not expect unanimous support by industry for these proposals. But I do hope we don't encounter automatic opposition either. This is not an adversary contest, a kind of game in which FDA proposes all the regulations it can think of and industry defeats as many as it can. Rather, the fundamental question has to be: What rules are necessary to safeguard the consumer? If we keep that principle in mind, it is much easier to deal with and resolve the disagreements that do arise between FDA and industry.

Now, of course, the FDA has taken on new responsibilities—product safety, shellfish certification, broader pesticide research, and other activities mentioned by Mr. Johnson. In all of these, too, it is the consumer who is our first concern. With the organization of the Consumer Protection and Environmental Health Service, I believe we are in a better position than ever before to translate that concern into effective action.

It's clear to me that we can be most effective when we have the cooperative support of industry in coping with consumer problem. Your participation in this Conference is evidence that we have the kind of dialogue going that can encourage this cooperative effort. I am looking forward to working with you in this endeavor.

Thank you.

Senator NELSON. Now, are you saying that you believe that the peer committee approach is a resolution of the kind of problem, the gray area problem, mentioned by Dr. Goddard and you?

Dr. LEY. Not a total resolution, Mr. Chairman. I believe there has been an improvement in the quality of information flowing into our files. We have taken vigorous steps to insure since Dr. Goddard's speech, and at his direction in the beginning, but with my total support since, that material of the quality he referred to is rejected upon initial receipt, sent right back to the manufacturer. So that there are efforts in progress.

The peer group is not the sole and only answer to this problem, and I must confess quite frankly that I have spoken to several major industry leaders in the pharmaceutical area very frankly in my office. And I pointed out to them that the major problem as I see it today in the development of new drugs is in the poor quality—I have used more vigorous words on occasion, sir—in the poor quality of data coming into our files in investigational drug studies.

Now, our discussions with the National Academy of Sciences are very important steps which would be an equally significant move to try to improve the quality of data. Although there are people who say that I am wrong, I firmly believe, and I believe the scientific com-

munity supports me, that there are classes of drugs for which we can write today very clearcut, definitive protocols of exactly what tests are required, exactly how many patients on which the tests have to be done, and exactly what statistical procedures have to be used to prove efficacy. One of the classes of such drugs I would present for the committee's consideration, is that of diuretics. I believe that the Academy, working in concert with the scientific community, with advisers from the FDA and industry, will be able to develop a set of guidelines for the evaluation of the efficacy and the safety of diuretics that can be applied across the board, with a very major saving both in terms of the numbers of patients and in terms of the risks to which these patients are subjected.

Diuretics are not the only such drugs that can be so evaluated. But again I do not wish to present this as a sole and major cure for the problem as I see it. There are other kinds of drugs, such as tranquilizers, for which such a protocol would be difficult, and indeed, I fear it would be impossible to design at this point in time.

Senator NELSON. Do I understand that you are going to proceed to establish peer groups throughout the United States?

Dr. LEY. That is our intent. I have a draft here that is not yet in completed form because of questions internally within the staff, which our General Counsel has prepared for my consideration for regulation-making requirements.

Senator NELSON. You have made the decision to go ahead?

Dr. LEY. I have. I must listen, however, to the comments that will arise in response to the proposal. I do not think it will be a welcome proposal.

On the other hand, I do not believe, Mr. Chairman, that we can exclude the subjects and patients of drug investigational work from this type of protective influence that every other research-oriented group in the country now requires.

Senator NELSON. The Public Health Service now uses peer groups?

Dr. LEY. Definitely. Throughout its entire program, internal and external.

Senator NELSON. Who did you say would select the peer groups?

Dr. LEY. The peer groups are selected by the institutions in which the studies are done. The selection of the peer groups is made an official matter of record and the minutes of the meetings of the peer group are available for inspection at any time.

Senator NELSON. Will the FDA require that the minutes of the actions of the peer group be submitted as a part of or independent of the IND?

Dr. LEY. This is a point that is currently under consideration, with several views on the part of my staff. I cannot answer this at the present time.

Senator NELSON. How would we know whether the peer group was just a perfunctory——

Dr. LEY. There would have to be as part of the submission of the investigational institution to the sponsor and from the sponsor to us a statement that such a peer group existed, that such a peer group had reviewed the material and that the minutes of the group were available and where. This is the minimum, it seems to me, that would be essential. This is the pattern that the Public Health Service would follow.

Senator NELSON. Would the FDA have personnel to do at least some reasonably broad sampling of the functioning of the peer group?

Dr. LEY. This would have to be sampled. I am concerned that we have not used to as great an extent as we possibly could the ancillary highly trained inspector, but nonmedical inspector, in our organization. This man has been specially trained for investigation into the clinical investigation area. We have not put him to as efficient use as possible. I believe that it will require a modest increase in manpower in this area and I am willing to commit him.

Senator NELSON. It seems to me that unless there is some oversight, every peer group may function under a different set of rules and you would not have any uniformity.

Dr. LEY. This is true. There must be some oversight apparent to the community, and I think it would also be of interest to point out to the committee that the peer groups in many of the medical centers that would be reviewing sponsored studies by firms would be the same peer groups that would be reviewing other investigational studies supported by Public Health Service research grants. The one place where this would probably not be true is in the prison situation, in which one of the findings in the Alabama report was that a peer group review is highly desirable for such a situation as that in Alabama.

Senator NELSON. You mean the Alabama Medical Association report was recommending a peer group review of that kind of activity, is that what you are saying?

Dr. LEY. Yes.

Senator NELSON. There was no peer group of any kind?

Dr. LEY. There was no significant peer group of any consequence in that situation.

Senator NELSON. How many investigators do you have in the FDA to do a field evaluation of the functions of the protocol, the performance of the protocol under the IND?

Dr. LEY. As indicated in my testimony, we have 140 nonmedical personnel who have been specially trained in this area. In the medical area, our total staff commitment not only includes Dr. Kelsey and Dr. Lisook sitting here behind me, but also includes all of the reviewing medical officers in the Office of New Drugs, into whose hands the IND studies come.

Senator NELSON. Are these field investigators?

Dr. LEY. These are not field investigators. These are headquarters personnel who perform the evaluating function that I indicated could be highly important, as in case No. 1, where adverse effects were not reported by one investigator, but strong effects reported by another. This is all part of our surveillance activity.

Senator NELSON. I understand you to say that you have 140 nonmedical field investigators. Is it their exclusive responsibility to monitor IND's or are they also your inspectors for the drug plants?

Dr. LEY. It is not their exclusive responsibility to monitor IND's. They have many other functions. As I indicated a few moments ago, I am concerned, and the staff is evaluating means by which we may involve 140 people more vigorously in the review of investigations. This is still under consideration within the Agency.

Senator NELSON. But so that I would have it straight in my own mind, are these 140 nonmedical inspectors, also the ones who do the

quality control inspections within the manufacturing plants of the drug companies?

Dr. LEY. Many of these are and many of these investigators are functioning in a very important role in our intensified drug inspection program in the field in that they focus attention on the studies reported to the Department by the investigator right as they exist in the investigator's file.

Senator NELSON. Excuse me, what was that again?

Dr. LEY. These 140 people are basically drug inspector personnel within the Food and Drug Administration. They have been exposed to a highly specialized additional training course which qualifies them uniquely for investigative work in the area of clinical investigation This means not only recordkeeping in the investigator's files and his method of conducting the laboratory work and the other work involved in the investigation itself, but it means they are also expert in evaluation of the sponsor's method of processing this type of information in their preparing it for submission to the FDA. These people have many functions to perform. However, they have unique training, they represent a large pool of personnel from which I believe we can divert a significant part of their effort into more intensive investigation of the investigator and investigation.

Senator NELSON. I am trying to get at the question really, of how many inspectors, how many man-hours are spent by your inspectors directly in the field evaluating the performance of the protocol by the investigator, not the inspector's work within the plant, not his inspection of the data that comes to the plant, but going out to the investigator, giving surveillance to his performance. On that question, I would also like to have you tell me how many IND's you have in—give us the last couple of years, and specifically, how many of those investigators were inspected for the performance at the place of the experiment, how many actually had a visit from the investigator, how many advisers had a visit to him directly and a review of how he is carrying out the protocol? Do you have that?

Dr. LEY. We can submit this information for the record, Mr. Chairman. It is in more detail than I have it here.

Senator NELSON. Yes, I understand.

Dr. LEY. I think it is important to point out that the man-years involved in the total process of supervising or oversight of the investigator and the investigation is in three separate categories—one, headquarters staff including the Office of New Drugs review of the investigational study submitted to us; second, in terms of the field staff. We can provide figures for both. Both figures are necessary to interpret the total effort we are putting in this area.

Senator NELSON. What I would like to know is if there are at any one time, in any one year 500 IND's pending, with experiments going on on 500 different drugs—in how many of those 500 experiments has an investigator gone to supervise the performance of the protocol by the investigator? How much time was spent on this task?

I am getting at this because I am concerned, as a consequence of the testimony of many witnesses, that there is inadequate supervision. If that is the case, I would like some estimate of what the Department thinks would be necessary in additional personnel to perform this function so that we may have, perhaps, some evidence on which to

base support for appropriations here in Congress to give the FDA more personnel to supervise that critically important aspect of the IND.

Dr. LEY. We will be pleased to provide this data for your committee, sir.

(The subsequent information was received and follows:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
Washington, D.C., October 20, 1699.

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

DEAR SENATOR NELSON: During our appearance before your Subcommittee on August 12, 1969, you requested that certain information be submitted for the record. The submissions are as follows:

1. How many "Notices of Claimed Investigational Exemptions for a New Drug" (IND's) have been received for the past couple of years?

Fiscal year:	
1968	859
1969	956

2. How many investigators, associated with these IND's were inspected at their places of business?

Fiscal year:	
1968	11
1969	11

3. How many man-years are expended by FDA in direct oversight of clinical investigators?

Fiscal year 1968:	
Bureau of medicine	3.2
Field	.6
Fiscal year 1969:	
Bureau of medicine	6.2
Field	1.6

4. Estimate the manpower and money necessary to provide adequate supervision over clinical investigators.

FDA is currently developing an integrated surveillance program of all the investigatonal phases of drug development and evaluation. It will include on-site visits to clinical investigators, inspection of clinical facilites and of laboratories used for preclinical testing, and surveillance over the monitoring activities of the sponsor of the investigational drug. The program will involve the Office of New Drugs in conducting the visits and inspections as well as continuing the efforts of the Division of Scientific Investigations in their oversight of suspect clinical investigators.

At present, the regulations place the responsibility for monitoring clinical investigators on the drug sponsors. The Office of New Drugs is currently undertaking a program to survey the adequacy of these monitoring efforts. Thus far, they have inspected one such sponsor and are evaluating the findings. We are planning a few more inspections of this nature to determine the feasibility of this new approach to oversigbt of investigational drug activities.

We anticipate that this new program will be available shortly. At that time, we will be in a better position to provide you with the estimated manpower and resources necessary for implementation of this program.

5. Is there anything in the Alabama Medical Association report on "The Use of Prisoners for Drug Trials in Alabama" (Southern Food and Drug Research, Inc., Dr. A. R. Stough, President) that is incorrect?

In general, the "Alabama Report" is thoughtful and factual. There are, however, some errors involving FDA's field of activity as follows:

(*a*) On page 10, the second paragraph contains the statement "In the present instance there is no reason to believe that the pharmaceutical firms failed to act in good faith or failed to discharge their responsibilities to the general public to develop safe, effective therapeutic agents. They contracted with approved clinical investigators to carry out approved research projects."

There may be some misunderstanding that the Food and Drug Administration approves clinical investigators and clinical research projects conducted by pharmaceutical firms. FDA neither approves investigators nor do we approve the firms' clinical research projects.

The pharmaceutical firms are expected to choose qualified investigators. The FDA may disqualify, however, an investigator from participating in clinical studies if he does not abide by the Investigational New Drug Regulations.

Further, pharmaceutical firms are required to conduct clinical investigations in accordance with the Investigational New Drug Regulations. We do provide comment and suggestions on their plan of investigational study if requested or if our review indicates it is needed. An IND Notice is terminated if the requirements of the regulations are not met.

(*b*) On page 11, the opening statement reads "It should be noted, however, that neither (i.e. the FDA nor the manufacturer) is primarily concerned with the rights and welfare of the institutionalized research subject."

The Federal Food, Drug, and Cosmetic Act under Section 505(i) and Section 130.3 of the New Drug Regulations place a definite and primary responsibility on both the FDA and the sponsor of an investigational study to assure that the health of the participants in such a study is protected. The sponsor must be sure that he selects capable investigators who can safeguard the subjects of the study, that adequate preclinical tests demonstrate that administration of the drug to man is justified, that there is a sound plan of testing (protocol) which minimizes risks to the subjects, that unexpected effects are promptly investigated and the study is stopped if they raise significant safety questions, and that each investigator agrees to obtain the consent of the subjects of the experiment (with certain exceptions specified in the law). The FDA in reviewing the submissions sponsors must make before initiating clinical trials, is required to assure itself that sponsors have met the above-mentioned requirements, as well as others, and to require cessation of the trials where appropriate safeguards are not observed.

6. Provide for the record the number of IND's (Notice of Claimed Investigational Exemption for a New Drug) in which Dr. A. R. Stough and his firm have been listed by the sponsor as clinical investigators for the last three years. The number of people involved in Dr. Stough's studies.

See Attachment A.

7. Provide same information as (6) for four other active clinical investigators.

See Attachment A.

If we can be of further assistance, please let us know.

Sincerely yours,

HERBERT E. LEY, Jr., M.D.,
Commissioner of Food and Drugs.

ATTACHMENT A

NUMBER OF "NOTICES OF CLAIMED INVESTIGATIONAL EXEMPTIONS FOR A NEW DRUG" (IND'S) IN WHICH DR. A. R. STOUGH AND 4 OTHER ACTIVE CLINICAL INVESTIGATORS HAVE BEEN LISTED BY THE SPONSOR AS INVESTIGATORS SINCE AUGUST 1966, WITH ESTIMATED NUMBER OF SUBJECTS

Investigator	IND notices	Subjects (estimate)[1]
A. R. Stough, M.D	72	2,681
Physician A	102	3,347
Physician B	41	1,707
Physician C	31	1,333
Physician D	19	861

[1] A large number of the IND notices are still active. The estimated number of subjects is based upon the annual reports which have been received, from preliminary reports submitted by clinical investigators, or from the number of patients planned for the protocol of investigational study.

Senator NELSON. On the question opened by Senator Dole, you had stated you were going to put in the record the memorandum of July 29 on Dr. Austin Stough?

Dr. LEY. Not quite, but I do wish, with your permission, to place into the record a summary of the Stough matter as I see it at this particular point in time.

Senator NELSON. Do you have a separate summary there?

Dr. LEY. I do, sir.

Senator NELSON. The committee has not had copies, is that correct?

Dr. LEY. I do not believe this has been provided to the committee earlier. I do have two copies additional here.

(Summary referred to follows:)

The New York Times recently has run two feature stories on drug testing by Dr. Stough in the Alabama Prison System.

Dr. Stough was engaged in doing the more routine parts of phase 1 studies for a number of drug sponsors. He was administering investigational new drugs to volunteers in the prison, drawing blood samples to determine the amount of drug that entered the blood stream and doing other associated laboratory studies. This is dosage range finding and gross toxicology. He was not engaged in the more sophisticated types of clinical pharmacology.

FDA personnel visited the Alabama facility in 1964 and our physician-inspector teams visited the facility again in 1967, and most recently in 1969 after a story about it appeared in the Alabama papers.

The findings in 1964 were that there were a number of minor discrepancies—poor record-keeping, inaccuracies in some of the records, and inadequate physical examination and medical supervision of the volunteers in the investigation. These deficiencies were discussed with Dr. Stough.

By 1967 these problems had been corrected except for minimal physician-subject contact. There is no requirement in the regulations which defines the degree of physician-patient contact for investigational studies.

The Bureau of Medicine concluded that the findings were not serious enough to warrant any action against Dr. Stough and his associate as investigators, based on current regulations. The studies going on in Alabama were providing useful information that was not available in other than prison environments.

The inspection report and the Bureau of Medicine evaluation were not required to be forwarded for review by the regulatory personnel. We are taking steps to see that in the future such reports are examined by compliance personnel.

Moreover, as previously noted, we are proposing an amendment to the investigational new drug regulations to require the establishment of review committees, of the type required in research funded by the Public Health Service, for institutions such as the Alabama Prison System where volunteers are involved in drug testing. This will better protect the welfare of the volunteers and assure a better quality of research data.

Senator NELSON. Was your memorandum from yourself to the Acting Director, Bureau of Medicine, subject, Austin R. Stough, dated July 29, 1969—was that released?

Dr. LEY. That memorandum from Dr. Jennings to me was in response to a request from my office to summarize the information as of that date. That was released to the press. I would have preferred that it not be released until I had the statement I have today. However, it did reach the press and did result in the second New York Times article.

The work that Dr. Jennings indicated was necessary I believe has been completed. You may wish to discuss this matter with him in terms of whether or not any of these studies were pivotal to a new drug approval. The evaluation was that they were not.

Senator NELSON. Well, from that memorandum, I would like to quote a sentence and ask your observation on it. I would ask that the memorandum dated July 29 from Dr. Jennings to Dr. Ley, subject, Austin R. Stough, be printed in full in the record.

(The information follows:)

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
FOOD AND DRUG ADMINISTRATION,
July 29, 1969.

U.S. Government Memorandum.

To: Herbert L. Ley, Jr., M.D., Commissioner of Food and Drugs.
From: Acting Director, Bureau of Medicine.
Subject: Austin R. Stough, M.D.

Dr. Stough is a clinical investigator who with his associate Irl Long, M.D., has been named in 139 IND's and 36 NAD's to date. A tabulation of these documents is appended hereto.

Dr. Stough first came to our attention in June 1964 in conjunction with a hepatitis epidemic in the Alabama Prison System which was subsequently proven to be caused by his poor technique in the conduct of a plasmapheresis program.

Dr. Stough has no formal training in clinical pharmacology or any specialty, but is a general practitioner who began work in the McAlester Penitentiary in Oklahoma in 1938. He performed an increasing volume of drug testing there until December of 1963 when unfavorable publicity and press criticism led to his expulsion from the Oklahoma Prison System. He subsequently set up shop in the Alabama Prison System, ultimately forming Southern Food and Drug Research, Inc., a corporation principally engaged in Phase I testing of investigational new drugs. In September of 1967, Dr. Lisook visited Drs. Stough and Long for the purpose of evaluating their facilities and techniques for the testing of investigational drugs. He concluded that Dr. Stough's practices were adequate under our regulations, although there was less physician-subject contact than would be desired.

In January of 1969 the *Montgomery Advertiser* and its editor-publisher, Harold E. Martin, ran a series of expose type articles concerning Dr. Stough's drug testing operation. Because of this adverse publicity Dr. Lisook undertook another visit to Montgomery on February 11, 1969. During the course of that visit he met with a special committee appointed by the Alabama Medical Association at the request of the State Board of Corrections. (See attached memo of conference)

The February 1969 inspection of Southern Food and Drug Research, Inc. was not materially different from that of 1967. Physician-subject contact again appeared to be minimal and the execution of the studies was primarily left up to medical technicians. Physical examinations appeared to be performed as required although they were somewhat cursory in nature. The administration of medication appeared to be properly policed. Laboratory records and progress reports appeared to be complete, for the most part, and in original form. There was no evidence to indicate that the tests were not actually performed, or that inmates were participating in the selection of subjects. The use of convicts to draw blood samples was acknowledged, but such practice was discontinued in the wake of the January 1969 publicity. It was noted that the interviews for subjective complaints by medical technicians were excessively brief.

On May 30, 1969, the *Birmingham News* carried a front-page story headlined "Medical Probers Assail Prison Drug Testing; Board Halts Program." Essentially the same information was found in a *New York Times* story of June 1, 1969. The basis for this publicity was the report of the special committee entitled "The Use of Prisoners for Drug Trials in Alabama."

The front-page story in *The New York Times* today, July 29, 1969 seems to be a recapitulation of previous newspaper articles and to contain no new information.

Dr. Lisook's memo to me dated June 11, 1969 is somewhat more detailed than this memo and he has more back-ground material in his files if you require further information.

Although Dr. Lisook's two investigations of Dr. Stough's operations disclosed no violations of our regulations, obviously we should be concerned that such an operation can exist under current regulations of FDA and DBS. Aside from the welfare of the subjects, the question of validity of the studies may still be raised—especially the possibility of concurrent testing of drugs.

JOHN JENNINGS, M.D.

DR. AUSTIN STOUGH

[Note: "D" denotes "Deleted" (completed study, etc.)]

IND/NDA	Drugs	Status	Date	Sponsor
3	Clomid	D		Wm. S. Merrell.
32	Tolinase		Nov. 15, 1968	Upjohn.
39	Periactin HCl		Feb. 19, 1968	Merck.
70	Indocin		Nov. 27, 1967	Do.
80	U 11,028	D		Upjohn.
81	U 9189			Do.
83	Aldomet		Oct. 24, 1968	Merck.
114	U 11,100	D		Upjohn.
127	Vectren	D		Parke Davis.
137	Cholcomycin Ointment	D		Do.
138	CI 546	D		Do.
143	Lincoln			Upjohn.
191(L)	Provest		Dec. 9, 1968	Do.
213	Thiabendazole	D		Mallinckrodt.
239	WY 535	D	Apr. 2, 1965	Wyeth.
247(L)	CL 912C		Aug. 28, 1967	Cutter.
248	WY 3263	D		Wyeth.
323	RO 5-2537			Hoffmann-LaRoche.
342	Tetracycline HCl			Lederle.
389	U 22,559A	D		Upjohn.
422	Mephenoxalone	D		Lederle.
426	Hydromox	D		Do.
428	Levoprome			Do.
436	Modaline Sulfate	D		Warner-Lambert.
442	Acetylcystein		Oct. 12, 1967	Mead Johnson.
492	Delalutin	D		Squibb.
524	Temposil	D		Lederle.
617	Penicillin Injection	D		Bristol.
619	Kantrex Injection		Oct. 2, 1967	Do.
626	Salutensin	D		Do.
631	I.V. Syntetrin Nitrate			Do.
637	I.M. Syntetrin Nitrate			Do.
654	Namoxyrate	D		Warner Lambert.
666(L)	Delestrec Injection			Squibb.
692	Dylate			Spencer.
723	Anavar	D	Sept. 19, 1966	Searle.
736	RO 5-4556		Dec. 27, 1966	Hoffmann-LaRoche.
777	Fenyripol	D		Neisler.
876	Arlef			Parke Davis.
891	SQ 9538		Sept. 14, 1966	Squibb.
1086	Depo Provera			Upjohn.
1090	Kanamycin			Bristol.
1154	P #286			Pitman-Moore.
1172	Quinestrol			Warner-Lambert.
1312	RO #55006			Hoffman-LaRoche.
1410	Product #157			Grove.
1616	Estergel Ointment			Merck.
1620	Ketalar Injection			Parke Davis.
1701	Tetracycline			Bristol.
1706	Coated Aspirin			Grove.
1713	Provera & Ethinyl Estradiol			Upjohn.
1790	SK&F #7690			Smith, Kline & French.
1793	U #18,425			Upjohn.
1809	Product #88-LASRT			Grove.
1895	U #19,176E			Upjohn.
2001	Lincocin Syrup			Do.
2147	Kenalog w/DMSO			Squibb.
2184	U #23,807A			Upjohn.
2214	P #23			Bristol.
2238	P #230			Grove.
2290(L)	CL #1190C		Feb. 20, 1967	Cutter.
2391	Dexoxadrol HCl			Upjohn.
2426(L)	SU #14,542			Ciba.
2477(L)	Voranil			Do.
2498(L)	Hetacillin			Bristol.
2501	SU #14074			Ciba.
2560	Triple Tetracyclines			Lederle.
2581	Hygroton/Potassium			Geigy.
2630	SU 13,686			Ciba.
2695	Minocycline HCl			Lederle.
2732	Formula #177 Aerosol			Johnson & Johnson.
2738	Potassium Hetacillin			Bristol.
2780	SU #8746			Ciba.
2844	SU #13,197		May 18, 1967	Do.
2928	Borcresine Phosphate		Sept. 15, 1967	Lederle.
2989	Potassium Hetacillin			Bristol.
3040	Lactulose Syrup			Warner-Lambert.
3139	FES Cap			Commercial Solvents.
3192(L)	THFES Cap			Do.
3196(L)	BA #31531			Ciba.
3256	Depo-Provera Injection			Upjohn.
3286	Profem			Do.

DR. AUSTIN STOUGH—Continued

IND/NDA	Drug	Status	Date	Sponsor
3366	Polycillin Injection		Aug. 18, 1967	Bristol.
3389	Guanadrel Sulfate			Cutter.
3436(L)	W #1673		Jan. 5, 1968	Wallace.
3455	BL-R #191			Bristol.
3533	U #18,490A		Sept. 14, 1966	Upjohn.
3547	Prolintane HCl		Apr. 16, 1968	Merck.
3585(L)	Trobicin Injection		Oct. 3, 1966	Upjohn.
3598	U#16, 178F		Mar. 30, 1967	Do.
3634	U#13, 906A			Do.
3643	U#25, 130E		Oct. 3, 1966	Do.
3683	BC #347		Aug. 31, 1967	Bristol Labs.
3687	Pacitran		Nov. 29, 1966	Ciba.
3692	BL-J #433		May 3, 1967	Bristol Labs.
3700	U#22, 394A		Oct. 13, 1966	Upjohn.
3733	U#12, 717F		Oct. 12, 1966	Do.
3765	U#24, 166A		do	Do.
3810(L)	Rifampin		Dec. 28, 1966	Pitman-Moore.
3848(L)	MJ #1992		Feb. 25, 1967	Mead Johnson
4045	Riker #761		Sept. 25, 1968	Riker Labs.
4097(L)	U#24, 973A C 14		July 7, 1967	Upjohn.
4136	SU #13, 437		Sept. 18, 1967	Ciba.
4215(L)	WIN #11, 464		Sept. 5, 1967	Sterling-Winthrop.
4266(L)	NDR #5204		Oct. 3, 1967	National Drug Co.
4285(L)	Dilabron		Oct. 11, 1967	Breon Labs.
4373(L)	Zaroxolyn		Jan. 30, 1968	Strasenburg.
4382	U#8839		Nov. 27, 1967	Upjohn.
4448(L)	Flagyl W/Nystatin		Jan. 8, 1968	Searle.
4736	CL #71563		Apr. 18, 1968	Lederle.
4788	DCR #515		June 4, 1968	Sandoz.
4803	U #13,906 A		May 10, 1968	Upjohn.
4814(L)	SCH 12169		Aug. 2, 1968	Schering.
4821(L)	NDR #5998-A		May 14, 1968	National Drug Co.
4830	CL #2422		May 16, 1968	Lederle.
4871(L)	U#25,927		June 4, 1968	Upjohn.
4884(L)	Anna P M		June 10, 1968	Pitman-Moore.
5018(L)	Pentids P #1200 A.S. Suspension		July 29, 1968	Squibb.
5046(L)	Riker #760		Aug. 7, 1968	Riker.
5087	U#26,225A		Aug. 22, 1968	Upjohn.
5096(L)	CL #65,562		Aug. 29, 1968	Lederle.
5135	U#3260 Suspension		Sept. 18, 1968	Upjohn.
5161	CL #71366		Sept. 30, 1968	Lederle.
5281(L)	R S #3540		Dec. 16, 1968	Syntex.
10579	TH&M Terpin Hydrate & Methoron HBr			Upjohn.
11020	Dantal Dihydrochloride			Searle.
11047	Cardrase			Upjohn.
13595	Neomycin-Fungizone			Squibb.
13615	Quide			Pitman-Moore.
13652	Acotral			Lakeside.
13675	Fungizone			Squibb.
13721	Kanomycin 3-phenyl-salicylate			Bristol.
13927	Hydromox			Lederle.
13992	Band aid antiseptic			Johnson & Johnson.
14005	Orgabolin			Organon.
14006	Maxibolin			Do.
14116	First aid spray			Johnson & Johnson.
14217	Maolate			Upjohn.
14241	Serc			Unimed.
14399	Norpramin			Lakeside.
14412	Provest			Upjohn.
15125	Bendroflumethiazide w/Reserpine and Protoveratrine A.			Bristol.
15171	Acutuss			Philips Roxane.
15294	Paranosaniline Pamoate			Parke Davis.
15500	Tolinase			Upjohn.
15867	Mellaril			Sandoz.
16009	Product 88			FGrove.
16058	Product 157			Do.
16131	Clomid			Merrell.
16178	Product 159 E			Grove.
16811	Renafur		Aug. 20, 1968	Norwich.
50057	Spectrocaine		Dec. 19, 1963	Squibb.
50058	Achrocidin		June 8, 1961	Lederle.
50098(L)	Polycillin-IM		Nov. 22, 1967	Bristol.
10162	Dalacin		Oct. 7, 1968	Upjohn.

UPDATE ADDENDUM

3281	Valium Injection		Jan. 29, 1969	Hoffman-LaRoche.
3592	CBA 93626		Jan. 21, 1969	Schering.
3617	Erythromycin Tab		Jan. 13, 1969	Upjohn.

UPDATE ADDENDUM—Continued

IND/NDA	Drug	Status	Date	Sponsor
3827	Depo Medrol		Apr. 16, 1969	Do.
5097	Protriptyline HCl and Perphenazine		Jan. 15, 1969	Merck.
5407(L)	SU 177,708		Jan. 13, 1969	Ciba.
5535	U-25030		Mar. 3, 1969	Uphohn.
16-845	Aristosol		Feb. 17, 1969	Lederle.

DR. EARL LONG

IND/NDA	Drug	With Dr. Stough	Date	Sponsor
188	Megestrol Acetate		Feb. 26, 1968	Mead Johnson.
191	Provost	X	Mar. 27, 1969	Upjohn.
247	Levoxadrol HCl	X	Aug. 28, 1967	Cutter.
453	Bandol			Squibb.
616	Penicillin		Apr. 25, 1968	Bristol.
666	Delestrec Injection	X		Squibb.
1669	Mebutamate		Mar. 22, 1968	Wallace.
1760	Polycillin		Dec. 11, 1967	Bristol.
1766	BL-P #1011		Mar. 23, 1967	Do.
2290	CL #1190C	X	Feb. 20, 1967	Cutter.
2426	SU #14,542	X		Ciba.
2477	Voranil	X		Do.
2498	Hetacillin	X	Mar. 13, 1968	Bristol.
3192	THFES Caps	X		Commercial Solvent.
3196	BA #31531	X		Ciba.
3436	W #1673	X	Jan. 5, 1968	Wallace.
3585	Trobicin Injection	X	Sept. 9, 1968	Upjohn.
3810	Rifampin	X	Dec. 28, 1966	Ciba.
3848	MJ #1992	X	Feb. 25, 1967	Mead Johnson.
4097	U #24, 973 AC 14	X	July 7, 1957	Upjohn.
4177	SC #17914		May 10, 1968	Searle.
4215	WIN #11, 464	X	Sept. 5, 1967	Sterling-Winthrop.
4266	NDR #5204	X	Oct. 3, 1967	National Drug.
4285	Dilabron	X	Oct. 11, 1967	Breon.
4373	Zaroxolyn	X	Jan. 30, 1968	Strasenburg.
4448	Flagyl w/Nystatin	X	Jan. 8, 1968	Searle.
4524	Persol Cream		Oct. 28, 1968	Carter-Wallace.
4557	MK #835		May 1, 1968	Merck.
4643	Megestrol Acetate		Feb. 13, 1969	Mead Johnson.
4814	SCH #12169	X	Aug. 2, 1968	Schering.
4821	NDR #5998-A	X	May 14, 1968	National Drug.
4871	U #25,927	X	June 4, 1968	Upjohn.
4884	Anna PM	X	June 10, 1968	Pitman-Moore.
5018	Pentids P #1200	X	July 29, 1968	Squibb.
5046	Riker #760	X	Aug. 7, 1968	Riker.
55096	CL #65,562	X	Aug. 29, 1968	Lederle.
5281	RS 3540	X	Dec. 16, 1968	Syntex.
1407	SU #177,708	X	Jan. 13, 1969	Ciba.
56-826	Bandol		Nov. 13, 1968	Squibb.
50024	Versapen		Aug. 16, 1966	Bristol.
50098	Polycillin IM	X	Nov. 22, 1967	Do.
50102	Dynapen Powder		Feb. 19, 1968	Do.
50103	Dynapen Injection		Feb. 20, 1968	Do.

Senator NELSON. In the last sentence, Dr. Jennings states that although Dr. Lisook's two investigations of Dr. Stough's operations disclosed no violations of our regulations, obviously, we should be concerned that such an operation can exist under current regulations of FDA and the DBS, and so on. "Aside from the welfare of the subjects, the question of validity of the studies may still be raised, especially the possibility of concurrent testing of drugs."

It seems to me that that sentence in itself is a strong indictment of the criticism of the methods being used by Dr. Stough when Dr. Jennings says that we should be concerned that "such an operation can exist under current regulations."

Dr. LEY. Mr. Chairman, the most effective measures to correct such problems as exist in the operation there is the peer review committee. That is, to my way of thinking, after reading very, very carefully the Alabama Commission report, the one major item that would have made that event in Alabama unlikely.

On the other hand, I do not wish to give the impression that I can or should attempt to place fault at any one level in the complex system that is responsible for oversight of such studies. Dr. Stough had certain responsibilities. The institution or prison had certain responsibilities. The Alabama Medical Society in turn had responsibilities, the sponsor did, and last but not least, we in FDA did.

Senator NELSON. What is the legal responsibility of the Alabama Medical Association?

Dr. LEY. The Alabama Medical Association does have an oversight function here in terms of the physicians operating within their State. They did become involved in what amounted to a peer review of the Alabama prison operation at the request of the warden. This is the responsibility that they perhaps should have been fulfilling earlier.

Senator NELSON. Do I understand, then, that you will make a proposal for a peer review committee?

Dr. LEY. That is correct.

Senator NELSON. Is this under statute?

Dr. LEY. This is a part of our regulations. I would propose that this be published as a proposal, with 30 days for comment. We undoubtedly, as I indicated, will have considerable comment. But I see no reason why the establishment of a peer review structure in experimental drug testing should not and can't be applied in this area.

Senator NELSON. Would it be one of the first orders of business, then, that once a final decision to establish peer review committees was made, they will be used in the experiments being conducted in the prisons in this country?

Dr. LEY. It would indeed.

Senator NELSON. I have read, as I know you have, a very comprehensive 22-page—what amounts to a peer review, I guess you would say—report from the Alabama Medical Association, signed by six persons, three of whom are M.D.'s, one a Ph. D. and one a lawyer and another one identified as Mr. Patterson, but not identified as to his profession.

Let me say that I read it as a very damning indictment of the conduct of studies by Dr. Stough. The medical group states on page 14: "The work of Dr. Stough and to some extent Dr. Long is, bluntly, unacceptable."

I would like to ask, because I could not get it straight from reading the news stories, as I understand it, Dr. Stough was doing drug IND studies for ethical drug houses, correct?

Dr. LEY. This is true.

Senator NELSON. He was also doing studies for the Division of Biological Standards, is that right?

Dr. LEY. I cannot speak for this, because I am not that familiar with the record. I do not believe that that operation, as I believe Dr. Murray told me, was in the Division of Biological Standards.

Senator NELSON. He was, as the news story appears, extensively collecting blood plasma.

Dr. LEY. This is correct.

Senator NELSON. Was that for the DBS?

Dr. LEY. That was a source of plasma for use in preparing gamma globulin, as the situation was outlined to me by Dr. Murray.

Senator NELSON. I realize that is not your field. But it was drawn for DBS, then?

Dr. LEY. It was drawn for production of gamma globulin by commercial processors.

Senator NELSON. I see. Under the supervision of DBS?

Dr. LEY. Again, you are getting into detail, Mr. Chairman, that——

Senator NELSON. All right. I will inquire of them.

(The subsequent information was received and follows:)

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., August 13, 1969.

Dr. RODERICK MURRAY,
Director, Division of Biologic Standards, National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare, Washington, D.C.

DEAR DR. MURRAY: The Alabama Medical Association and the New York Times have reported on the plasmapheresis program recently carried on in various state prisons by the Southern Food and Drug Research Company.

It is my understanding that Drs. Stough and Long, officers of the company, and their assistants were collecting plasma for use in preparing gamma globulin, an activity which comes under the jurisdiction of the Division of Biologic Standards.

It would be greatly appreciated if you would send me a detailed description of the past and present activities of Southern Food and Drug in this field, your relationship to these activities and your findings with respect to the quality of the work of its personnel.

Sincerely,

GAYLORD NELSON,
Chairman, Monopoly Subcommittee.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
Bethesda, Md., September 12, 1969.

Hon. GAYLORD NELSON,
U.S. Senate,
Washington, D.C.

DEAR SENATOR NELSON: This is in reply to your letter of August 13th concerning the activities of Southern Food and Drug Research Company in relation to the collection of plasma for processing to albumin and globulin. The events referred to occurred in 1964 and we have had some difficulty in identifying the records relating to this matter since our information came to us through the reports filed by the processors of the plasma to albumin and globulin.

What follows may seem lengthy but this description of the elements involved in the production of albumin and globulin are essential to an understanding of what is involved as far as the safety and effectiveness of these products is concerned.

The "biological products" provisions of the Public Health Service Act apply to the safety, purity and potency of such products. In the case of albumin and globulin, which are prepared from human plasma, these criteria are met if the final product is safe, pure and potent. Thus, for example, the residual blood present in human placentas has provided a valuable source of these materials (particularly immune serum globulin) for many years. On the basis of this and other experiences, it has been fully accepted for the past 15 years or more that the method of processing plasma to globulin and albumin renders the final product safe for administration. There is no recorded instance of hepatitis having developed following the administration of albumin or globulin prepared by the Cohn method used by industry (alcohol fractionation followed by heating developed by Dr. Edwin Cohn and associates during the period 1940–1947). Since the incidence of hepatitis following blood transfusion is 0.1 to 1.0%, it is

believed that a plasma pool used for fractionation, representing usually 1,000 or more donors must have some hepatitis virus in it. There is no way of preventing this. Even if a pool does contain such virus, it is clear that a safe, pure and potent product is assured by the method of processing plasma to albumin and globulin.

Plasma for fractionation is frequently obtained by manufacturers under the so-called "short supply" provisions of the regulations concerning biological products. Under these provisions the manufacturer establishes procedures with the suppliers, determines that these are adhered to and informs the Division of Biologics Standards of the arrangements, together with the names of the suppliers operating under these provisions—usually a great many sources of various kinds such as licensed and unlicensed blood banks, plasmapheresis centers, blood collecting stations, etc. Personnel from the Division check on these suppliers from time to time to determine adherence to the agreements between the manufacturer and the supplier which spell out the procedures to be followed. Copies of these agreements are filed with DBS.

There are no provisions within Sec. 351 of the Public Health Service Act, which addresses itself only to the safety, purity and potency of final products, for the development of requirements for the protection of the blood donor except as they might affect the safety, purity and potency of the final product. If the donor is injured by the bleeding process used to obtain plasma for fractionation; e.g., by suffering anemia, infection or physical damage, recourse may be made to local laws—laws relating to malpractice, etc. In the case of products where the procedures may affect the safety and purity of the final product, as in the case of blood for transfusion, regulations are adopted.

When the Division of Biologics Standards became aware in June 1964 of the occurrence of a number of cases of hepatitis in the Alabama prison, presumably related to the plasmapheresis program, it conferred with the National Communicable Disease Center which collects epidemiologic data on infectious diseases, including hepatitis, and attempted to investigate the plasmapheresis operation. However, an on-the-site inspection was not possible because operations had been indefinitely suspended.

In order to be sure that the safety of the albumin and globulin had not in some way been compromised, the following actions were taken:

(1) An embargo was placed on any lots of albumin and globulin which may have been prepared from plasma pools which contained any plasma coming from this source. This was done on July 2, 1964. The manufacturers complied.

(2) Surveillance of hepatitis in relation to products already released to the market was instituted by the manufacturers and by the National Communicable Disease Center.

Since 1964 there has been a considerable voluntary tightening of the plasma collection procedures used under the "short supply" provisions. These included more frequent inspections by representatives of the manufacturers and the formulation of more detailed instructions to be followed by the supplier of plasma. Manufacturers have provided us with detailed statements of the procedures used. Those operations which we have inspected since this time have been satisfactory.

Our records indicate that in 1963 three manufacturers of albumin and globulin were receiving plasma from Dr. Stough and his associates. In 1964 there were two. Since 1964 only one manufacturer is indicated as having obtained plasma intermittently from this source.

There is no indication from the record to indicate that the plasma supplied by Southern Food and Drug Research Company was not suitable for producing satisfactory albumin and globulin.

If we can provide any further information in this matter, we would be happy to be of assistance.

Sincerely yours,

RODERICK MURRAY, M.D.
Director, Division of Biologics Standards.

Senator NELSON. You have read the medical association comment, has the FDA done a comparable study in depth of the work being done by Dr. Stough, in the kind of depth that was done by the Alabama Medical Association peer group, so called?

Dr. LEY. We have very recently completed a detailed review of all results Dr. Stough obtained in his studies in the Alabama prison system. In our context and in our framework—that is, in the framework of the investigational drugs followed—comparing his results with other results of other investigators, looking at comparable results from related drugs, and so forth, we find in the sense of a scientific investigation no reason to question the basic validity of Dr. Stough's observation. Indeed, in several instances, he was highly critical of drug products because of adverse reactions which he reported and which were reported by other people. So we have conducted a review. But it is not in the context of a commission report.

Senator NELSON. Let me understand you—the review was done on the written material submitted to the FDA?

Dr. LEY. Right.

Senator NELSON. My question is: Has the FDA sent its own team of investigators to do an on-the-spot evaluation of the performance of the protocols he has?

Dr. LEY. This we have, Mr. Chairman.

Senator NELSON. A team?

Dr. LEY. A team. I think at this point, my statement would be very appropriate, because it tells you what we have done.

Senator NELSON. All right. So you may wish to have in mind some points raised by the medical association, let me give you a couple of points from there.

As to your review and your conclusion as to the adequacy of the written material you have, what's your response to the story in the New York Times that, for example, they are paying the prisoner—he gets paid $1 a day—and I understand from the story that his monthly stipend is 50 cents. It was a strong motivation to get the $1 a day. How can you tell from the studies you reviewed, the written materials submitted to your office, how can you tell that the side effects on these prisoners were reported when the reporter says that one of these prisoners, or maybe more, was sick from the drugs, but declined to report it because he did not want to lose the $1. How do reports from your office discover that?

Dr. LEY. Our reports and our investigations do not specifically approach this type of question. This is a question of not only the quality of informed consent, because the money provided to the patient offer an unusual stimulus for him to stay in the program and an unusual stimulus for him not to exercise his right as a subject to withdraw from the experiment if the effects were exceedingly unpleasant or unsatisfactory to him.

The points raised in the Times article are more matters of consideration by an appropriate peer review group in the Alabama situation. The questions that were raised there are not questions that can be answered by our investigative team of an inspector in a position to visit the prison for a day or two. It is impossible to get that type of information by an outsider coming in for a relatively short period of time. The appropriate group for resolving the questions raised in terms of remuneration would be a peer review group.

Senator NELSON. What about the question of the prisoner not reporting toxic side effects which would certainly be critical to an evaluation

of the drug and are not found in your files—the patient who does not report it because he wants to continue to get the money?

Dr. LEY. The basic problem here, Mr. Chairman, is that the remuneration to the prisoner was too much. This meant that the prisoner had a very strong pressure not to report and not to withdraw from the study. Therefore, he would decline to say that he felt any adverse reaction. This is bad for the prisoner in that it exposes him to unnecessary risk, it is bad for our records in that it does not provide us full information. If the stipend system had been set by the peer review group at a much lower level, there would have been no such insistence on the prisoner's not reporting because he wanted to stay in the study.

Senator NELSON. I am going to ask that the full report of the Alabama Medical Association study of the use of prisoners for drug trials in Alabama be printed in the record at this point.

(The study referred to follows:)

THE USE OF PRISONERS FOR DRUG TRIALS IN ALABAMA

INTRODUCTION

Statement of the Problem: It has been well said that while conflict between right and wrong is melodrama, conflict between right and right is tragedy.

It is right that the health of the public be protected by drug testing. Following extensive animal experimentation, such as that now being conducted by (or for) all of the ethical manufacturers of pharmaceutical products, there inevitably arrives the time when someone has to be the first human to receive the new drug. We strongly endorse the policy of the Food and Drug Administration which insists that in most instances the someone be, not an enfeebled, sick man, but a healthy human volunteer. Who should that volunteer be? We shall shortly return to that question.

It is also *right* that every precaution be taken to safeguard the health of the prison inmates. We believe that this has been done in principle and in policy but that under the existing circumstances, it has not been possible to do so in detail.

At first glance, it may seem that there is an inevitable conflict between these two "rights". The major effort of this committee has been directed toward this dilemma. In this effort, we have been aided by the complete support of the governing body of the Medical Association, and by the cooperative attitudes of the Food and Drug Administration, of the State Health Officer, the *Montgomery Advertiser*, the members of the Board of Corrections, the Commissioner and staff of the prison system, the representatives of a number of leading pharmaceutical manufacturers, and of a variety of consultants from inside and outside our State. We wish to thank these groups and individuals. Without such support and cooperation, it would probably have been impossible for us to arrive at any practical conclusions and recommendations.

BACKGROUND INFORMATION

It appears that the Southern Food and Drug Research, Inc. has been operating a research program in the Alabama Prison System since 1962 with the approval of Commissioner Frank Lee and the Alabama Board of Corrections. The president of Southern Food and Drug Research (known between 1963 and 1967 as JEMCO, Inc.) is Dr. Austin R. Stough who is a graduate of the University of Oklahoma and of the Medical College of the University of Tennessee. He conducted research programs in the Oklahoma prison system and the Arkansas prison system before coming to Alabama. Dr. Irl Long who was previously in general practice in Montgomery and who is still prison physician for Kilby Prison is associated with Dr. Stough in providing medical direction for Southern Food and Drug Research.

The original emphasis for Southern Food and Drug Research was on a plasmapheresis program but this was discontinued in 1964 following an outbreak of hepatitis which involved 376 prisoner participants with three deaths. (A Public Health Service investigation showed that the outbreak was definitely

linked with the plasmapheresis program and a significant break in aseptic technique was found which accounted for this.) In 1963, however, the Food and Drug Administration set for the various drug houses much stricter standards for drug testing and these included a greatly increased demand for Phase I testing (Phase I testing is that done on healthy humans after completion of the animal experimental work). As a result, proficient investigators with adequate facilities were in considerable demand and Southern Food and Drug Research then concentrated its attention in this area.

Over the years since then, the drug houses seem to have been generally satisfied with what was done in Alabama and the Food and Drug Administration has had no specific complaints although they queried the number of investigations being done at any one time as being perhaps too many for adequate medical supervision by the limited medical staff of Southern Food and Drug Research. Internal control over the program by the Board of Corrections and its officers appears to have been limited in amount with the Medical member of the Board (Dr. McLaughlin) briefly reviewing the protocols for each new drug trial and occasionally mentioning them to members of the Board.

Membership on the Board of Corrections is not a full-time position. With their primary interest to attend to, it could not be expected that members of this Board be completely and constantly aware of every transaction affecting the prison system at a given time. A busy physician could not devote the time required to properly evaluate the protocols without neglecting his private patients.

The Commissioner and his wardens apparently gave Dr. Stough and his group ready cooperation with very few questions being openly asked. The prison physicians for the other two prisons involved in the drug testing program (Dr. Edwards at Tutwiler and Dr. Mracek at Draper) generally required that they be kept advised of new drug testing programs in their own prisons when these were initiated.

While most of the work done by Southern Food and Drug Research was for private drug companies, other programs were occasionally undertaken for agencies such as NASA and on a subcontracting basis for the Medical College of Albany, New York. Conversely, a very limited use has been made by the University of Alabama Medical Center of prisoners for drug trials and the Red Cross has, at infrequent intervals, taken blood from prisoners.

In January, 1969, the *Montgomery Advertiser-Journal*, over the byline of Mr. Harold E. Martin (Editor and Publisher) launched a series of attacks at the drug testing program being conducted in Alabama prisons. In addition to hinting at excessive profits being made, at the expense of the health of the prisoners by Southern Food and Drug Research, certain additional medically oriented accusations were made:

1. Although the inmates signed a waiver they were not told of the possible effects of tests while the prisoners' strong need for extra money largely invalidated the requirement of informed consent.
2. Physical examinations were not being performed before each program as required in some protocols.
3. A doctor was not present during many of the potentially critical periods of reaction.
4. Some of the experiments left the men too sick to perform their regular duties.
5. Prison inmates drew blood and performed other technical procedures.
6. The contrast between the facilities for the private concern's testing program and the extremely inadequate facilities available for treating sick prisoners was shocking.
7. A number of quite serious reactions had occurred among prisoners but these had received little attention.
8. The administration of the program with prisoners sometimes, giving false histories and not taking the medicine provided for them, made the results of the testing program somewhat unreliable.

The newspaper articles were not entirely negative and they did point out that needed research was carried out, inmates did receive money to buy cigarettes and other needs, and the Prison Welfare Fund received some monies which could be used for programs that the State did not provide. (At Kilby and Draper twenty percent of the money paid to the prisoners went to the Prison Welfare Fund). The newspaper suggested that the entire program be placed under the authority and supervision of the University of Alabama Medical School, that the participants be properly remunerated, that profits from the program should

go for improvements in the prison system, that the testing program be so scheduled as not to interfere with the work or training at the prison, that the participants be clearly informed of possible dangers involved in the program, that the controls over the program provide for good scientific evaluation and that good medical supervision be exercised at all times.

Following this adverse publicity which carried distinct connotations of laxity on the part of the Board of Corrections and possible dishonesty on the part of certain of their senior employees, the Board of Corrections adopted the following resolution.

"That the Chairman be authorized to appoint a committee of two or more persons qualified to determine from a medical standpoint, and not connected with the Board of Corrections, to investigate any drug testing programs conducted in the State prisons, to determine whether the programs are properly supervised to protect the health of the participants, both in testing and in the event of any after effects of the testing, to determine whether any prisoners are being abused in any way, and to report to the Board their findings."

Upon receipt of this request, this committee was appointed by the governing body of the Medical Association. The report constitutes our findings.

FINDINGS

The findings of the Committee may be summarized under the following headings:

1. Prison testing facilities
2. Equipment and staff (Southern Food and Drug Research)
3. Drug house relationships
4. The situation in other states
5. The present medical program (Alabama Prison System)
6. Errors of fact

1. Prison Testing Facilities

Kilby, Tutwiler and Draper Prisons were visited during the course of the investigation. Private conversations were held with the three wardens, the three prison physicians (two of these were seen elsewhere than in the prison for which they were responsible), Dr. Stough, the staff providing medical care in the three prisons, technicians involved in the testing program, and a number of prisoners who were on or had been on one or other of the testing programs together with a number of more junior prison officials.

At Kilby Prison a list was seen of prisoners who had been selected by the Southern Food and Drug Research from their records as being suitable subjects for a new test which was being started that morning. No person in the prison system had any hand in selecting this initial list. From about 60 names which had been submitted, the warden had deleted about ten because, so he advised us, these persons could not be spared by their division heads from their official prison occupation. Most of the remaining 50 prisoners had been called into the testing room in the prison that morning in groups of about six persons. While blood was being taken from them (apparently for laboratory testing) they had received a rapid explanation of the purpose of the test, (there was considerable variation in the understanding of what had been said) with the statement that the drug being tested was safe and should the laboratory tests be satisfactory, they would be asked to sign a waiver-consent form. All this had seemingly been done by technicians with no physician being present as far as could be determined. Two of the four prisoners who were interviewed indicated that they had never been examined by a physician while they were in the prison although they had been on several drug trials. One of these prisoners told of tests with an anti-hypertensive drug which had had to be discontinued after three weeks (the trial was supposed to run for four weeks) because of severe reactions among those taking the pills. He himself had hung on to the end although he had been feeling very ill and had not complained of this illness, because it would have meant his losing the pay which he was hoping to receive for his participation. The majority of the prisoners interviewed indicated that the only reason they participated in the drug trials was because of the money which they were paid.

At Kilby, the original medical screening of convicts and the treatment of those who fell ill appeared to be largely in the hands of Mr. Howell, a man with very little previous medical training. His prior experience before entering his present position had been that of a venereal disease inspector. This man is supplemented in his duties by a number of part-trained inmates who are used as orderlies.

It was stated, with pride, by this individual who functions as hospital director that he himself was able to deal with nine out of every 10 patients who came to him so that the doctor was not bothered.

Mr. Howell has the title of Medical Technician. However, it is apparent that he has been permitted to usurp responsibilities far in excess of his qualifications. It has been learned that this individual is responsible for the filling of requisitions for drugs from the other prisons within the system. In this capacity he has made substitutions for the drugs requested. Such decision should be made by a licensed physician. It is apparent to this committee that with proper controls this situation could not have existed.

Conditions in the so-called hospital at Kilby were appallingly bad and would not have been acceptable fifty years ago, let alone today. One felt that a little extra effort and a little additional money would have made a tremendous difference if only the drive had been there. The importance of this hospital at Kilby is that it turned out later that persons having severe reactions to any of the drug trials in any of the prisons were transferred to this hospital for more intensive care.

The situation at Tutwiler Prison where only women are housed was immeasurably better than at Kilby. Both the warden and the hospital matron knew what was going on and had details of each protocol in front of them. Only relatively innocuous drugs such as certain hormonal products were tested at Tutwiler (the potentially dangerous drugs were tested at Draper and Kilby where only men are housed). The subjects in each trial knew the purpose of the trials and reported regular and adequate supervision. Housing and care were generally satisfactory and the morale of staff and prisoners was obviously high. It was notable that these prisoners received a larger weekly allowance than was the case in the other two prisons and appeared to make good use of this. We were told with pride by the prisoners of patients with cancer, which had been diagnosed early as a result of the testing program and that these patients were now receiving proper treatment. The difference in this prison was more than could be accounted for by the nature of the trials being undertaken, or by the fact that this was a woman's prison.

The situation in Draper was similar to that which had been found at Kilby, though not as bad. The difference was probably related to the dedication of the prison physician and to the strong sense of responsibility of the warden. There was no question here but that inmates had been used as technicians until very recently, while severe drug reactions were not being given the attention (medical or experimental) which their condition deserved. Supervision for patients who had been "stopped up" in the special room constructed by Southern Food and Drug Research, appeared to be almost entirely non-medical in nature and no really adequate provision had been made for any serious, unexpected, severe reaction. Once again, it appeared that most of the prisoners were volunteering purely for monetary reasons and were staying on the tests even after disturbing reactions had occurred simply to be paid more. There was some question whether a physician was being called on to decide what reactions were serious enough to constitute a demand for a patient to be withdrawn from a trial or whether this decision was in the hands of a technician. Here also, it appeared that the drug trials were given priority over the normal business of the prison and this division of authority could hardly have benefited the status of the local prison officials who were doing, apparently, a good job under difficult circumstances.

Your committee believes that by and large, the research studies completed and published in highly respected journals by staff members of Southern Food and Drug Corporation represent creditable, useful, and practical contributions to medical science. However, this good should not be permitted to hide the manifest defects in the present system.

The Board of Corrections with its physician member has naturally assumed that any doctor conducting experimental studies on human subjects would take the utmost precautions to safeguard the health of such subjects. Their confidence has been gravely abused.

It is the opinion of the committee that the prison testing facilities in Kilby and Draper do not measure up to minimum standards and compare unfavorably with what has been described to us as existing in several other states (see later in this report). Within Alabama, the limited testing done on prisoners at the Clinical Research Center of the University Hospital under the direction of Dr. Clifton Meador (now Dean of the Medical School) provides a striking con-

trast to what was observed in Kilby and Draper. In this University program, a few prisoners were selected for good behavior and understanding of what was involved. They were housed in the same quarters where other non-prison volunteers were housed with no guards. None took advantage of the easy opportunity to escape and since discharge from the prison at least one former prisoner has revisited the Research Center to express his gratitude at being given this opportunity for moral rehabilitation.

This committee was confronted with a seeming conflict of interest when it viewed the dual role of Dr. Irl Long serving as both senior prison physician and as an officer of Southern Food and Drug Research. Even Dr. Long readily acknowledged that a potential conflict of interest could exist. This unconscionable situation, regardless of reason, should never have been permitted to come into existence. This situation places all persons concerned in an untenable position exemplified by the necessity for the investigation.

2. Equipment and Staff (Southern Food and Drug Research)

The laboratory of Southern Food and Drug Research occupies the second floor of a building at 306 Arthur Street in Montgomery, Alabama. Space seems adequate and work tables, casework, shelves, record storage areas and equipment seemed sufficient for the work done. Reagents appeared fresh, were well labeled, and stored in an orderly manner. Major equipment consisted of microscope, large centrifuge, freezer, refrigerator, flame photometer, water bath, spectrophotometer, P.H. meter, Coulter counter, and a dual channel autoanalyzer for doing several routine chemical procedures using several manifolds. Procedures determined with the autoanalyzer consisted of BUN, sugar, alkaline phosphatase, total bilirubin, total protein, and albumin. Several enzymes were being determined by manual methods. CBC's and urinalyses were done by routine methods including a Coulter counter for cell counts. The refrigerator contained Dade commercial control sera and some homemade pooled sera.

We examined a series of alkaline phosphatase and bilirubin values directly from the autoanalyzer chart paper and saw one set of standards and one control for about twenty unknown patient samples. The control was calculated from the chart and showed an error of about 40% on the alkaline phosphatase. This was pointed out to the laboratory director and he excused it on the basis that commercial controls were sometimes wrong and that they could depend more on their own values. (In our experience this is occasionally true but it requires repeating the tests with other controls.) His attitude to us was unacceptable and reflected poor technique. The technician operating the analyzer on the day of our inspection had limited knowledge of the instrument.

All personnel were certified by American Medical Technologist which has limited significance in our opinion, but most had received military training in laboratory schools. These military programs are frequently quite good, and the laboratory director seemed well informed. We conclude that the laboratory is adequately equipped, staffed by people with minimal, if not marginal, acceptable training and results are generally but not always accurate. It probably compares favorably with many small hospital laboratories in Alabama but lacks the better qualified personnel and more careful quality control seen in better run laboratories.

Some tests such as Pap smears and PBI's have been done by Dr. Robert Adams of the Montgomery Baptist Hospital for the past four years and Dr. Adams has given free consultation about laboratory procedures to Dr. Stough by personal contact and telephone on several occasions. Random samples of the other procedures have at other times been sent to Dr. Adams' laboratory for comparison of results. Our conclusion that Dr. Stough operates an acceptable but not always reliable laboratory was shared by Dr. Adams who has privately recommended to Dr. Stough better supervision of the laboratory and indeed of the entire testing program.

3. Drug House Relationships

Reputable drug firms are concerned with developing and producing effective, safe medications. Their record in carrying out this function is unassailable. In their search for new therapeutic agents they maintain an impressive laboratory operation with a competent, highly trained research staff. All newly isolated or synthesized entities to be evaluated for drug potential are carried through an exhaustive battery of tests in several species of animal subjects providing toxicity data and general pharmacological profiles to serve as a basis for prediction of human responsiveness to the same agent.

The preclinical or animal work required of the drug developer is not specified in detail by the FDA and may vary within limits depending on the nature of the compound. The studies, however, must leave no "blind spots" in the animal pharmacology. It is generally accepted that the need of the manufacturer to intimately and thoroughly know his product and the responsibility of the FDA to protect the public from drug hazards is adequate proof that the manufacturer has done everything possible to provide, by animal studies, predictive information for use in human studies.

Regardless of the sophistication and exhaustiveness of animal studies, however, the definitive test of what the drug will do in the human is learned only by use in humans. The predicitive value of animal studies is less than absolutely established. Litchfield, in a retrospective study of six drugs evaluated in laboratory animals and man, found inconsistencies but concluded that some predictive value could be shown. Penylbutazone threshold difference between rabbit and man is more than forty fold. A compound shown by Brodie to anesthetize the rat satisfactorily so that infusion for 8 hours was followed by complete recovery in 10 minutes was, in a careful study in the first human subject, found to require 48 hours for recovery after a 10 minute infusion. Thus, there is inherent in the clinical testing to follow some usually small but inassessible hazard.

It is reassuring to remember, however, that the compound's activity is in the physical and chemical properties of its molecule. A clinical pharmacologist thoroughly familiar with the physical and chemical nature of the drug and with appreciation of the fact that the body's ability to dispose of a drug often depends on any enzyme system with broad or narrow substrate limits, will be prepared for dealing with blood levels that might result from the human's not possessing a polarizing enzyme with spectrum broad enough to include it. Clinical testing should either be done by an investigator trained in clincal knowledge of the new and potentally hazardous test material; or there should be extensive conferences between preclinical and clinical investigators and not just a mere presentation of the animal data reports with the assumption that they will be read and perceived.

It is our opinion that Phase I studies, in general, and, in particular, those involving a first human testing, do not give sufficient importance to either the choice of the investigator or the briefing of the investigator. This is particularly relevant for agents of an entirely new action category or having a new chemical configuration. There is the impression often that protocols are passed to any available clinical investigator to be carried out in a routine sterotype manner. A clinical investigator may thus be doing a job in which he feels competent from having performed perfunctorily in the same capacity for many years but with very little understanding of the role he is performing. FDA and pharmaceutical manufacturer's monitoring is provided but this evaluation may be too superficial and too remote to provide maximum safety. Less than ideal Phase I testing inevitably increases the risk for those volunteers used in Phase II (the first testing on selected sick patients). In a recent discussion of a new drug product, Dr. Gilgore of Pfizer Laboratories remarked that—

"For the early Phase II studies we want our investigators to be the most experienced available. Careful review of the literature and discussion with physicians at scientific meetings are important aspects in our investigator selection process. We selected four well-recognized experts in the field as our principal Phase II investigators. With these we discussed the experimental procedures to be followed and with collaboration of statisticians, designed the clinical protocol. . . . After pilot studies were completed we called our investigators together for a 'think tank' type of discussion at which their results were received."

In contrast the only mention of selection and briefing of Phase I investigators is that "two were selected."

In the present instance there is no reason to believe that the pharmaceutical firms failed to act in good faith or failed to discharge their responsibility to the general public to develop safe effective therapeutic agents. They contracted with approved clinical investigators to carry out approved research projects. However, there are some points for possible criticism, (1) There may have been a too superficial monitoring of the clinical work which they support, (2) They demonstrated some lack of discretion in selection of their Phase I investigator. Thus, there was a need to consider the number of projects to which the prospective investigator was already committed, (3) Their initial conference sessions may not have provided for adequate grounding of the investigator in all the significant basic properties of the test material, a particularly important point when the

limited training in basic pharmacology of both clinical investigators (Drs. Stough and Long) is considered.

That the drug manufacturers are interested in conducting and supporting research programs of quality is confirmed by a consideration of two clinical programs established and operated by two of the major firms, the Upjohn Company and Parke-Davis at the Southern Michigan State Prison. These programs involved an initial expenditure of perhaps one half million dollars for facilities and are generally believed to be first class, both in providing for optimum safety and welfare of the human subjects and in providing dependable clinical data.

There is no reason to doubt that excellent programs are desired by the drug manufacturers or that they would support such programs. Despite this, both the drug firms and FDA have given tacit approval to the research in Alabama prisons, an approval based on their confidence in the reliability of data so obtained.

It should be noted, however, that neither is primarily concerned with the rights and welfare of the institutionalized research subject. There is within the body of the law some provision for protecting the welfare and rights of prisoners used as research subjects, but in the absence of sufficient funds and some watchdog mechanism, these rights may be abused. There is the justifiable view that the drug manufacturer is not abandoning any moral or ethical responsibility in assuming that the welfare of institutionalized human subjects used in testing its products will be adequately underwritten by the administrators of the institutions or by other state agencies, boards, or commissions charged with that responsibility. The states in which prison inmates are used as experimental subjects provide examples of very adequate provision for welfare of the human subjects through "human use" committees and "human experiment review boards" which are concerned primarily with protection of the human subjects. That, except at the Medical Center, there is no such firmly structured monitoring group in Alabama should not be considered to extend the responsibility of the drug manufacturer to assume this neglected duty. There is good reason to believe, however, that the pharmaceutical manufacturers would much prefer to have their clinical programs conducted under an officially supervised system in which the welfare of the human subject is assured.

The committee is of the opinion that drug companies would also prefer a system which would provide for on going "quality control" during a drug testing program and a certainty that all possible toxic reactions, whether real or only apparent were being fully reported. An agency which would establish clinical research standards and policies and critically assess the safety and propriety of all procedures and the conducting of these would serve the cause of drug research and the principle of inividual rights.

In summary it may be concluded that the pharmaceutical firms are generally not subject to criticism for the present state of the clinical research program under investigation. They have contracted with approved clinical investigators to do approved research on compounds which they have developed and for which they have provided very thorough preclinical testing. That they may have been unwise in their selection of a clinical investigator is a point for criticism but is understandable. That they have not shown greater interest in the welfare of the subject used in the clinical investigations is explicable since they would understandably assume that such an obligation would be underwritten by alert state agencies. There is evidence that the pharmaceutical firms would prefer to have their clinical research program conducted under a system by which adequate state provision for prison inmate welfare would be assured.

4. The Situation in Other States

During the course of this committee's work, a survey was made on the use of inmates for drug testing in the prison systems, of other states. This survey was made by written inquiry to the commissioners or their counterparts of the 49 other prison systems. At the time of this writing 35 responses have been received.

Twenty states do permit drug testing within their prison systems. Fifteen states do not permit testing; however, the State of Tennessee has proposed legislation which would permit testing within the system there.

In those states where testing is permitted, their programs appear to be well structured along two main lines, in order to insure (1) ultimate protection of the health and safety of the human subjects and (2) minimum interference with the operational aspects of the prison itself.

The protective mechanism in most instances is centered around a professional committee which passes judgment on each testing program that is proposed. Such

a committee then makes a recommendation to the prison board which must have final authority before testing can be conducted.

In these states without testing programs the reasons, where given, for their non-existence were usually a lack of proper facilities and medical facilities in particular.

The one general area of agreement in those opinions expressed or inferable is that drug testing is essential. Further, the presence of drug testing programs in a prison affords another means of rehabilitation through the provision of a channel by which the prisoners can make both a humane and financial contribution to society and their families.

The programs in other states have far superior controls, both medically and administratively, to those presently found in the Alabama system. The relative lack of controls could well account for the vast amount of testing done in the Alabama system.

The appendix to this report contains examples of some procedures used in other systems in which the committee feels have considerable merit.

5. The Present Medical Program (Alabama Prison System)

We believe that the physicians responsible for the health of the prisoners at Atmore, Draper, and Tutwiler Prisons have done a *magnificent* job when their work is considered in relation to the pitiful and almost scandalous lack of facilities, funds, and personnel available to them. At the expense of personal economic loss, lack of time with their families and almost complete sacrifice of opportunities for recreation and relaxation they have proven their dedication to the Hippocratic tradition. We applaud the degree of voluntary devotion, to their own concepts of their obligation to society, displayed by these three prison physicians.

Certain aspects of the various prison medical facilities have been described earlier in this report. They, with the exception of Tutwiler, are unacceptable. The Tutwiler dispensary while superior to that in the other prisons, could be improved.

6. Errors of Fact

Respect for the Board of Corrections and for Commissioner Lee requires that the committee report that certain errors of fact did appear in the newspaper articles concerning the drug testing program. These include:

(1) The ownership of the ward constructed at Draper. This building is used by Southern Food and Drug Research, Inc. and was paid for by the corporation. It is now property of the Alabama Prison System.

(2) The "blood draws" allegedly taken at Atmore did take place, but these were donations to the American Red Cross. We were unable to confirm any plan to expand the drug testing program to expand the drug testing program to the Atmore facility.

(3) At no time has an expansion of the testing program been planned to include the testing of foods. Southern Food and Drug Research, Inc. did offer (this offer was accepted) $7,000 toward the purchase of new kitchen equipment badly needed at Draper.

(4) No modern laboratory facilities were found to exist at any prison facility. The laboratory of Southern Food and Drug is in Montgomery.

It is not this committee's responsibility to pass judgment upon the motivation behind the printing of these stories. We do not believe these articles were errors of intent; however, they are errors of fact. The implications of some of these articles were not substantiated in this committee's findings.

IMPLICATIONS

Our investigations have shown substantial defects in the drug testing program as administered at present in Alabama prisons. This does not, however, change our opinion that drug trials using prisoners can and do serve an essential purpose. They benefit the Nation and provide the prisoner with an opportunity to contribute something back to society, to earn some extra needed money and to improve living conditions in the prisons through a well developed welfare fund. In addition, a well conducted drug testing program would provide extra medical coverage for prisoners with the possibility of the early diagnosis and treatment of disease and better diagnostic facilities then might otherwise be available. Actually this has frequently happened in Alabama.

Considering the present situation we regard it as being distinctly unsatisfactory. The prisoners' welfare is not being adequately safeguarded and the validity of the drug trials themselves must occasionally be seriously in doubt. The chief deficiencies are undoubtedly the lack of an adequately trained staff, the lack of sufficient interest in the prisoner as a patient, the lack of medical supervision, the unique pressure toward signing a "consent form" because of the need for money, unsatisfactory conditions for the treatment of those prisoners who do fall ill and the lack of any adequate peer review of protocol which are submitted. For the staff and facilities which are available, there is no question but that far too many trials are being conducted at the same time. Thus, at the time of our visit it appeared that no fewer than seven separate trials were being conducted in the three prisons we visited.

Faced with the present situation one is tempted to look back and ask, "How did this happen?" It is not our intention, however, to rake over old coals, except where such a review might lead to improvements in the future. In general, we would comment that supervision over the program has been inadequate and the responsibility for this must fall to some extent on all senior administrative levels. Men, no matter how worthy, simply cannot do what they wish to do, without the needed funds. The work of Dr. Stough and, to some extent, Dr. Long, is bluntly unacceptable. Others seem to have been involved more through innocent acceptance than through anything else. In retrospect it is easy to see that a request to the State Health Officer for an adequate control inspection might have saved a lot of grief, but this overlooks reality.

It is only right that prisoners, as wards of the state, should, *in the absence of a drug testing program*, receive medical care of the same general quality as that received by the average citizen of the state.

We believe that with very little help from the State, a sincere attempt has been made at Atmore prison to give this level of medical care. The dedicated physician providing this care has paid not only with time and at the probable price of his own health but, in part, out of his own pocket. It is totally wrong that a physician should, because of his own dedication be forced to meet an obligation that should rest firmly on the shoulders of the taxpayers of Alabama.

Where *there is a drug testing program* the obligation is different. Here the responsibility is to provide the quality of care that a volunteer ordinarily receives at a first class research institution. The fact that the volunteer is a prisoner does not alter this. Because there are fewer prisoners and because (see above) the drugs tested are relatively innocuous, the care of Tutwiler has been of high quality. Again the cost has been met in part from the pocket of a dedicated physician.

The situation at Draper is different in some respects and similiar in others. There are many more prisoners, many more testing programs, and drugs that are far more likely to produce adverse effects are being tested. Despite the strong attempt and the out-of-pocket contributions of a third dedicated physician who like the other two, has the full support of his warden, it has not been possible to provide the minimally acceptable standard of care that could probably have been provided had there been no testing program.

The responsibility for the greatly increased cost of a higher standard of medical care that should be a direct consequence of drug testing is not that of the taxpayers of Alabama. It is directly or indirectly the responsibility of the companies whose drugs are being tested. There is one large difference, the Alabama taxpayers have, as yet, shown no desire to meet their responsibility while the drug manufacturers have seemed willing to meet theirs.

We do not know what the expense of this difference between the cost of average quality health care without drug testing and superior care with drug testing will be. We are certain it will be substantial. Nevertheless, we have hopes that the drug companies will do their part.

It seems to us now that with the exception of the noted errors of fact and their perhaps graver errors of implication the *Montgomery Advertiser* was correct in most of its criticisms of the present drug program. There were insufficient controls over the drug testing program in allowing Dr. Stough a free hand within the prison system. The responsibility for this omission of controls to protect the prisoners must rest by virtue of their authority ultimately on the Board of Corrections. But we repeat that no man or group of men can possibly meet a responsibility that requires funds when they are not provided by the State with even minimal necessary funds.

ALTERNATIVES

As the problem has been described, we are faced with the dilemma of "right" versus "right." It is certainly "right" that new drugs should be evaluated before release to the general public, it is "right" that this evaluation should be meaningful—that is, it should be done in a thorough, scientific manner by competent individuals. It is "right" that the individual who is to participate in the trial (whether he is a prisoner or not) should do it purely on voluntary basis with full knowledge of the hazards involved.

In this area we are to be guided by the principles outlined in the Nuremberg Code, the Declaration of Helsinki, and the American Medical Association's Ethical Guidelines for Clinical Investigation—see Appendix. It is "right" that the prisoner with few rights of any kind should receive at least the average medical care available to free citizens, and be protected from those who might abuse his position and sometimes his ignorance to the detriment of his health for experimental purposes. It is certainly good if not right that prisoners be given a chance to earn some money (especially considering the pittance they receive otherwise in the Alabama Prison System). It is also good that prisoners so motivated may enhance their self esteem by making a positive contribution to the general public welfare by participating in a medical research program. (Our interview with Dr. Clifton Meador, the Dean of the Medical School, shows that a well-run program by properly motivated people may have a definite rehabilitative benefit to the prisoners in their ability to relate to the free society).

If there is so much right and good about the program, then what is our problem? Just as it is good that a well-run private enterprise such at A.T. and T. runs a superb telephone service in most of the United States, it is also right that such a monopoly should be regulated for the benefit of the customer who has no choice. By the same reasoning the highly desirable drug testing program might be well run by reputable free enterprise (such as ethical drug firms presumably do in Michigan) or by nonprofit research organizations as long as the research is monitored adequately by the officially designated commission or regulatory board. There are, however, certain practical problems which make such a free competition system awkward. These stem from the necessity that a unit capable of conducting such research establish major facilities such as clinical laboratories, research laboratories and offices in the vicinity of the research site and maintain a staff of highly qualified, carefully selected personnel. This constitutes a highly specialized functional unit, the existence of which would be without purpose in the absence of contracts for research. It is doubtful that even an altruistic private organization would be willing to make such investment without assurance of continuing contracts. If there was such, a free competition system would seem impractical or would likely revert to a monopoly system which would be subject to criticism.

A foundation established by a state institution such as a major university would be a logical alternative. Such a foundation would serve as a functional unit with laboratories and other necessary fixed facilities and with clerical and administrative staff directed by a clinical pharmacologist qualified to conduct human drug research. This foundation would be under control of a board of appointees qualified in medico-legal aspects of human experimentation, with the foundation director serving as permanent chairman. The controlling board would be charged with the responsibility of reviewing all protocols from pharmaceutical firms, or others submitting clinical research projects, assessing hazards inherent in the projects and critically evaluating the safeguards to be provided. The controlling board would also be responsible for seeing that all research subjects were aware of hazards and entered the programs voluntarily.

To protect themselves from any possible imputation of a "conflict of interest," the controlling board of the responsible foundation might advantageously appoint a Prison Experimental Review Committee to advise them on any potential risk to the health of the prisoners. The members of this Committee should not be related to the research foundation and might include a competent practicing physician appointed by the Board of Censors, a lawyer nominated by the Attorney General, and a designee of the State Health Officer. Since our suggestion does not envisage a monopoly for the responsible foundation (though the bulk of research investigations would be channeled through them) the proposed Committee could also advise with regard to other groups which wish to conduct their own research in the Alabama prison system.

Moving from the general to the specific, the two major university-related nonprofit organizations in Alabama which might fittingly establish the research foundation to which we have referred, are the Auburn University School of Pharmacy and/or of Veterinary Medicine and the University of Alabama Medical School. The authorities of the University of Alabama Medical Center and Medical School have, however, stated that directing and operating such drug testing programs is not within their sphere of interest. On the other hand, they would be happy to do all that they reasonably could do to aid in providing proper medical care to the prisoners and in protecting them from the possible harmful effects of drug testing. Preliminary discussions with Auburn University have been encouraging since this University has all the necessary potential and excellent leaders. This committee thanks both universities for the interest and attention they have given to this matter.

We are thus suggesting that all research protocols from drug companies and others be submitted to a new research foundation (hopefully sponsored by Auburn University) which would review these protocols.

After approval by the Foundation Controlling Board (with advice from the Prison Experimental Review Committee) the Board of Corrections would consider the proposal from the point of view of prison organization; and if they approved, submit it to the Medical Director and Warden of the Prison in which the experiment is to be conducted. Any one of these groups or individuals would have the right to reject the program with *written* justification for their decision. (This might reduce the number of programs or participants from the present excessive level, but it would introduce adequate safeguards for the health of the prisoners.)

Note that we have refrained from mentioning Southern Food and Drug Research and Dr. Stough. Obviously such a proposed system of controls would require considerable changes in his present operation. In a free enterprise system properly regulated he would have every right to submit his programs to the research foundation for consideration. Other interested parties might do likewise. No firm or individual should hold an exclusive contract to conduct experiments within the prison system. Each would be judged on its merit, safety and efficacy.

We are assuming, however, that in the vast majority of instances the research foundation would be asked not only to review the protocol, but also to undertake the research envisaged in the protocol. It would seem reasonable to assess the firms submitting research projects not only for direct costs, but also to cover the costs of the additional safeguards to the prisoners (including those of the Prison Experimental Review Committee) required by the research foundation and the Board of Corrections.

Pursuant to an amendment of the initial request made by the Board of Corrections, this committee has considered what it believes to be suitable alternatives to the present drug testing procedure in whole—or certainly in part—where needs are apparent.

These suggestions have been incorporated in Figure 1. Admittedly, both planning and money will be needed to implement an ideally structured program. The numbered items are discussed further in the text of this report, following immediately after Figure 1.

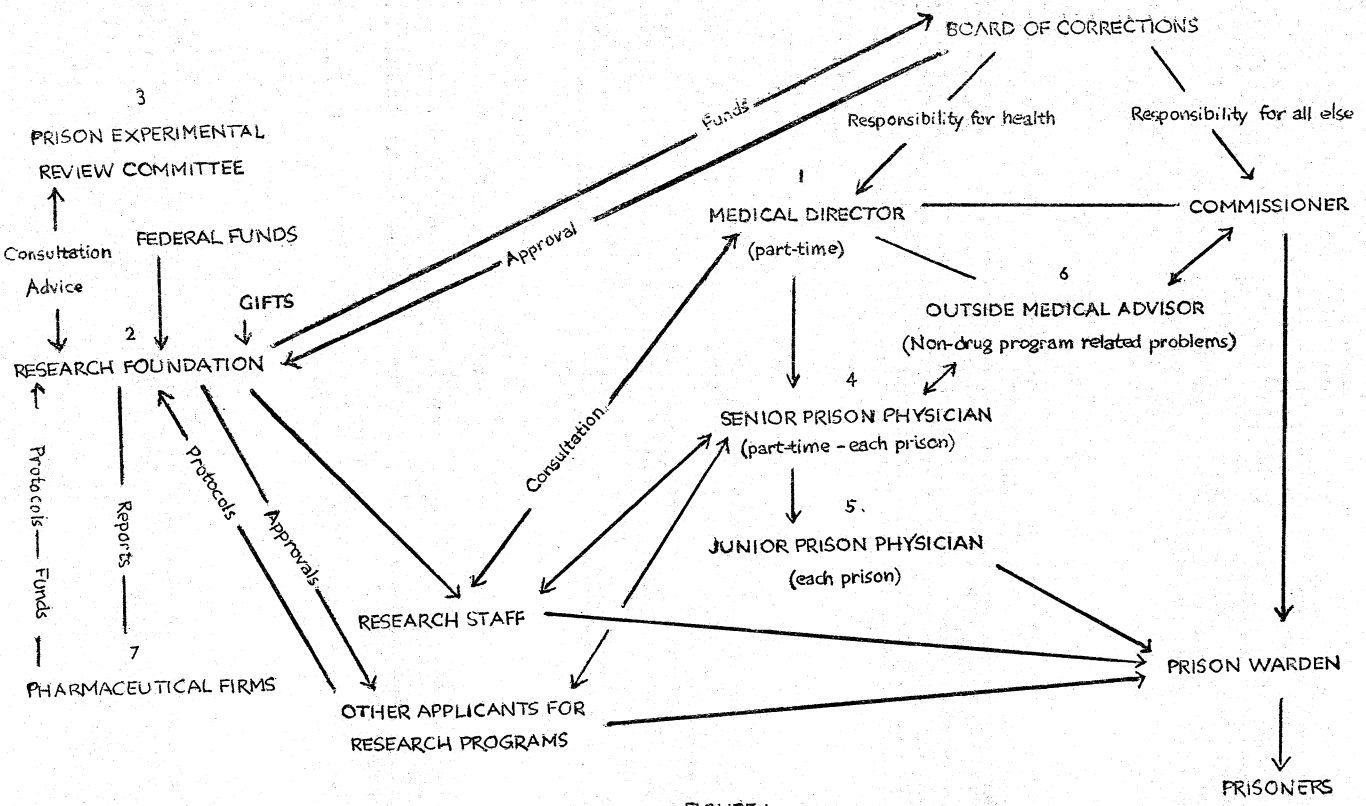
BOARD OF CORRECTIONS
Funds
Approval
Responsibility for health
Responsibility for all else
3
PRISON EXPERIMENTAL
REVIEW COMMITTEE
1
MEDICAL DIRECTOR
(part-time)
COMMISSIONER
Consultation
Advice
FEDERAL FUNDS
GIFTS
2
RESEARCH FOUNDATION
6
OUTSIDE MEDICAL ADVISOR
(Non-drug program related problems)
4
SENIOR PRISON PHYSICIAN
(part-time - each prison)
Consultation
Protocols
Approvals
Protocols — Funds
Reports
5
JUNIOR PRISON PHYSICIAN
(each prison)
RESEARCH STAFF
PRISON WARDEN
7
PHARMACEUTICAL FIRMS
OTHER APPLICANTS FOR
RESEARCH PROGRAMS
PRISONERS

FIGURE 1

(1) As we see it the chief problem that may stem from the lines of responsibility and of authority that are illustrated in the diagram (Fig. 1) included in this report relates to the Medical Director.

Should the Medical Director for the entire prison system of Alabama be directly responsible to the Board of Corrections or indirectly through its highly respected Commissioner? There are obvious potential advantages and disadvantages in each method. We believe that this is a decision that only the Board should make. However, since it is our present impression that the Commissioner would prefer not to assume any responsibility in health matters, the diagram as presently drawn, indicates direct responsibility of the Medical Director to the Board. Obviously, the Board should have complete authority to make any changes it wishes as regards such an arrangement. We are suggesting that the Medical Director be part-time but that a substantial part of his income come from the Board of Corrections. He should receive no direct payment from any research group.

(2) The Research Foundation has been discussed elsewhere. The Foundation would share with the Board of Corrections the responsibility for obtaining funding which would make adequate supervision of all drug tesing programs in the prison system a reality.

(3) The Prison Experimental Review Committee has also been discussed elsewhere. It is essential that this Committee take an active interest in what is happening and not degenerate into a rubber-stamp mechanism giving approval as a matter of form.

(4) The Senior Physicians for each prison would continue as at present to be part-time, but an increased remuneration is strongly recommended. It is proposed that this be achieved by augmenting their salaries by additional funds received indirectly (see later in this report) from the Research Foundation through the Board of Corrections.

(5) It is contemplated that the Junior Physician would be a resident on leave from a medical center for one year. This doctor would be paid by the Board of Corrections an adequate salary plus the benefits accorded other full-time prison system employees. An additional sum of money would be placed in escrow with the academic institution or hospital from which he is on leave to supplement his residency stipend during his final period of study.

(6) We have noted earlier in this report that the University of Alabama Medical Center has volunteered to do all that they reasonably can to aid in seeing that prisoners get proper medical care. This committee recommends that the Department of Public Health and Epidemiology at the Medical Center be asked to name a medical advisor to the prison system who would be outside the prison system. In addition to advising on the delivery of medical care, he could advise on matters of public health, communicable diseases, sanitation and the relative importance to be attached to health expenditures in a limited total budget.

(7) We have indicated earlier that the responsibility for the greatly increased cost of a higher standard of medical care that should be a direct consequence of drug testing is not that of the taxpayers of Alabama. It is suggested that the Board of Corrections (with appropriate advice) determine an estimated total cost for providing this extra care and that this cost, through the Research Foundation, be debited back to those drug firms making use of the Alabama Prison System for drug testing. It seems possible to the Committee that this cost might well be more than the present total cost of providing medical care in the prison system.

It must be emphasized that if this arrangement was achieved, this would not relieve the prison system of its own financial responsibility for providing acceptable medical care to prisoners. Indeed, this should provide a stimulus for much needed improved support from within the prison system.

SUMMARY

It is the unanimous opinion of this committee that the drug testing program is almost essential and should be continued for the benefit of the prisoners and society in general. However, as presently conducted the program does not provide adequate safeguards for the health of the prisoners and leaves something to be desired in quality of results obtained. In order to alleviate these problems, we have made suggestions for certain structural and organizational changes in the program which should produce a system for drug testing that might serve as an example for the nation.

Early in our report, we likened our task to that of observing and commenting upon a "play" in a theater. Perhaps it is not inappropriate to pursue that analogy.

It has been our privilege to sit on the front row. We have observed a drama that has displayed certain minor aspects of comedy and many features of melodrama. But the major impact has been that of tragedy. There has appeared, over and over again, conflict between right and right.

From our posts of vantage we have watched the entrances and the exits of the characters and the unfolding of the plot of this drama, we have constantly asked ourselves one question: "Who if anyone, is the villain in the Play?"

From time to time we have made tentative judgements as indicated earlier in this report, but our final judgement indicates that our search has been successful and that the greatest villain has been identified. At times, he brazenly occupied the spotlight; at others he has been seen flitting in the shadows. More often his presence has been felt even while he remained hidden in the wings. That villain is human nature. The same character is also the knight in shining armour, the hero of the play.

COMMITTEE MEMBERS

Tinsley R. Harrison, M.D., Chairman, Birmingham.
J. N. Clanton, M.D., Huntsville.
Peter N. B. Peacock, M.D., Birmingham.
Byron R. Williams, Ph. D., Auburn.
Reginald T. Hamner, L.L.B., Montgomery.
L. P. Patterson, Montgomery.

Senator NELSON. I would like to ask this question: You have, I understand, taken a careful look at the Alabama study.

Dr. LEY. I have.

Senator NELSON. Do you have any reason or any evidence that would refute any conclusions or any statements made by the Alabama Medical Association in this report?

Dr. LEY. This is a very difficult question to answer off the cuff. Much of the criticism or comment of the Alabama commission is aimed at specifically this area of informed consent, the degree of stipend or the amount of stipend available to the prisoners—all items which, technically, fall outside the present existing regulations of the Food and Drug Administration. So that when the statement appears here, "The work of Dr. Stough and to some extent of Dr. Long is bluntly unacceptable"—I must caution the committee and any other persons interested in the subject that this sentence, although it may be quite appropriate when you consider everything that was considered by the commission, is not appropriate on the basis of our review of the scientific details of the reports of doctors found in our file. However, it is very difficult to go line by line and make this sort of comment throughout the report.

I believe that in general, the major thrust of this report is that there was inadequate, incomplete understanding on the part of both Dr. Stough and on the part of the institution, the prison, of some of the responsibilities which each had in this particular situation in which prisoners were used for investigational studies.

Senator NELSON. But they make a substantial number of observations which, of course, are not related to paperwork that was submitted in the studies by Dr. Stough.

Dr. LEY. One of them that bothers me specifically, Mr. Chairman, is the remark about the quality control procedures utilized in the clinical laboratory, performing laboratory studies on blood specimens of the patient. Even the commission, however, recognized that the laboratory personnel were minimally trained for the work, but were probably no different from the majority of personnel in most medical laboratories in the State of Alabama.

Senator NELSON. I have been taking excerpts. I do not want to leave the impression that everything in here is negative as to Dr. Stough. It is not. That is why I wanted to print it in full in the record. And I am not asking you to endorse or give an opinion, either, on everything they said, because obviously, your team did not do the same kind of a peer evaluation that this team did. But if there were anything in here that you knew of or were certain of that you thought was not correct, I would think it would be helpful for the record to put it in.

Dr. LEY. I know of nothing right at this moment. I would appreciate the opportunity to review it once more and perhaps submit a statement for the record if there is.[1]

Senator NELSON. We are very pleased to have you do so. I want to skip to Senator Dole now so he can ask his questions.

I then can conclude that you feel it is very important to establish a peer group to evaluate the performance of the protocols not only in teaching hospitals, and so forth, but as soon as possible in all the prison experiments being done in this country?

Dr. LEY. I do indeed. I think this is a very important matter.

Senator NELSON. Senator Dole?

Senator DOLE. Let me observe, Mr. Chairman, that this committee is very appropriately named the Monopoly Subcommittee. The chairman monopolizes selection of the witnesses and all the time. I believe on the part of the minority, certain changes should be made. We also have an interest in the subject matter and it is unfortunate that 99 percent of the time is taken by the chairman.

Second, with reference to the article, the memorandum from Dr. Jennings to you, Dr. Ley, do I understand this contains a list of drugs and companies which own the drugs?

Dr. LEY. I believe I only have a superficial memorandum here. There was an appendix and attachment which have been reviewed in greater detail since this memorandum.

Senator NELSON. I intended to ask that that appended list be printed along with Dr. Jennings' memorandum. The list is here so that Senator Dole may see it.

Senator DOLE. Would this information have been available to anyone who requested it?

Dr. LEY. In terms of the listing of the studies which Dr. Stough had been involved in by manufacturer and by IND number?

Senator DOLE. Yes.

Dr. LEY. This type of detailed information would ordinarily not be available to the public or to the members of the press in this form.

Senator DOLE. Now, the article that I referred to should be made a part of the record, the New York Times article of August 5. It also states that many of the drugs were listed in code.

(The article referred to follows:)

[From the New York Times, Tuesday, Aug. 5, 1969]

DRUG AIDE ADMITS TO DOUBTS ON TESTS

(By Walter Rugaber)

WASHINGTON, Aug. 4.—A leading official of the Food and Drug Administration has acknowledged that scores of drugs now on the American market have undergone safety and efficacy tests of questionable validity.

[1] See pp. 5678–5679.

Doubts about the tests, conducted in a number of Southern prisons by one of the nation's most active evaluators of new pharmaceutical products, were apparently felt within the Food and Drug Administration as long as two years ago.

Despite the shortcomings, the agency made no move to regulate the tests or to disqualify the physician responsible for most of them, Austin R. Stough. Dr. Stough is now based in Montgomery, Ala.

Dr. John Jennings, acting director of the agency's Bureau of Medicine, argued that two inspections of the prison drug testing programs had turned up no violations of the agency's regulations.

But Dr. Jennings went on in a recent memorandum to declare that "obviously we should be concerned that such an operation [as Dr. Stough's] can exist under current regulations."

The memorandum went to Dr. Herbert L. Ley Jr., Commisioner of the Food and Drug Administration. It was dated last Tuesday and was made available today by a source outside the agency.

The document briefly recounted the history of Dr. Stough's activities, beginning with a 1964 hepatitis epidemic "subsequently proven to be caused by his poor technique in the conduct of a plasma-pheresis program."

In addition to drug testing in the Alabama and Oklahoma state penitentiaries, Dr. Stough took blood from the inmates and extracted the plasma for use in a large number of the nation's gamma globulin products.

Gamma globulin is widely used to improve a patient's immunity to various diseases. One Federal Government source has estimated that Dr. Stough's plasma could have produced a fourth of the national supply.

A study by the National Communicable Disease Center at Atlanta showed that the 1964 epidemic afflicted hundreds of prisoners in Oklahoma and Alabama and in Arkansas, where Dr. Stough also worked.

Dr. Jennings noted that Dr. Stough's plasma and drug testing operations had been stopped in Oklahoma "when unfavorable publicity and press criticism led to his expulsion" from the prison there.

The plasma program continued in Arkansas, however, until late in 1967. It was halted in the Alabama prisons in 1964, but Dr. Jennings noted that Dr. Stough "set up shop" there for drugs tests, and these continued.

Dr. Alan B. Lisook, the lone physician regularly employed by the Food and Drug Administration to make field investigations of drug testing activities, visited Dr. Stough only twice.

"The February, 1969, inspection of Southern Food and Drug Research [Dr. Stough's company] was not materially different from that of 1967," Dr. Jennings wrote in his memorandum.

"Physician-subject contact again appeared to be minimal and the execution of the studies was primarily left up to medical technicians."

"Physical examinations appeared to be performed as required although they were somewhat cursory in nature. The administration of medication appeared to be properly policed.

"Laboratory records and progress reports appeared to be complete, for the most part, and in original form. There was no evidence to indicate that the tests were not actually performed, or that inmates were participating in the selection of subjects.

ENDED AFTER PUBLICITY

"The use of convicts to draw blood samples was acknowledged, but such practice was discontinued in the wake of the January, 1969, publicity. It was noted that the interviews for subjective complaints by medical technicians were excessively brief."

The January publicity consisted of more highly critical articles in The Montgomery Advertiser and The Alabama Journal.

A committee of the Alabama Medical Association found that physical examinations were not only "somewhat cursory" but also occurred in some instances which no doctor on hand.

"Interviews for subjective complaints," said by Dr. Jennings to have been "excessively brief," are considered essential by clinical pharmacologists judging a new drug.

"Although Dr. Lisook's two investigations of Dr. Stough's operations disclosed no violations of our regulations," Dr. Jennings said, "obviously we should be concerned that such an operation can exist under current regulations of F.D.A. and D.B.S."

D.B.S. is the Division of Biologics Standards, another agency within the Department of Health, Education, and Welfare. It has responsibility for plasma programs, but its officials contend that its regulations cannot be used to protect blood donors.

"Aside from the welfare of the [prison] subjects," Dr. Jennings observed, "the question of validity of the studies may still be raised—especially the possibility of concurrent testing of drugs."

"Concurrent testing of drugs" apparently refers to testing more than one experimental drug on the same person at the same time. Dr. Jennings could not be reached for elaboration on this point.

Attached to the memorandum was a list of some 175 experimental drugs tested by Dr. Stough and an associate. The list also named the companies for which the work was carried out.

This information had been repeatedly sought by The New York Times when it was preparing an article on Dr. Stough's operations. The article was published in last Tuesday's editions.

The memorandum and the list were made available by the staff of the Senate Subcommittee on Monopoly of the Small Business Committee after part of the information had been given by the agency to a medical newspaper.

In the form that the list of drugs and conmpanies was provided, it was generally meaningless. Many of the drugs were listed by code names and there was no indication of what Dr. Stough reported about them.

It is understood that most of his reports were favorable even though a number of the drugs involved were controversial. Some have been criticized on the ground that they caused serious side effects.

The Food and Drug Administration may provide a more comprehensive view of Dr. Stough's tests when officials appear before the subcommittee at a special hearing scheduled for next Tuesday.

Senator DOLE. Did the FDA give the key to the code to any outside person, or did the FDA break the code for any outside person?

Dr. LEY. The listing in the code as so stated is only for purposes of this list. The file for each one of these products contains a complete disclosure of the components of the medication. We did not, to my knowledge, make this information available in the public area, nor should we.

In many cases, the products are listed as a generic or a trade name. The code is used frequently in investigational work early in the investigation prior to the coining of a trade name for a product. But we did not provide the compositions corresponding to the codes to the press or to the public.

Senator DOLE. Do you know whether or not—do you know, Dr. Ley, when this list of drugs was furnished to this subcommittee?

Dr. LEY. I do not know without questioning the staff. I do not know.

Senator DOLE. The reason I ask the question is that much information furnished to the subcommittee reaches only certain members of this subcommittee and is rarely made available to the minority side. This is unfortunate, hence I wonder if this was given to the chairman or Mr. Gordon, a majority staff member, with any restrictions on its usage with reference to information? Were there any restrictions placed on the report when it was made available?

Dr. LEY. Ordinarily, such items as this are provided to several committees having oversight or general interest in agency operations. Some committees, without mentioning them, I think have files that are as good or sometimes better than ours.

Senator NELSON. May I respond to that question so Senator Dole will have it clear?

Dr. LEY. Yes, sir.

Senator NELSON. The statement, the release was made public to the medical press. After it was made public, the committee counsel, who

is very alert, sought and got copies of what was public knowledge. It was available to the minority just as well as to the majority.

I might add to that that all statements that come from the witnesses are supplied to the minority. If we find some information separately, apart from that, we have no obligation to distribute it to the minority, any more than the minority distributes some independent information furnished by a drug company.

Senator DOLE. Let me say in response to that that I was not under the impression these are partisan hearings. If Mr. Gordon is not professional staff and does not wish to furnish information, we will take proper steps to require the information be furnished.

Senator NELSON. The information was made public, Senator.

Senator DOLE. Part of the information was made public. The same is true of statements of every witness. They come to us at 5 o'clock the day before the hearing or later.

Senator NELSON. If you have any instance that you are not getting it, call it to my attention. I was conducting hearings for 2 years, Senator, long before you came here and I have never heard any compliant.

Senator DOLE. That is because no one ever showed up on my side.

Senator NELSON. That is my fault; is it, sir?

Senator DOLE. No; but I intend to be here. If we are going to conduct these hearings in the public interest, we had better erase the partisan lines and——

Senator NELSON. If you want to call a meeting of the committee to describe any specific unfairness or injustice that is done, Senator, I will be glad to attend it. If you have a specific case in mind, make it specific. Let's not have general charges that you cannot support.

Senator DOLE. I have attended many sessions and perhaps it is time that we have some understanding on how we divide the time on this committee, not 99 percent to you and 1 percent to others who may attend.

Senator NELSON. I am here 99 percent of the time alone and we have not decided to give it to the majority or the minority.

Senator DOLE. We can remedy that, too.

There is a report from Alabama; I don't know when that was furnished to the committee. It has never been made available to the minority. We have not had a chance to review that report.

Senator NELSON. That was not sent to the committee at all. It is a public document that anybody alert can get. I regret very much that the other side has not been conscientious, but this is not part of any testimony. I do not think that everything I am able to discover or read I am obligated to spoon-feed to anybody else. All documents, all testimony, goes to the minority. If you have any complaint about that, be specific about it.

Senator DOLE. I have mentioned a couple of specific things now.

Senator NELSON. What were they?

Senator DOLE. The Alabama report.

Senator NELSON. That is public in Alabama. We sought it and got it.

Senator DOLE. If we are going to operate as a committee, we should operate as a committee. If you are going to operate as a one-man act, we ought not to call it the Monopoly Subcommittee.

We ought to have a hearing on the monopolistic activities of the majority if we are going to get into this.

Senator NELSON. Fine. You set the date, Senator, and I will be there.

Senator DOLE. Today we are going into an area involving a legislative matter pending in another committee. The question with reference to the peer review committees has been discussed at great length. As one member of this subcommittee, there may be some merit to this suggestion. I am not certain whether the FDA could ever be in a position to supervise all of the new drug investigations. But I was curious in reading a statement that there are some 15,000 new drug investigators. Who are these people generally? Are they engaged in phase 1 or phase 2 or phase 3 of the investigations?

Dr. LEY. Senator, they may be engaged in any one of these phases. Customarily, we find more frequently the general practitioner engaged in phase 3 testing which has as its objective, indicated in the testimony, to determine the effects of the drug as it would normally be given in clinical practice. So we do have this provision. But this is only in very general terms. We may have certain people with general medical backgrounds doing a type of work that we consider quite appropriate, what Dr. Stough is doing in Alabama.

Senator DOLE. What field is Dr. Stough in? A general practitioner?

Dr. LEY. Dr. Stough's training was that of general medicine.

Senator DOLE. Is he engaged in that practice now?

Dr. LEY. He is not. His total activities are those of drug testing. In this sense, he is unique among—not totally unique, but a rare animal among the total group of investigators.

Senator DOLE. Do you have a list or catalog of 15,000 investigators? Is that material available? Do you keep a record of those?

Dr. LEY. We have this material. It is not as convenient or accessible as we wish until we finish the computerization of it. But it is available in part in our file.

Senator DOLE. These are on a State-by-State basis, I assume?

Dr. LEY. No, we do not have a breakdown on this basis. These are some of the problems we hope to solve by the computerization of the file. It is on an alphabetical ground, I believe.

I am pleasantly surprised. The staff tells me that the names of the investigators are presently computerized. The additional information about training facility, and so forth, is not yet available by that basis. This is available, but it requires deep research of the record.

Senator DOLE. What purpose is served by your having a list of all the investigators? Do you review that list occasionally?

Dr. LEY. Two purposes, Senator, are served by this list. First of all, we may by this technique identify those investigators who have the largest numbers of investigations in progress. Second, it gives us the opportunity, if the man whom we disqualify is listed as an investigator by a sponsor, to say no, you may not utilize it. It serves these two functions.

Senator DOLE. Do you have any record of the compensation paid by, say, Dr. Stough to the clients he has?

Dr. LEY. No, that is not part of our record in any place.

Senator DOLE. There is no effort made to determine that?

Dr. LEY. I do not think that would be a legitimate item under the regulations or the law. I would have to turn to Mr. Goodrich.

Senator DOLE. The reason I raise the question is because of an earlier question by the chairman, that it is a temptation on the part of the investigator to make improper findings depending on whom he represented. It might also be a factor in the amount he is paid.

I also understand that he made reference to a certain prisoner in Alabama who perhaps was paid too much for participation in testing. I am wondering what he was paid, what the going rate was in Alabama. Perhaps this may be in the report which we may receive.

Senator NELSON. $1 a day.

Dr. LEY. Dr. Lisook tells me that the fee varies depending on the test, and I suspect, as usually is the case, on the number of times the prisoner has to be bled. But an average figure across the board would be somewhere about $1 a day.

Senator DOLE. I understand that in the State of Kansas, there was some testing done in the Kansas State Prison at Lansing, but it was terminated by prison officials partly because prisoners could make more money taking pills than by working and some preferred to stay in their cells and take pills than engage in any other activity.

I also understand that in the State of Wisconsin, one of the prisoners has gone to court demanding the minimum wage.

Senator NELSON. A very progressive State.

Senator DOLE. Right; but it is a very real factor and I am not certain whether you can compensate anybody properly. I assume all the tests, most of the tests in institutions are in the phase 1 category, is that correct?

Dr. LEY. Most of the prison-type testing is in phase 1; yes, sir.

Senator DOLE. Now, out of 15,000 new drug investigators, there have been a total of 11, I guess, suspended. I assume there are two possible answers. One is that this is only one-tenth of 1 percent of the total, that the obvious response might be that you do not have an opportunity or the facilities or the funds to properly review the other 14,989. Is that a fair assumption?

Dr. LEY. I am not satisfied with our total effort in this area today, Senator. This is a problem, of course, with every administrator, trying to balance one need against another. I would like to see more effort in this. On the other hand, I do not believe that anyone can be expected to visit every one of the 15,000.

There are other aspects to this overall problem that are equally important. Another one would be that we need some more effective means of getting information directly to the clinical investigator.

This pamphlet is an example of the effort, of our direction. It is not a translation in terms of lay language. But it is a good job. I would like to see this type of information distributed more widely to the investigators by FDA rather than rely totally on the sponsor to provide this. But there are educational activities which are very important in this area which I think we should be doing more of.

Senator DOLE. Well, assuming that a law is passed, the one the chairman is interested in, now pending before another committee—this is not a legislative committee—there is still no assurance there would not be some mistakes. The passage of a law in itself does not assure anything.

Second, there should be a presumption that drug companies are seeking good quality drugs and that the investigators are generally

men of integrity, assuming there may be a few who do not follow the regulations. This may also be true in politics and in other things. But there is not any ironclad way—this is the point—to make certain mistakes are not made. There is always that possibility that we are going to make mistakes in whatever we do.

Do you have any suggestions in addition to the two specific suggestions you make on page 11 and the one you discuss on page 7 with reference to the peer review committees?

But I believe as one who is, as has been noted, a very junior member of this committee, that the steps that have been taken have merit and they will be met with some opposition, but at least we are stepping off in the right direction.

Senator NELSON. I guess I asked you, do you know how many IND's are currently pending?

Dr. LEY. There are currently approximately 2,700.

Senator NELSON. In the past 12 months, how many IND applications have been submitted?

Dr. LEY. 900 during this last fiscal year.

Senator NELSON. How many IND's does Dr. Stough's corporation have?

Dr. LEY. 114. We would have to do a search to provide the information for the record on how many are currently active this past fiscal year. That we can provide. I do not have it immediately in front of me.

Senator NELSON. I would appreciate it if you could submit to the committee the IND's that Dr. Stough has had submitted and handled in the past 3 years vis-a-vis all others.

Dr. LEY. We will be pleased to make this available.

Senator NELSON. Then the number of people involved if you have that.

Dr. LEY. This will be available.

Senator NELSON. Could you submit the same for the next four or five investigators with the largest number of IND's?

Dr. LEY. There is no problem with this except for the total number of subjects. This will require considerable effort.

All right; yes, sir.

Senator NELSON. You may submit that for the record.[1]

Counsel has some questions.

Mr. GORDON. Dr. Ley, in your statute, you have something about obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision or under the supervision of investigators responsible to him; also, that it is necessary to obtain the consent of such human beings or their representatives except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings.

Last summer, the Washington Daily News carried a series of articles on testing of drugs on humans. Let me read some of it to you.

In 1963, Welfare Department physicians tested two new drugs on 67 elderly patients at the city's District of Columbia Village facility.

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[1] See pp. 5678–5679.

The tests were part of what the Washington Daily News has found to be a pattern of clinical research with humans, but possibly more important, they may depict the impotence of regulations in the field.

The trials with the drugs were conducted nearly 16 years after an international tribunal had set the norm that humans must volunteer to take part in medical experiments and months after this norm was codified by the United States, yet the Welfare Department physicians did not seek individual consent from the patients involved.

Then further down:

Welfare medical director Dr. Jack Kleh claims drug tests did not undergo the department's review policies because they were "controlled by the Food and Drug Administration and was, therefore, in the scope of responsibility of the research committee." Yet a FDA spokesman claims that they only "monitor" such tests and the burden of obtaining releases from patients is placed squarely on the drug company involved and the physicians it engages to conduct the tests. Dr. Kleh reports these two drugs were handled by Welfare Department doctors.

Now, I understand that in orphanages, children—at least occasionally—are used for human experiments. What I would like to know is how does this problem of informed consent apply to elderly patients in institutions or to children?

Dr. LEY. The consent in this category of elderly patients and children is a difficult problem. If you turn to section 130.37 of our regulations, we have a definition of consent which means that a person involved has legal capacity to give consent and so situated as to be able to exercise free power of choice and is provided with a fair explanation of pertinent information pertaining to investigation of drug, et cetera.

Obviously, this definition does not apply to the case of children or to persons who might be not in full possession of their mental faculties. This is a very serious and controversial area of discussion among medical investigators today. There are many studies that should be done in children if children are to receive the drugs which are available to the adult. Under normal circumstances, the guardian of the child has the right to provide consent for participation by the child in such studies. Similarly, in the case of a person who is incapacitated, senile, or otherwise not mentally capable of giving consent, the guardian or nearest relative would have this power to grant consent for investigational study.

Mr. GORDON. Dr. Ley, who is the guardian of, say, a retarded child in an institution?

Dr. LEY. This would depend upon the situation. If the child's parents are alive, I believe the parents would be the legal guardian. I would have to turn to counsel for further comment on it.

Mr. GOODRICH. That would vary from State to State, Mr. Gordon. In some instances, the superintendent of the institution would be the legal guardian; in other instances, the director of welfare. But in all instances, there would be someone who would be the legal guardian.

Mr. GORDON. But the point here, I think, or at least one of the points is that the relationship between a parent and his or her child would not be the same as a legal guardian to one of his wards, say a superintendent of an institution. I do not think he would have that love or feeling toward the child. The situation is quite different, I think.

In another article in the same series, a doctor claims that there is a widespread practice of using institutionalized patients and indigent persons in public hospitals to try out medical techniques which physi-

cians would not attempt on private patients or persons in a private hospital. Would you comment on that?

Dr. LEY. I can only comment to the extent that the words used in that article are obviously the opinions of the writer. I would like to state that the peer review approach which the Public Health Service has been utilizing for its research grants and these regulations on informed consent have done much within the past 2 years to modify this circumstance.

I would also like to go emphatically on the record, because FDA was responsible for one study in the District of Columbia Village complex, that one study was conducted with full regard to patients' consent and informed consent was obtained with every subject in that particular study. That was the only study that FDA had direct responsibility for.

(The articles referred to follow:)

[From the Washington Daily News, June 24, 1968]

OLD STANDARDS AND NEW THINKING ON TESTING—CLINICAL RESEARCH ON HUMANS: INEFFECTIVE LAWS

(By Nicholas Horrock)

In 1963, Welfare Department physicians tested two new drugs on 67 elderly patients at the city's D.C. Village facility.

The tests were part of what The Washington Daily News has found to be a pattern of clinical research with humans, but possibly more important, they may depict the impotence of regulations in this field.

The trials with the drugs were conducted nearly 16 years after an international tribunal had set the norm that humans must volunteer to take part in medical experiments and months after this norm was codified by the United States, yet Welfare Department physicians did not seek individual consent from the patients involved.

Tho both drugs were new and not approved for public sale, the Welfare Department's Research and Education Committee did not first review the projects and doctors neither sought nor received individual permission from the patients to conduct the tests.

EXPLANATION

Welfare Medical Director Dr. Jack Kleh claims the drug tests did not undergo the department's review policies because they were "controlled by the Food and Drug Administration and was therefore not within the score of responsibility of the Research Committee."

Yet an FDA spokesman claims that it only "monitors" such tests and the burden of obtaining releases from patients is placed squarely on the drug company involved and the physicians it engages to conduct the test. Dr. Kleh reports these two trials were handled by Welfare Department doctors.

One of the two drugs, a pain killer produced by Squibb Company, has never been cleared for public sale. Dr. Kleh suggests it may have been withheld because it caused gastric disturbances in patients.

But he strongly argues that neither of the two drugs was dangerous nor had "serious adverse effetcs."

(The other drug tested was a psychotrophic agent used to control "agitated" senile patients. Developed by Wallace Laboratories, it was later approved for public sale.)

OUR PROBE

During the course of a two month investigation, The Washington Daily News has found a series of tests such as the 1963–D.C. Village experiments, a pattern that includes trials of such concoctions as a diet pill, a patent medicine, a shampoo and an acne treatment.

In a number of the tests it was difficult to discover any logical benefit to the patients involved, in others it was impossible. Subjects for these experiments included juvenile delinquents, retarded children and retarded adults.

The Welfare Department was unable to document that obtained consent of patients or relatives in a number of these tests.

There are nearly 4,000 persons in the city's welfare institutions, most of whom cannot legally give their consent to anything.

They are, in effect, a captive audience; totally dependent upon the Welfare Department for medical care. They cannot choose their physician, approve or disapprove of a treatment technique or agree or disagree to take part in a medical experiment.

OLD STORY

The controversy over regulating medical experiments with humans is not new. Nor is the aspect of controlling experimentation on humans in institutions. In 1948, the Nuremberg military tribunals set forth a 10-point code for clinical research with humans as a reaction to the horrors depicted in Nazi death camps.

The first point reads "The voluntary consent of the human subject is absolutely essential."

Despite the semantic strength of the "code," it was more than 15 years before the philosophy of getting a patient's consent was actually codified in the United States.

It was not until Congress passed a series of amendments to the Food, Drug and Cosmetic Act which strengthened control over the testing and marketing of new drugs. Specifically the legislation empowered the Food and Drug Administration to require drugs be tested for efficacy as well as safety and set down a framework of required "clinical" investigations.

HILL ACTION

New York Sen. Jacob Javits was successful in attaching a rider to this bill which required that the doctors employed by the drug companies or other testing agency explain the test to a patient and obtain consent.

The 1962 law, however, actually shut only a few doors. In the initial regulations written by FDA, the manner of consent, that is whether written or oral, was not specified.

Furthermore it permited doctors to waive getting consent when they believed it was "justifiable" not to inform a patient.

At the same time human experimentation regulations have been painfully evolving, medical research in this country had skyrocketed.

Freeman H. Quimby, a science research specialist at the Library of Congress, prepared a report for Sen. Javits last year that found the American drug and medical research industry was spending 20 times as much in medical experimentation than it had in the 1940's. He estimated the gross expenditure at $2 billion.

He also found: "a growing need for larger numbers of human subjects per clinical trial so that the efficacy, side effects, and precautions for the increasing volume of the new drugs and biologicals can be established with statistical rigor before approval for general use by practicing physicians."

Dr. Henry K. Beecher, a Harvard medical professor, and critic of the standard of medical ethics in research work claims physicians are doing research work under other pressures:

"Medical schools and university hospitals are increasing dominated by (medical) investigators. Every young man knows that he will never be promoted to a tenure post or to a professorship in major medical school, unless he has proved himself as an investigator. If the ready availability of money for conduct research is added to the fact, one can see how great the pressures are on an ambitious young man."

In 1964, the World Medical Association met in Helsinki, Finland and adopted a set of standards for research on humans. This was later called the "Declaration of Helsinki," and won quick support from major U.S. medical associations. It specifically noted that consent should be obtained from relatives or legal guardians if the patient was incapable of rendering it. It said written consent was preferable.

TROUBLES

But two years later, when FDA Commissioner James Goddard issued a policy guide calling for "written consent" forms, the medical associations weren't so ready to go along.

"It is impossible for the commissioner to codify realistically, in the form of a policy statement, the legal requirements for valid consent under the myriad

varying circumstances which exist . . ." wrote American Medical Association Executive Vice President Dr. F. J. L. Blasingame.

In a sense the variation in attitude reflected a mainstream of the human experimentation argument.

The medical profession has generally taken the position that it must regulate itself and that stiff inflexible laws on experimentation would retard medical research and are unnecessary.

[From the Washington Daily News, June 25, 1968]

RIGHTS OF TEST PATIENTS VERSUS SOCIETY'S GOOD—MEDICAL TEST DILEMMA: WHOSE NEED GREATER?

(By Nicholas Horrock)

Willowbrook State School rambles lazily over wooded acres on the Jersey side of Staten Island in New York.

It is, many people guess, the largest institution for care of the mentally retarded in the world and its crowded dormitories house more than 5500 youngsters.

It has also become a symbol in a national controversy over the use of human in medical experimentation: over what one New York State Senator charges has turned the children of Willowbrook into "human guinea pigs."

ITS USE

Twelve years ago a team of research physicians from New York University began a series of investigations into the cause and treatment of hepatitis and measles. Among the methods employed in research was the purposeful giving of hepatitis and measles to children in the institution.

Outside of medical journals the testing received little critical or public attention until 1965 when a Harvard physician, Dr. Henry K. Beecher, mentioned the experiments in an attack on the medical ethics surrounding human research.

The following year, however, State Sen. Seymour B. Thaler, a lawyer and Democratic representative of Queen's residential Forest Hills area, charged the manner in which the tests were administered was unethical.

"The price of being poor or mentally incompetent in New York State," he argued in a recent interview, "is being a human guinea pig.

"I suspect this largely true thruout the country."

He claims that there is a widespread practice of using institutionalized patients and indigent persons in public hospitals to tryout medical techniques which physicians would not attempt on private patients or persons in a private hospital.

But along with Sen. Thaler's charges comes a dilemma. Can the medical research be regulated to protect humans enlisted for tests without stifling the progress for which so many millions are grateful?

Physicians, both those in research and in patient care, maintain that at some point all drugs and all new techniques must be tested on humans. They claim that if these tests had not been conducted such drugs as quinine and measles vaccine could not be used.

Last year Sen. Thaler introduced two bills designed to control human experimentation.

One of them, which a national drug publication suggested might be a "model for legislation in other states," called for voluntary informed consent in writing in all experimentation.

It barred parents from offering up their children to medical experimentation unless it was an "emergency" in "which immediate treatment was necessary for the physical or mental ailment with which the subject was suffering" and made court review mandatory for other experiments on minors.

The bill, Sen. Thaler said, "got nowhere. Everybody was against it." He said it met widespread opposition from medical societies and from the State Department of Mental Hygiene.

He then introduced what he regards as "compromise" bill calling for "registration" of all research projects, disclosure of where the financial support comes from, written consent of patient or guardian, review of projects by a State Health committee, and medical "insurance" for any subject who suffers further illness as a result of the test.

This legislation, Sen. Thaler said, got a "little farther." It passed the Senate, but was defeated in the state assembly. He has reintroduced the measure and called for public hearings on experimentation in the state.

MAJOR CRACK

By scheduling hearings at which state hospital officials, medical associations and individual doctors can testify, Sen. Thaler may have opened the first major public debate on the need for legislation to control human experimentation.

It is a debate in which Dr. Saul Krugman feels his position is already clear.

"The most important factor in assuring ethical and careful medical experimentation is to have physicians with great integrity."

Dr. Krugman is the physician in charge of the Willowbrook experiments and to him the attack levelled by Sen. Thaler and the news media was uninformed and ruthlessly harmful to medical science.

"No one ever came to me and asked about our work. Sen. Thaler never called me. The first I heard of the charges was when a newscaster called me at 11 a.m and asked me to prepare a retort by the 6 o'clock news."

SCIENCE

According to Dr. Krugman, the Willowbrook experiments were approached with the greatest of scientific care and responsibility.

He claims the project was cleared by University Hospital officials, state school doctors and review boards of Federal agencies and that furthermore the physicians had permission of the parents.

Dr. Krugman acknowledges that the method of obtaining consent has changed, and now reports that a doctor takes time out to brief parents carefully on all aspects of the experiment before consent is asked. It is still obtained in writing, he said.

[From the Washington Daily News, June 26, 1968]

SELF-DISCIPLINE OR FORCE OF LAW?—THE RACE IS ON TO REGULATE MEDICAL TESTS

(By Nicholas Horrock)

The Department of Public Welfare this week is expected to release a new policy proposal governing the use of human beings under its care in medical research.

The policy review was instituted by Dr. Jack Kleh, Welfare medical director, after a series of articles in The Washington Daily News revealed that retarded children, juvenile delinquents and the elderly were being used in tests of such drugs as a diet pill compound, tranquilizers an acne treatment and a patent medicine.

In many of these cases, the department could not document that it sought or received the consent of the patient or the family; in other cases it acknowledged it did not.

In its reviews, the District's Welfare Department has embarked on a problem which has received ever-increasing attention by legislators, physicians, and the general public.

Thru a series of interviews with doctors here and in other states, lawyers, and legislative experts, The News developed these points of stress.

Consent—The bulwark protection encompassed in all treatises on human experimentation since 1946 is "consent." It is a philosophy that a person must understand the hazard of the drug or operation he will undergo and must "consent" voluntarily to take part.

Many research physicians argue that the layman cannot truly comprehend the risks of an experiment and that "informed" consent is often impossible, yet it has remained an unwavering requirement.

Institutionalized guinea pigs—Medical researchers as well as many other sources contacted maintain that the human in an institution, (the prisoner, the mental patient, the retarded), present special problems to a reseacher looking for subjects for an experiment.

The British, for example, virtually exclude all these persons from medical experimentation at all.

As one British physican serving with a government organization here explained it, even the use of inmates of a penitentiary in medical tests raises serious questions about whether the subject actually "volunteered" or was pressured to get involved because of the promise of reward.

He said that the absence of absolute quality of consent among prisoners undermines their scientific value for experimentation.

Possibly more important, however, was his opinion that medical research in Great Britain has not been retarded by the stiff standards in selecting subjects for tests.

Discipline—Herein lies the nub of the greatest controversy about medical experimentation. Who decides if a test on humans is necessary, if consent is "informed" and if all other procedures are valid.

By and large the medical profession both here and abroad have jealously guarded its right to decide what's good for the public. But other voices are creeping in.

In New York, a state senator is proposing a law to oversee human experimentation; in other areas laymen (ministers, social workers) are being placed on medical research review committees to take part in review of projects.

Critics of the medical profession claim its internal discipline is not strong enough to afford the public real protection against the incompetent or overzealous researcher. They cite, for example, one of the few instances in which physicians have been "censured" for research foul-ups—a New York case in which two doctors were given a year's "probation" by the state licensing agency for administering live cancer cells to patients without consent.

As one critic charges, "These doctors never even lost a day of practice . . . is that disciplining them?"

He and others foresee a race in which the profession moves to tighten internal controls before the lawmakers take over.

Senator NELSON. That is a rollcall. I will have to leave. If there are any questions from either the minority or the majority or any of the members, if they want to submit them to Dr. Ley to respond for the record—yes, Mr. Duffy.

Mr. DUFFY. Doctor, there has been some considerable publicity about a study that FDA has released recently. If you would care, perhaps you might submit a statement in regard to that.

Dr. LEY. I would not wish to submit a statement as Commissioner, because that is a very preliminary study. My staff will not finish comment on it until September. At that time, we probably will have a statement.

Mr. DUFFY. All right, thank you.

Senator NELSON. That will conclude the hearing for today.

(Subsequent information follows:)

WAYNE STATE UNIVERSITY,
Detroit, Mich., October 28, 1969.

HON. GAYLORD NELSON,
U.S. Senate,
Old Senate Office Building, Washington, D.C.

DEAR SENATOR NELSON: It has come to my attention, through Geoffrey Cowan of the Center for Law and Social Policy in Washington, that your Committee is about to publish recent hearings with Dr. Ley and other data about new drug testing. I would like to urge you to include our critical review of proposed FDA regulations for peer group review of clinical investigation of new drugs in human beings. These recommendations to FDA from the Council of Health Organizations were prepared by myself and Dr. Henry K. Beecher. They include a proposal to strengthen the entire area of new drug evaluation with special reference to protection of human subjects and scientific adequacy of testing.

The Council of Health Organizations which has undertaken to advise in this matter is composed of three organizations, the Medical Committee for Human Rights, Physicians Forum and Physicians for Social Responsibility, comprising approximately 10,000 doctors, nurses and other health professionals. I will ask our Washington counsel to forward our full statement to you for consideration.

The impact of the Nelson Committee is excellent in the health institutions which I have visited recently.

Sincerely,

PAUL LOWINGER, M.D.,
Associate Professor.

COMMENTS OF THE COUNCIL OF HEALTH ORGANIZATIONS ON PROPOSAL FOR PEER GROUP COMMITTEE REVIEW OF CLINICAL INVESTIGATIONS OF NEW DRUGS ON HUMAN BEINGS

On August 22, 1969, the Food and Drug Administration published a Notice of Proposed Rule Making concerning Peer Group Committee Review of Clinical Investigations of New Drugs on Human Beings. 34 Fed. Reg. 13552–53. The notice stated that interested persons had 30 days to submit written comments on the proposal. By letter of September 17, 1969, the Council of Health Organizations ("The Council") requested an extension of time for the filing of its comments. A 30-day extension was granted.

The Council is a coalition of medical organizations, including the Medical Committee for Human Rights, The Physicians Forum, and Physicians for Social Responsibility. The Council represents the interests of more than 10,000 health personnel on issues of national health policy. The Council and its constituent organizations are concerned with the social aspects of health care and the responsibility of the health professions in the society.

Since many of our members are actively engaged in new drug testing, the Council has a special interest in the FDA's methods of insuring the safe and effective development of new drugs. We are familiar with the tragic consequences of unsafe or inappropriate new drug tests. We know that testing must be more effectively regulated, not only in order to produce good scientific data, but also to protect the safety and welfare of the human test subjects. The drug industry appears to share this view. The drug manufacturers and new drug investigators who had filed comments on the FDA's proposal by the time these comments were prepared, do not question the basic thrust of the proposal—more effective review of new drug tests on human subjects.

The Council considers the FDA's proposal grossly inadequate. While it appears to recognize the problem, the proposal is hopelessly fragmentary and vague. Unhappily it does not represent a meaningful step toward effective regulation. On behalf of thousands of members of the health professions who have a professional interest in adequate drug testing, the Council urges the FDA to reconsider its proposal and to seize this opportunity to take effective action.

In these comments the Council will analyze the problem of new drug testing on human subjects, set out the inadequacies of the FDA proposal, and suggest some methods for establishing meaningful review committees

In the preparation of its position, Dr. Henry K. Beecher served as a consultant to the Council. A statement released by Dr. Beecher on October 6 regarding the FDA proposal is appended thereto.

I. THE PROBLEM

The ethical and practical problems inherent in new drug testing on human subjects pose a dilemma which requires great sensitivity to resolve. America prides itself on new developments in medical science and people have come to expect new scientific advances each year. Doctors and patients across the country anxiously await the development of new drugs—yet for all those who await the benefits of new drug testing, who is willing to share the risks? The FDA must daily deal with the tension between the government's obligation to safeguard the rights and safety of test populations and its obligation to assure that the safety and efficacy of new drugs has been demonstrated by human experimentation before new drugs are made available to the general public. As members of the health professions, the members of the Council of Health Organizations appreciate the difficulty of finding suitable and acquiescent patients, of fully informing them of the nature of the test and how it may affect them, and of providing adequate medical supervision once a test is underway.

The welfare and safety of the test population for new drugs has never been adequately protected. Every few years some freshly revealed drug testing abuse shocks the conscience of the nation. The studies conducted on prison inmates by Dr. Austin Stough have been the focus of recent attention. Five years ago the public was aroused by the case of 22 elderly, seriously ill patients at the Jewish

Chronic Disease Hospital in Brooklyn who were injected with live cancer cells as a part of a research project. In 1966, Dr. Henry K. Beecher published under the title "Ethics and Clinical Research" in the New England Journal of Medicine, 274:1354–1360, a study of 22 cases of questionable testing practices.

Those of us in the health professions know that the pressure on a new drug investigator to produce results are often so intense that it is all too easy to treat subjects in an assembly line fashion. Moreover, the investigator, by virtue of his role, does not have sufficient detachment to weigh objectively the sensitive questions involving the rights and welfare of the human subjects of his tests.

These problems are most acute in tests involving the poor, the dispossessed, and the helpless. Since few people are anxious to participate in medical experiments, drug investigators understandably make heavy use of those people least able to resist the investigator's request. Such people are especially valuable to the investigator when they can be tested and observed in institutionalized settings such as orphanages, prisons, mental hospitals, and homes for the elderly. Experiments in hospitals also tend to utilize the poor since they are, in effect, wards of the state and have no private physician to protect their interests.

The FDA's 1967 regulations requiring informed patient consent (21 CFR § 130.37) address this problem—but they do little to protect society's outcasts. What does it mean to require the informed consent of orphans, the senile, the mentally ill, or their respective guardians? How much information must they be provided? What kind of independent decision can a prisoner make when he believes that his consent will secure favorable treatment and better prospects for parole?

Some outside group, independent of the investigator and the new drug sponsor, is needed to protect the rights and safety of human test populations. The FDA has proposed that "peer group committees" be established to function as an independent reviewing body. We agree that much good could be accomplished by an experienced, independent review committee operating under a clear mandate to safeguard the test subjects' rights, safety, and welfare. Yet the FDA proposal would not establish such groups.

The National Institutes of Health have led the way in the development of peer group committees to review experimentation with human subjects. In a well-thought-out pamphlet entitled "Protection of the Individual as a Research Subject," Public Health Service, May 1, 1969, the responsibilities and characteristics of the peer group committee are set out in considerable detail.

The peer group review committees proposed by the FDA are loosely patterned after the PHS–NIH peer groups, but the detailed provisions of the PHS–NIH scheme—which assure the effectiveness and independence of the PHS–NIH peer groups—are omitted from the FDA proposal. What is more, while it may make sense to establish a peer review committee in a hospital or university setting, the FDA proposal does not address itself to the difficult problems of adapting the peer group concept to such institutions as prisons or orphanages.

It is arguable that the peer group review concept is inapplicable as a real solution to the problems of testing in institutions in which medical research is not normally carried on in a professional setting. Perhaps it will prove to be too cumbersome and expensive in practice. However, for the present, the review committee approach, if constituted along the lines proposed by these comments, holds sufficient promise so that it should be established.

The Council recognizes the complexity of the issues involved in policing new drug testing. The Council proposes that the Food and Drug Administration, perhaps with the cooperation of the NAS–NRC, establish a procedure—which might include FDA hearings—for developing information and soliciting opinions which will enable the FDA to formulate a long-range strategy to assure the welfare of test subjects—including appropriate guarantee of the scientific necessity and adequacy of new drug testing. In conducting the study, the Food and Drug Administration should solicit the participation of public groups—consumer, patient, para-professional, and health care groups—as well as drug manufacturers and new drug investigators.

Detailed information should be accumulated on new drug testing: which kinds of institutions are most frequently used; which classes of the population normally are used for new drug experimentation; what percentage of new drug tests are conducted in scientific and professional settings as opposed to other institutional settings; what percentage of new drugs are tested by individual practitioners not operating in any institution. The inquiry should explore the way that the peer group review system has operated under the NIH–PHS system.

The FDA should also consider alternative or supplemental approaches to this problem, including solutions which are less oriented toward individual institutions than the peer group review committee. It may be that the FDA itself should set up a number of regional panels to oversee and review the testing of new drugs.

II. ANALYSIS OF FDA PROPOSAL AND SUGGESTED AMENDMENTS

The FDA Peer Group Committee proposal was apparently developed in the wake of the testimony of Commissioner Herbert Ley on August 12, 1969, before the Subcommittee on Monopoly of the Senate Select Committee on Small Business. In testifying on the use of human subjects for new drug testing, Commissioner Ley stated that the FDA was developing a "peer group" proposal, which, he indicated, would help insure the scientific adequacy of new drug tests and help protect the rights and safety of test populations. While the Council agrees that action is sorely needed in both of these areas, the Council submits that the proposed peer group committee proposal does not deal effectively with either. Our major objections fall into four categories:

1. The composition of the review committee would not assure sufficient competence or independence;
2. The responsibilities of the review committee are almost totally undefined;
3. The authority of the review committee is undefined;
4. The range of the new drug testing situations covered by the committee proposal—which is limited to Phase 1 and 2 tests in institutional settings—is too restricted.

The Council urges adoption in lieu of the proposed regulation, of a more detailed and carefully articulated system of review committees, to be implemented at once, to provide supervision of new drug testing in all appropriate situations.

1. *Composition of the review committee*

(*a*) *Criticism of FDA proposal.*—The regulations fail to spell out methods by which review committees may be selected to assure that the committees are truly independent and competent to review the testing of new drugs on human subjects.

In the present FDA proposal, the selection process is totally undefined and the possibility that the committee would be a "rubber stamp" is left open. The entire committee apparently could be chosen directly or indirectly by the drug sponsor or by the investigator. Apparently the FDA anticipated that the selections would somehow be made by the institutions, though this requirement does not appear in the regulations.[1]

Even were it established that institutions would name their own committees, major questions about committee membership would remain. Neither the regulations nor Dr. Ley's testimony specify whether the committee members would come from within the institution itself, what their qualifications should be, or whether their qualifications could be reviewed by the FDA.

Other significant questions are raised by the FDA's use of the Public Health Service peer group committee model, since those committees are specifically designed for the universities, research institutions, and hospitals which do research with NIH funds. There is reason to doubt that the same model without modification would suit the prisons, orphanages, or homes for the aged where new drugs are often tested. The NIH–PHS program is grounded on the assumption that all members of the hospital community share a professional concern about experimentation with human subjects. As a result, the staff has the competence and motivation to make certain that the hospital selects a knowledgeable, concerned, and objective review committee. There is no evidence that any similar widespread concern and competence exists in other kinds of institutions. As a result, an investigator operating in a prison or orphanage might have inordinate influence in choosing the members of the committee. Furthermore, if the committee members come from within the institutions—as the NIH–PHS committee members often do—there is little likelihood that they would have either the requisite interest or competence. It is unclear who on the staff of a prison, for example, is

[1] Dr. Ley testified before the Subcommittee on Monopoly of the Senate Select Committee on Small Business on August 12, 1969, that the review committees would follow the model of the committees which the Public Health Service has required institutions receiving NIH grants to establish. He said: "The peer group set up by the Public Health Service is a group of physicians, lawyers, ministers formally appointed by the institution—the hospital in the present contract [sic], although it would be equally applicable to a prison situation—formally appointed as the reviewing body for all investigational work dealing with human subjects carried on in that institution."

a "peer" of the investigator. In our view, to speak of a "peer group" in a prison is a non sequitur.

For the review committee concept to work, the committees will have to be genuinely independent. The proposal pays lip service to the concept of independence in requiring "assurance that the review committee does not allow participation in its review and conclusions by any individual involved in the conduct of the research activity under review (except to provide information to the committee)." But independence requires something more. It requires that the committee be selected in some objective manner and it requires that its members have a degree of experience and expertise which staff members at institutions like prisons and orphanages may not have or recognize.

(*b*) *The Council's proposal.*—Some institutions in which new drugs are tested have preexisting peer group committees, established to meet the Public Health Service requirements. At present, most and perhaps all of those committees review all research done by their institutions, including tests of new drugs. If those committees are functioning adequately,[2] they presumably could continue to oversee research on new drugs undertaken within the institution. This would avoid administrative duplication and help assure supervision by a group with some experience and sophistication. The names and qualifications of persons on such committees should be submitted to the FDA on Form FD 1571.

For institutions which do not already have peer group committees, the FDA's regulation should establish guidelines for instituting review committees. A description of the selection process and the requisite qualifications for committee memberships should be included. In prisons, orphanages, and homes for the aged, the institution staff would probably not include enough appropriately trained personnel to compose a competent review committee, nor would they have the expertise or resources necessary to select a review committee which could, in the language of the proposed rule, "assure complete and adequate review of research."[3]

Participation by the investigator or the sponsor of the research in the nomination or selection of peer group members should be explicitly prohibited in the regulation. The regulation should require among the members of the commitee at least the following: experts adequately qualified to assess the potential medical benefits of the research and consider potential benefits against risks; an attorney selected, perhaps, by the local bar association; an independent physician having no connection with the institution or the investigator, selected, perhaps, by the local medical association; qualified representatives of appropriate universities; and representatives of the community. The names and qualifications of all members of the review committee should be submitted to the FDA on Form FD 1571 for its approval. The mode of selection of the committee should also be explicitly stated. The FDA staff should be available to assist institutions which lack the necessary competence in constituting a review committee.

In some cases a single review committee might review the new drug testing in a number of institutions in the same area. Several institutions might jointly establish a single review committee, or one institution might accept a committee established by another institution.

2. Responsibilities of the review committee

(*a*) *Criticism of FDA proposal.*—Like the Public Health Service peer group committees on which they were modeled, the FDA committees ought to have their purposes and functions carefully outlined in agency regulations. Unfortunately, the FDA proposal leaves the responsibilities of the review committees unspecified. There is, indeed, much confusion about the appropriate subject matter for the committees. In one sense their power seems very broad: they are "responsible for initial and continuing review and approval of the experimental project;" the investigator must "report to the commitee for review any emergent problems or proposed procedural changes which may affect the status of the investigation;" and "no change will be made without committee

[2] The adequacy of the functioning of existing peer group committees is a matter which the FDA should consider.

[3] The Public Health Service states in a similar context:

"The membership [of a review committee] should possess not only broad specific competence to comprehend the nature of the research, but also other competencies necessary in the judgments as to the acceptability of the research in terms of institutional regulations, relevant law, standards of professional practice, and community acceptance. The committee's maturity and experience should be such as to justify respect for its advice and counsel." *Protection of the Individual as a Research Subject,* Public Health Service, May 1, 1969, p. 6.

approval except where necessary to eliminate apparent immediate hazards." Any "modification of the experimental design on the basis of experience gained" must also be made with the approval of the review committee. Yet just what all of this reviewing will mean is not clear.

The central concern of the FDA proposal seems to be to assure the safety and welfare of human subjects of new drug tests. As stated in the preamble to the proposed regulation, the committees are to assure appropriate supervision and "adequate safeguards for the health of human [test] subjects." This is an appropriate function for an independent peer group committee and closely resembles the purposes of the Public Health Service committees.

Commissioner Ley suggested in his testimony before Senator Nelson's Subcommittee on Monopoly of the Select Committee on Small Business on August 12 that the review committees would also provide a check on a test's scientific adequacy and necessity. This aspect of the review committee's role is totaly ambiguous in the FDA proposal. The scientific quality of new drug testing badly needs to be improved,[4] and some consideration of the scientific adequacy and necessity of a new drug test is essential to a consideration of the rights and welfare of test subjects.

(*b*) *The Council's Proposal.*—The regulations should set forth in some detail the legitimate concerns and method of operation of the review committees.

The review committee should, at the least, explicitly be given powers analogous to those of the committees established under the NIH grants. The NIH–PHS regulations require that its committees shall assure that—

(*a*) the rights and welfare of the individuals involved are adequately protected,

(*b*) the methods used to obtain informed consent are adequate and appropriate, and

(*c*) the risks to the individual are outweighed by the potential benefit to him or by the importance of the knowledge to be gained." *Protection of the Individual as a Research Subject,* Public Health Service, May 1, 1969, p. 1.

All of these considerations deal with the welfare and rights of the patient population. The assessment of the relative benefits against risks also calls for some scientific expertise and understanding of the particular area of medicine in which the experimentation is taking place.[5]

The review committees will have to be especially vigilant to insure that, in the words of the NIH–PHS regulation, "adequate and appropriate" methods are "used to obtain informed consent." Major problems were left unresolved by the FDA regulations adopted in 1967 (section 130.37) concerning consent by test subjects. For example, obtaining the consent of children in orphanages and the senile in homes for the elderly is a delicate matter at best. Often their legal guardian is the state. Members of such groups would benefit from a review committee acting in their interest to make sure that the state safeguards their rights.[6] The committee should also consider whether the information to be given to a test subject is adequate for him to make an informed judgment, in light of all the circumstances.

There are other areas in which the review committee's responsibilities will be especially great. It ought to develop enough information to allow it to be satisfied that the investigation provides maximum assurance of patient safety and that members of the test population receive adequate supervision and medical attention.

3. The authority of the Review Committee

(*a*) *Criticism of FDA proposal.*—No enforcement power is specified in the FDA's proposal. While the review committees are made "responsible for initial and continuing review and approval of the experimental project," the proposal does not describe what happens if a committee disapproves of a project. The

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[4] The FDA can impose new testing standards by devices specifically designed for that purpose. The new regulations providing "Hearing Procedure for Refusal or Withdrawal of Approval of New Drug Applications and for Issuance, Amendment, or Repeal of Antibiotic Drug Regulations; Interpretive Description of Adequate and Well Controlled Clinical Investigations" which the FDA published in the Federal Register on September 19 are a useful step in this direction. (21 CFR § 130.12, § 130.14, and § 146.1).

[5] The Council believes that it can never be ethical to ask a person to take the risks associated with new drug testing if the tests themselves are unnecessary or will not, because of their design, yield significant results. Hence, any committee charged with protecting the rights and safety of test subjects must have the capacity to review the scientific aspects of the tests.

[6] Indeed, it is arguable that such groups should never be used in new drug testing where there is no expected benefit to the subject.

proposal provides no mechanism by which the committees could prevent the investigators from taking what they regard as unwise action. Nor does it effectively give such power to the FDA itself, since the proposal provides no method for even informing the FDA of committee findings or concerns.

When Senator Nelson asked how the FDA would know "whether the peer group was just perfunctory," Dr. Ley answered:

"There would have to be as part of the submission of the investigational institution to the sponsor and from the sponsor to us a statement that such a peer group existed, that such a peer group had reviewed the material, and that the minutes of the group were available and where. This is the minimum."

Actually, this "minimum" is not included in the FDA proposal. The proposal does not require the investigator or the sponsor to insure that minutes either be kept or be made available.

(*b*) *The Council's proposal.*—The regulations should state that no new drugs can be tested without the approval of the review committee. When it does not approve of a particular aspect of a new drug test, the review committee should report its findings to the institution as well as the investigator. In appropriate cases the review committee should immediately reports its conclusions to the FDA.

The review committee should analyze the testing program for research at the outset, before any work has begun. If the review committee concludes that any aspect of the program shows insufficient concern for the interests and welfare of the test subjects, it should be empowered to disapprove the program or require modification. In addition, the review committee should in a systematic way periodically review the testing procedures. The FDA proposal requires that the investigator return to the review committee for review when he is changing his protocol. But it is equally important that the review commitee from time to time review the progress of the tests on the basis of reports from the investigator and other data. For example, other developments in the scientific community might obviate the necessity for the particular experiment being undertaken; or preliminary test results might reveal unanticipated danger to test subjects.

The regulation should state that review committees should review the reports submitted by investigators to the new drug sponsors to make certain that such reports are complete. The review committee should also make a report detailing all of its findings and conclusions, copies of which should be sent both to the institution involved and the FDA. Minutes of review committee meetings should be kept and made available to the FDA on request.

4. Coverage of the review committees

The most glaring omission of the proposed regulation is the failure of the FDA to deal with phase 3 testing problems or to provide a review mechanism for noninstitutional tests of new drugs. Any comprehensive scheme adopted by the FDA to safeguard the rights of human subjects on whom new drugs are tested must deal with phase 3 problems as well as phase 1 and phase 2. In addition, the FDA should devise a method of bringing noninstitutional investigators under the surveillance of a review committee, perhaps through regional review committees.

III. CONCLUSION

For the reasons stated in these comments, the Council urges substantial revision of the proposed amendments regarding peer group committee review. As presently drafted, the proposal gives the delusive appearance of dealing in a meaningful way with a major problem. See *New York Times*, August 13, 1969, page 1.

The Council and its members are prepared to assist the FDA staff in the drafting of a meaningful review committee proposal and in undertaking an analysis of other approaches to this problem.

(Whereupon, at 12 noon, the subcommittee adjourned, subject to the call of the Chair.)

APPENDIXES

APPENDIX I

STATEMENT OF EDWARD R. PINCKNEY, M.D.

I am Dr. Edward R. Pinckney and I am here at your request to discuss the role of medical advertising in relation to the practicing physician's knowledge of drug use—that is, the role the pharmaceutical company plays in its attempt to influence rather than honestly educate the doctor who prescribes drugs. There is no question that drug advertising has a profound effect on both the cost as well as the quality of medical care by causing overuse and misuse of drugs. The one particular aspect of drug promotion I would like to emphasize is the role of the scientific medical publication that carries medical ads within its pages and the influence of those ads on the doctor, which eventually reflect on the health and safety of the doctor's patient.

In the past 15 years I have been an editor of five different medical journals, including *The Journal of the American Medical Association.* I have written, and had published, more than 100 scientific articles and editorials in medical journals, and I have written (jointly with another physician) one book for the medical profession. I have written four other medical books and authored a daily and Sunday newspaper column for the general public all stressing how best to utilize physicians, drugs, and other medical services. Academically, I have held professorial positions on the faculty of two medical colleges, and while teaching at Northwestern University Medical School, I was chairman of Preventive Medicine and Director of the Comprehensive Medical Clinic. I have also been in the private practice of medicine, specializing in internal medicine.

To begin, I would like to state that in spite of any laws or regulations that now exist that allegedly control medical advertising, it is my opinion that the primary responsibility for the ethical and accurate advertising of drugs to the medical profession lies within, and on, the editorial board—and especially the editor—of the medical journal that carries the advertisement. I say this because the medium of the scientific journal is really the only medium over which there can be peer control and especially because this is the one medium that can command the professional respect of the practicing physician. (Unfortunately, many physicians do not "respect" governmental agencies.) I unhesitantly state that the problems related to drugs, such as their use without proper scientific indication or the use of combinations that tend to cause more harm than good or even the dangerous "side effects" that offset the intended therapy, come more from the lack of ethical standards within the leading medical organization than from a manufacturer trying to make a profit from his product.

To be sure, there is the standard cliche retort by some physicians that drug use can only be decided by the prescribing physician at the moment of diagnosis and that only prescribing physicians can take into account all the various judgemental factors that exist at that time that lead to the drug to be used. Of course, there can be no argument about this; at the same time, it is my belief that this same physician's judgment has been wrongly influenced by what he has read in advertisements for the drugs he uses. And, since most physicians learn about drugs, especially the newer drugs, through advertising it is not wrong to concentrate on this medium of information.

Mention must be made at this point of the "detail man" or drug company representative who visits the doctor personally to promote his company's products. Even with laws on the books, it is virtually impossible to control the detail man's "pitch." While it is a known fact that drug companies spend the major portion of their advertising dollar on "detail men," what is not often publicized is why. Simply put, this is the one approach to the doctor where there need be no negative emphasis on the drug being "pushed." I

can say, as a result of my own direct experience with "detail men," that rarely, if ever, do drug company representatives mention, let alone stress, the known side effects of the product they are promoting.

I must also say, at the outset of my statement, that I really cannot blame the pharmaceutical manufacturer for trying to promote his product for profit; profit is primarily why he is in business. If someone has a product to sell, it is only natural that he wants that product to be known as the best there is and not, willingly, disclose any defects. But before you refute this opinion with still another cliche that drugs are different because they effect a person's health, think how the law allows, and even excuses, "puffing" in real estate sales where an entire family's health and well-being can virtually be destroyed because no one dares stop a real estate agent from grossly exaggerating the merits of a home that, after purchase, turns out to be a real "dud."

So it is that I feel strongly that if drug companies are going to be forced to be completely honest, the way to achieve this goal is not primarily through legislation but through a form of professional control that is respected and followed by the medical profession. You have had legislative controls of drug ads on the books for years now and, even including the ones that went into effect last month, the result of the laws has not brought about any improvement as shown by lessened drug reactions, hospitalizations as a result of overuse, and misuse, of drugs and really, what is worst of all, failure to be cured because of use of the wrong, or ineffective, drug (an example might be the use of an antibiotic against a bacteria that is resistant to the drug, or the use of a drug without providing the proper environment). What we have not had, however, no matter what you may hear, is absolute professional control over the way a drug is advertised; control that is depended upon by physicians because they respect the authority in control.

Again, it is my opinion that the majority of physicians learn about new drugs through advertising as opposed to postgraduate courses on drugs or scientific articles in medical journals. And the relation of drug information on advertising pages compared to editorial pages offers a good example of what I mean. A randomly selected issue of *JAMA* (as *The Journal of the American Medical Association* is best known) contained advertisements for nearly 100 drugs and other therapeutic products. Within that same issue of *JAMA*, the editorial section contained only five specific references to drugs, four of which were letters to the editor. I probably should mention how I "randomly" selected the particular issue of *JAMA* (May 26, 1969); it arrived in the mail on the same day I received your request to testify.

But returning to the "editorial" material within a medical journals pages, it must be stressed that insofar as editorial material is concerned (the scientific article or report on a case) if the title of the article does not catch the doctor-reader's eye because he cannot see any relationship to his own immediate needs, then he is not as apt to read the article—even if it contains extremely essential information about a drug from the strictly scientific point-of-view. In contrast, advertisements for drugs make a direct appeal to the doctor-reader, implying an answer to his most commonly seen patient-problems.

At this point I should like to take a "typical" ad, from the same randomly selected issue of *JAMA*, and demonstrate just how misleading it can be (Exhibit A).[1] This ad appeared right up front in the magazine, within the section I and many other physicians turn to first: "Medical News."

The product advertised is Ananase, a tradename for an enzyme product claimed by the manufacturer to: "reduce inflammation and edema," and to speed up the healing process. As you know, inflammation is the way the body—or more specifically some tissue of the body such as skin—reacts to injury. We say a tissue is "inflamed" when it is red, hot, swollen and painful. More often than not these are the symptoms complained of by the patient. This particular ad makes a distinctly separate claim that its product is effective against edema, or swelling of tissue usually without redness or heat. I am sure you are all familiar with the fact that a swelling on your skin can be quite painful even if not red or hot. At the same time, edema can also be simple swelling of tissue filled with fluid as is seen when the ankles become swollen as a consequence of heart or lung disease, varicose veins, or just standing too long. The eyelids can be edematous, or swollen, after rubbing, lack of sleep or too much liquids and/or salt.

[1] Exhibits retained in committee files.

Also, inflammation, or injury, say to the skin, need not always come from an accident; the act of surgical incision is considered of equal injury. This is pointed out because the ad stresses that surgical, or post-operative, patients recover faster if the promoted drug is administered.

A physician, reading this ad and accepting it at face value, would be justified in prescribing this drug in the firm belief that his patients would recover much, much faster after surgery or after virtually any form to injury, or if suffering from edema not necessarily related to injury. In the best interests of his patient, he would certainly be tempted to utilize this product for his patient's benefit and, in fact, might even be considered negligent for delaying his patient's progress by failure to prescribe the drug.

But now let us look at this ad more closely. The first definitive implication within the ad's "copy" is that it reports on *three* different studies or evaluations of the product. This is indicated by the three separate "references" near the end of the ad's reading matter. Such references are an extremely important part of most ads for drugs (the exception being ads that are only intended to remind physicians of the *name* of a previously advertised drug; a way of repeating the fact that the product exists and its purpose). These references allegedly tell the doctor that the product has been tested and obviously found superior (or why advertise). They also intend to indicate the extent of the testing and ostensibly the efficacy and safety of the product. In other words, the references in an ad lend authenticity and professional backing to the product supposedly by impartial clinicians (clinicians meaning doctors who work directly with patients—either their own or in clinics, as opposed to academicians and theoreticians).

Note that the second and third references are papers by the same author. In the second paragraph of this ad (the fifth line) there are the words: "In another study . . ." which alludes to number 3 in the references. In actual fact, these words are untrue. The "another" study is nothing more than a continuation of the same study numbered 2 in the reference list. The author of the study himself calls his first 24 patients (cited in the ad as reference 2) a "progress report" leading specifically to reference 3. Thus, the two seemingly separate studies, so indicated by the ad and implying greater (diversified) testing of the drug than was actually performed, are in reality one and the same study by the same man.

Now let us look at the specific study referred to in the ad, as actually reported by the doctor in his published article. The ad, in the second paragraph, makes the point that the treatment period of "inflammation following surgical procedures" was much shorter for patients who received Ananase. The ad does *not* say that the same article reports, with equal emphasis, that only 29.2 of these patients who allegedly healed faster had an "excellent" or even "good" response—as compared to the average response. This measure of the *quality* of the response to the drug, following surgery, was the poorest result obtained in this doctor's study. It is not therapeutically significant when less than one of three patients who take a drug show no better results than if the drug were not taken at all.

That this drug company was well aware that a doctor would look for some indication of the quality of response to the drug, can be proved by the fact that the third reference, or later report on the same study, calls attention to the quality of results. Evidently to nullify the lack of quality that did not accompany the claimed shortened time for healing, in the second reference, the advertiser takes data from the third reference to show that 27 out of 46 patients (still only a bit more than half) were judged to have "superior" results. Of even greater interest, is that in this third reference, which is used for quality claims, the doctor reports that far *less* than half the cases of inflammation from contusions, abrasions, abcesses and perforating wounds—a form of surgical wound, achieved so-called "superior" results. This observation was *not* mentioned in the ad. The question arises, why did the drug company not use the corresponding figures from the *same* report in the ad?

Obviously the ad is intended to promote the time factor in healing. Why, then, does the ad not tell that the doctor who made the study used to support the company's claims also stated unequivocally that when he measured the number of days it took to heal "soft tissue trauma," another term for inflammation, the time for healing for those who took the advertised drug was identical—*not faster*—to the number of days it took similar patients to heal who did not take the drug. Thus the drug did not accelerate the healing process here but this fact is ignored in the ad.

Also missing from this ad is the type of surgery performed (the technique used), the part of the body operated upon, the type of post-operative dressing or bandage used and many other factors that any surgeon will tell you without which it would be worthless to try and evaluate the effect of any particular drug on healing.

If all appropriate information about this drug is to be offered to the physician, it then becomes of interest to know why the company did not cite a very late reference (in the medical journal *Angiology* for January, 1969) of another study of their drug. In this study, where Ananase was tested against a placebo, not one of the symptoms of inflammation showed any significant statistical difference, or improvement, whether treated by the drug or by the fake, inactive, substitute. As a matter of fact, when the patients in this latest study were evaluated by doctors who did not know whether the patient was receiving Ananase or not, the evaluating doctors felt that over 70% of those who took the placebo had improved over what they normally would have expected. Should a doctor, reading this ad for possible use on his own patient, be told this information before he decides to employ the drug? Of course he should.

Believe me, gentlemen, this ad is not unusual. In fact, in order to emphasize my point that advertisers only use information they want to, and exclude all pertinent data, let me show you a different ad for the same product. (Exhibit B) This ad stresses "a superior therapeutic response with Ananase in 4 out of 5 cases—of hematoma." The reference to back up this claim was used in the previous ad (Exhibit A). In this ad, however, the other reference in the previous ad (the one that reports on the entire study by the same man) is omitted! A look at the results obtained in that reference (which was good enough to use in a different ad) will easily show why it was forgotten. In the omitted reference the same doctor stated that out of 59 cases of hematoma (a swollen black and blue result of injury) and contusions (bruises), only 28, *or less than half*, obtained "superior" results when they were given the drug. 31 patients received the drug but the results were no better than would have been expected had the drug not been used. This is certainly *not* a "superior" response in 4 out of 5 cases, as the ad claims.

Finally, if a doctor wants a complete picture of the drug, Ananase, he might read *The Medical Letter*, a private publication on drugs without advertising support. Volume 4, page 60, of *The Medical Letter* contains a report on the use of Ananase, the specific enzyme in the advertisement under consideration. The editorial board, and its professionally respected consultants state, without equivocation, they "find no satisfactory evidence of the effectiveness of Ananase." What is important about the published findings as they appear in *The Medical Letter* as opposed to the claims in the ad is that both cannot be right. And this is not merely a quaint controversy where two opposing parties offer divergent opinions with no real consequences dependent on who is right. It is of great importance to the patient who may well pay a great deal of money (either directly or through some government or private agency) for something that does not work. What is even worse, use of this drug could delay proper healing by depending on something ineffective or it could cause a severe sensitivity drug reaction that subsequently would cost the patient a great deal more money and anguish than did the original illness.

Now it must be admitted that this ad saw print in spite of the regulation on drug advertising that exist. This brings me back to the matter of editorial control over advertisements in scientifice medical journals. If conditions that governed the AMA 15 years ago were still in effect, this type of ad would never have appeared in an AMA publication. It was just about 15 years ago that the AMA abolished its council approval for products to be advertised in AMA media. In 1953, just preceding the removal of council control over advertised products, the AMA sponsored a survey made by Ben Gaffin & Associates to specifically determine why advertising revenue was falling. The result of the Gaffin study was quite blunt in showing that *the* major cause of why the AMA received less and less money from advertising was because of the meticulous scrutiny given to any product to be promoted in an AMA publication. Drug manufacturers resented not being able to say anything they wanted to about their product in AMA publications so they simply took their advertising dollars elsewhere where their claims were not questioned.

Although it is circumstantial, to be sure, the AMA initiated a study to find out why they were taking in less and less money through advertising. The study revealed that the strictness of the AMA Council on Drugs—the council wanted

proof of an advertiser's claims—was the reason. There followed, close upon the results of the survey being made known, the sudden demise of virtually all AMA "screening" of drugs. And then AMA advertising revenue began to climb again.

While on the editorial staff of *JAMA*, I noted many discrepancies in the ads published within *JAMA's* pages. I brought these to the attention of the editor and each time I was referred to the "advertising review committee," which was not part of the editorial department of *JAMA*. In reality, the "advertising review committee" (and this was after the abolishment of council review for all AMA advertised products) was nothing more than one woman, medically untrained, who glanced at the ads, and seemingly did nothing more than admire them for overall appearance. Not once was any overtly misleading statement in an ad corrected. I can say, therefore, that although the AMA claimed to have "advertising principles," such principles never really existed in fact.

I remember quite distinctly pointing out specific discrepancies in certain medical ads such as the use of alleged references to support a product, even though the "cited" reference did not exist or was one reference that was duplicated and even triplicated to appear to be separate and distinctive supportive studies. In far too many instances, when tracked down, all the alleged references turned out to be one small study supported and paid for by the company advertising the product. There were instances where a reference was cited as if in absolute scientific support for the drug advertised, yet if that reference was researched it turned out to be nothing more than a general discussion of the overall chemically related group of drugs, of which the advertised product might be considered a part. Some references merely turned out to be a one word mention of the generic name of the product being advertised, and it is interesting to note that the same drug company that denounced the use of generic products did not hesitate to refer to that generic product in support of its ad.

In other words, the reference cited in ads which were intended to indicate general clinical testing, acceptance and success of a drug—in order to influence the potential prescription for that drug—were not at all what they implied. And unless the doctor-user of the drug traced down the multitude of references, he naturally assumed widespread support for the advertised product.

As a result of my own studies and investigations, I wrote an editorial for *JAMA* (writing editorials was a major responsibility of mine while on the *JAMA* editorial staff) pointing out some of the things I felt were misleading to physician readers. I can, if you desire, read the editorial, but I have attached it as an exhibit (Exhibit C). The editorial was eventually published in THE NEW PHYSICIAN, the official journal of The Student American Medical Association (SAMA), of which I became editor.

Needless to say, the AMA never allowed publication of that editorial. It was specifically vetoed by the present Executive Vice-President of the AMA, who at the time I wrote the editorial, was the man who approved all such editorials before publication. Rather than try and quote his words to me, at that time, I would prefer to quote his printed words, since they say essentially the same thing. In Volume 13, page 10, of the BULLETIN OF THE AMERICAN WRITERS' ASSOCIATION, Dr. Ernest B. Howard, now administrative chief of the AMA, was asked if advertising should be eliminated as a source of drug informataion. Dr. Howard answered: "No. Advertising is the medical journal's principal source of revenue, and I hope it will continue for many years to come."

I cannot help but feel that such an atttiude on the part of the administrative side of the AMA best illustrates another pertinent finding of the Gaffin study on medical journal advertising made for the AMA; that is, the relationship between the editorial department of *JAMA* and the administrative department of the AMA proper. As the Gaffin study revealed: "It is obvious that there necessarily exists a basic conflict of interests between the business office, whose primary purpose is increasing advertising revenue and the editorial office, whose primary purpose is in turning out as professional a publication as possible. Often, what will increase advertising revenue will decrease professional standing."

And that, Mr. Chairman, is what, in my opinion is essentailly wrong with drug advertising today. The professional standards of medical publications have suffered at the expense of bringing in advertising revenue. Frankly, as an AMA member, I also take issue with the concept that the primary purpose of the business office of my association should be to increase advertising revenue, and I feel safe in saying that I am not alone in this attitude. The primary purpose of the AMA, to me, is to represent medicine from a scientific point-of-view and to

offer the medical profession the most *unbiased* information on all forms of therapy.

May I digress for a moment here and say that the information I am offering today is not something I have just decided on. I should point out that I offered some of this information to the Food and Drug Administratin twice in 1963. Had some of my suggestions been adopted then, or had those that were adopted been enforced, an ad such as the one I have exhibited could never have been printed to mislead today's prescribing physician.

Now, let me reinforce my testimony with another ad from the same issue of *JAMA* from which I obtained the Anarase ad, and but a scant 14 pages away from it. Please keep in mind that most physicians will accept this ad at face value simply because it is in *JAMA;* they assume it has been screened for absolute accuracy (Exhibit D).

This ad is for Mandelamine, a chemical to use against infections in the urinary tract (kidneys and bladder). This ad uses five published references to support its claims. Although the ad cites the first reference for one purpose, it is of interest to note that another, important, part of that first reference is not only omitted, but is even contradicted in the ad.

In the ad it is pointed out that an acid urine is essential for the antibacterial activity (of Mandelamine). The ad goes on to say that maximum efficiency of the drug occurs at pH 5.5 or below. I am sure members of this committee understand the terms acid and alkali; the letters pH followed by a number being a specific indication of whether something is acid or not—in this instance we are considering urine. Normally, most people on an average diet will produce urine with a pH of 6, or slightly acid (7 being the neutral dividing point between acid and alkali). When we eat an excess of proteins, it tends to make the urine more acid; while vegetables and citrus fruits do the opposite, that is, make the urine alkaline or with a pH greater than 7).

Now you might possibly remember that at the beginning of my statement I mentioned it was possible for a drug to fail in its intended effect because of improper environment. The use of Manelamine illustrates what I meant; if the drug is not used in a very acid environment, it has no therapeutic effect. This, in turn, is not only a waste of money for the patient but could be even more dangerous than the original infection since an ineffective drug allows the infection to grow and become worse.

To come back to the ad, the first reference used in the ad to support the company's claims not only *stresses* the need for acidifying the urine, it specifies just how acid the urine must be. The original article, indicated by reference number 1, says the pH must be "less than 5." This is *very* acid, and more often than not must be achieved by adding another chemical (e.g., methionine, ammonium chloride, lysine) or forcing the patient to drink a great deal of cranberry juice or take large doses of Vitamin C. In other words, to use this drug without making equally sure the patient's urine is very acid is not only likely to be ineffective but could even be considered negligent.

Now look at the ad again. The ad states that maximum efficiency occurs at pH 5.5 or below. The ad does not hestitate to use reference 1 to support some of its claims, but it evidently does not agree with that same reference when it comes to acidifying the urine. While it may not seem much in the way of numbers, there is a great deal of physiological difference in a pH of 5.0 or below and 5.5. Actually it is as if the acid strength were doubled when the lower figure is used. If the reference's claims for how acid the urine must be is correct, then the doctor who reads only the ad will wrongly feel he is doing a proper job if his patient's urine reaches an acidity of pH 5.5, as the ad says. Thus, by following the ad alone, the doctors may well prescribe an ineffective drug. What is flagrantly missing from the ad is the fact that the doctor must monitor his patient's urine—at the very least once a day—in order to achieve and maintain the proper pH.

In another portion of this same ad, where the effectiveness of this drug is boasted about, it is important to note the "fine print" statement that in a true scientific sense actually discredits the very claim the ad is making. The ad admits, almost as an aside, that those who benefited most from Mandelamine also received greater amounts of antibiotics for greater periods of time. How can you honestly measure the effect of one drug when other drugs were used at the same time? And, with certain antibiotics, especially ones used most often to treat the identical urinary infection for which Mandelamine is recommended, it is best to have an alkaline urine—one that would render Mandelamine completely ineffective.

This brings me to the matter of reading a complete advertisement, without consideration of searching out and reading the supportive references. Do you know how long it takes the average physician—with his knowledge of medicine—to read this particular ad, and to read it for meaning? I asked five different physicians to read the ad so they felt they understood it. The average time was 4 minutes. This may not seem like much in itself, but if you multiply just the ads in the *one* journal where this came from, you would require that average doctor to spend over 6¼ hours on the advertisements alone. And this would not even include a glance at the editorial material—the doctor really should read; nor does this 6½ hour reading time include advertising pages for items other than drugs which make up another 105 pages for another 7 hours. And this is only one of the minimum of ten medical journals that arrive on the doctor's desk each and every week.

I make this point because I want to stress that even if an ad does contain an abundance of information, it cannot be assumed that the physician can or will read much more than the promotion-styled headlines. As a further extension of the reading experiment, I found it took me just about 24 hours of reading time to get through this one issue of *JAMA*. Now add on the time it took me to track down the reference to these ads (with great help of the Los Angeles County Medical Association Library). I can fairly estimate the search took another hour and the reading another three hours.

And as an incidental note, of the five doctors who read the Mandelamine ad for me, for timing purposes, not a single one could immediately, or correctly, name a "ureasplitting bacteria" as so importantly specified in the ad. Thus it is easy to see that a careful follow-up to this ad would require a great deal of reading before the drug could properly be used. But if the reader accepts all the claims, and directions, at face value thinking it absolutely accurate, he could fail to treat his patient successfully. And this is where the editorial board of the medical journal that published the ad comes to the fore.

If the editorial board of *JAMA*, through its experts and consultants who have access not only to the complete references used in an ad, but also to references not used by the drug company, took the trouble to review the claims of the ad, and clarified any discrepancies before publication, the physician-reader could actually practice better medicine. More so, if the editorial board saw to it that the most important adverse or relevant facts about the drug were given the same eye-catching attention as are the alleged indications for the drug, I do believe the incidence of drug failure as well as drug danger would decrease markedly. What is more, I believe that simple overuse of drugs, without any scientific reason for the use, would diminish allowing not only a great saving in the costs of drugs to patients but a great saving in life.

At one time, when the AMA did carefully screen its ads, even the Gaffin report reported that AMA council approval of an ad "relieves the physician of much of the personal responsibility which he assumes when it is absent." But, and this is a big but, if the leading medical publication in this country refuses to adhere to strict standards in advertising you cannot expect any other publication, nor any other form of medical advertising for that matter, to adhere to any standards. And I think it is plainly obvious that the AMA has all too willingly succumbed to virtually no standards when it comes to the advertising it accepts. And since it was the AMA that initiated and paid for an expensive survey for the primary purpose of increasing advertising revenue, there seems little doubt that revenue has taken precedence over professionalism.

Let us look at another ad from the same issue of *JAMA* (Exhibit E). Quite obviously this ad is for Serc a chemical that allegedly "helps control the frequency of episodes in those patients with a high level of recurring attacks (of) vertigo of Meniere's disease." One year ago this month, the Food and Drug Administration announced it was taking action to stop the sale of this specific product. Just two months ago there were many emphatic public pronouncements about the FDA's move to withdraw approval for Serc. This information was also given attention in various medical publications that reach physicians. Yet in the May 26, 1969 issue of *JAMA*, there is an ad for Serc. The ad obviously implies the drug is effective and cannot help but nullify the FDA's recommendations. This ad could easily have been cancelled (there was ample time after the most recent FDA announcement) if the *JAMA* editorial board had any consideration for its readers. The real issue, however, is whether a journal with the ostensible status of *JAMA* should even carry an ad for a drug under question. Only a stronger desire for revenue as opposed to pro-

fessionalism would have allowed such a disservice to the medical profession. At this point it seems quite proper, and most appropriate, to discuss the AMA in relation to its evident honesty, authenticity and accuracy. Since it is my belief that unless and until the AMA takes the lead in setting standards for ethical adverising, no other form of medical advertising will feel it has to conform to any ideals, I do think a few examples of how the AMA operates, in connection with its publications, are in order.

Let us look at another example of the apparent dishonesty that seems to result in that conflict between the editorial and the business side of medical publications. For many years the AMA has sent out, *free* (the AMA uses the word complimentary), two, not one mind you, but two, copies of *Today's Health* magazine to every AMA member. Now, it is recognized that one indication to a potential advertiser whether he wants to advertise in a magazine is that magazine's *paid* circulation or the number of people evidently willing to put out their own money to buy the magazine. The greater the paid circulation, the greater the chance that the reader will actually go through the pages and see the advertisement; the more consumers that will be reached. If, therefore, you want to impress an advertiser in order to solicit his business, what you need to do is show a real reader interest in your publication. Can you imagine a potential advertiser's attention if your paid circulation suddenly—almost overnight—more than doubles? I am not talking about an increase from 3,000 to 6,000, I am talking about 350,000 to over 700,000! Well this is what happened to *Today's Health* several years ago. When the AMA decided to send out *two* free copies of *Today's Health* to all its members, it suddenly showed a rise in *paid* circulation of about 400,000. And it so reported these figures to the Post Office Department year after year, as required by law. Yet, in spite of the fact that such a statement was false and even though this matter was brought to the attention of the Post Office Department, nothing was done to the AMA to make it tell the truth. For if the truth were known, the required statement of circulation would indicate more free copies than paid for copies.

To be sure, the AMA can claim the *two* free magazines are part of its dues structure, but it has, in print, said these are "complimentary" copies. And the membership was never asked if it wanted the magazine in return for payment of dues.

Because we are discussing the AMA publication, *Today's Health*, I would like to give another indication of the accuracy and authenticity of the information published by the AMA. In the February, 1969, issue of *Today's Health*, the last two lines on page 78 read: "Date over-the-counter drug supplies when you buy them. Some lose their effectiveness when they are stored, or they may become toxic." Now this is an extremely serious statement for the AMA to make. If it is true, then it should be documented by the use of names of products that could become poisonous after any period of time. If it is not true, then the AMA should be taken to task for such irresponsibility I tried to obtain additional information directly from the AMA but to no avail. I then asked a former editor of *Today's Health* who was returning to the AMA to secure the source of this startling statement as well as the names of such products. He told me, after a vain attempt within AMA headquarters that there did not seem to be any basis for this alarming pronouncement—other than to entice people to get rid of "old" drug products and buy new ones.

I do think this committee will agree that if there are any products being sold over-the-counter that prospective patients can easily obtain and that might, at a later date, specifically be the cause of illness, the medical profession should be made aware of same. I then contacted the FDA and was told they knew of *no* basis for the AMA's statement. Just as I have tried to emphasize the fact that the AMA is not strict and responsible about what they allow advertised in their publications, so do I feel that such a profound, yet seemingly erroneous, declaration published in *Today's Health* is another concrete example of AMA irresponsibility.

To go back to the matter of paid circulation of AMA publications and the relation of allegedly paid subscribers to advertising revenue. When I was on the *JAMA* editorial staff, there was a definite problem with the circulation of other AMA scientific publications. Some were so small (only a few thousand paid subscribers) as to be relatively unprofitable to the AMA. In addition, the small circulation tended to keep authors from submitting manuscripts for these "specialty" journals of the AMA (papers submitted to *JAMA* were shunted to other journals to supply them with editorial content.)

Many ways were considered to raise the paid circulation of all AMA publications—with primary purpose again to bring in to the AMA additional advertising revenue. The drug companies were quite frank in telling the AMA that they could not see advertising in a medical journal that had no real paid circulation. And here it must be noted that the lack of paid circulation was a definite index of the lack of interest by physicians for, at that time, *JAMA* came to them without actual subscriptions; it was part of the dues structure. So now that the advertisers had advertising restrictions removed, they now wanted to know that other AMA publications had wider distribution.

What did the AMA do? They followed the *Today's Health* "gimmick" and literally forced another free copy of one of its other publications on every member. As a result, *The Archives of Internal Medicine* circulation increased ten fold, when, in fact, the increase was really the result of giving it away. The same was true for other AMA scientific publications. And, when advertisers felt the magazines were going into the hands of so many more readers, they, in turn, increased their advertising in more AMA publications. The result: even greater advertising revenue for the AMA.

It must be noted that AMA members were never offered the alternative of rejecting the free copies forced upon them, thereby reducing their dues (e.g., $12 a year for one of the Archives; $12 a year for the *two* copies of *Today's Health;* and $10 a year for the *AMA News,* which literally duplicates information sent out by free publications to all physicians). Were this choice alone allowed, the dues of every AMA member could be cut in half. Instead, the AMA continues to raise its dues and force its publications on its membership.

I am sure you are all aware that, for most doctors, membership in the AMA is compulsory, not voluntary, so the mailing of these publications as part of membership insures a relatively large circulation with its attendant large advertising revenue. To be sure, the AMA will tell you *they* have nothing to do with the fact AMA membership is compulsory, but the fact remains that a simple directive from the AMA prohibiting this practice would stop it immediately. This has never been done for it has been fairly estimated that if AMA membership were not so fixed that it is literally required to practice medicine, more than half the present membership would resign. The same AMA that fights so hard for so-called "free choice" of a physician has never allowed the physician to make a "free choice" in regard to his membership.

How does compulsory membership work? In all too many areas, a physician cannot obtain a hospital staff appointment (the right to treat his own patients in the local hospital) unless he is a member of his County Medical Society. The County Medical Society requires that membership must include membership in the State association. The State Association then requires that membership *must* include membership in the AMA. So, to take care of his patient in a hospital, the doctor must be a member of the AMA. He is not given the option of joining only those associations he would choose; he has no choice. Thus a great many doctors, with nothing to say about it, indirectly contribute to the false circulation figures of the AMA's publications, and, consequently contribute to increased AMA revenues and thus to what seems to be deliberate carelessness in advertising standards.

And if the AMA will not set the highest standards for medical advertising, you cannot expect any other medical publication to follow suit—especially where such standards could interfere with obtaining the advertising dollar. Naturally, if the AMA continues to refuse to take the lead in setting advertising standards that have meaning to the practicing physician, then the only recourse is legislative action to achieve the same result. That standards are absolutely necessary, there can be no question. The very fact that just one misleading advertising exists that could eventually cause harm to a patient is sufficient justification.

What could AMA standardization mean? If it were known that the AMA did not allow an ad in its pages unless that ad met all professional requirements (this does not limit ads; it merely means that equal eye-catching attention is given to all the important aspects of a drug), the doctor would know that a product advertised in an AMA publication had been reviewed with his (the doctor's and the patient's) benefit in mind as opposed to the revenue for the AMA being of primary concern. An AMA ad should mean that the claims can be justified. In contrast, an ad in some other medical publication that was not found in AMA pages would clearly indicate to the doctor that the ad had not been screened by AMA physicians and was, therefore, not to be accepted at face

value. It is my contention that if this fact were known among the medical profession, other pubications would soon follow the AMA's lead, and what is more important, drug companies would be much more careful about what they say in their ads.

What I hope I am really stressing is that the AMA should return primarily to scientific activities and that the business end of AMA should end its rule of the professional end. I frankly do not see how the present AMA administration can deny that there is a most unwholesome relationship between it and the drug manufacturers; the AMA today virtually exists more for the benefit of pharmaceutical companies than it does for its membership. As an interesting sidelight here, several years ago the total membership of the AMA (in spite of compulsory tactics) decreased. Rather than let that fact become public, the AMA then gave away, without even asking, free membership to physicians in Government service military, public health, etc.). This, in turn, raised the total number of members so as to give the impression that AMA membership was on the increase. Of course, such an action also raised the circulation of its publications—again appealing to potential advertisers.

Naturally, the question comes up, what if drug companies again refuse to advertise in AMA publications because of scientific and ethical scrutiny—as they did two decades ago? Two answers appear. First, can you imagine the attitude of physicians across the country if they knew that an ad in an AMA publication relieved them of a certain amount of legal responsibility, while an ad in some other publication left them a bit more open to question? It is quite possible that advertisers would recognize this aspect of liability and be more apt to conform to standards. But, second, does the AMA really exist to make money from drug ads? Is not the proper role of the AMA, an organization ostensibly to protect the patient's health and welfare, to disseminate scientific information to its membership? In a real sense, why should the doctors of this country prostitute themselves in order to bring their professional association money to use in nonprofessional (e.g., political) activities?

I feel I must stress the fact that there is no medical advertisement so urgent that it cannot be put off until the claims are verified and that all aspects of a clinical study are reviewed to balance the claims and put them in proper perspective. The FDA was charged to do this for the past 5 years, yet there are many, many misleading ads in medical publications every day. When the AMA allows such ads in its publications it becomes a panderer of drugs rather than a scientific evaluator. And here I must stress again, at the risk of repeating myself, that too many doctors believe that if an ad is in an AMA publication it has been properly screened. I think I have shown this to be false. Furthermore, the very fact an ad does appear in an AMA publication has tended to make doctors believe that the company whose ad is in *JAMA* must be all right. That, too, just is not so. The AMA has actually pushed the idea that an ad in one of its publications implies "official" acceptance; at the same time the AMA has done nothing to earn that reputation. You know, if nothing else comes out of these hearings other than the fact that you have made physicians aware that, at present, they must read every ad for a drug with innate bias, you will have performed an extremely valuable service for the people of this country. In a sense, you may have achieved more than any legislation could accomplish.

Thus far, my testimony has hopefully given you evidence that although drug manufacturers obviously mislead physicians as a form of "puffing," (either by not telling the whole truth or by not stressing the dangers of their products), the real culprit behind the *dissemination* of this misleading information is the medical journal that publishes the ad. As I said, it is virtually impossible to control the detail man. At a recent medical meeting (California Medical Association) the detail man for a drug company told me: "Although the FRA requires us to say, in ads, that the dosage of our drug is 1 capsule four times a day, (and the written ad even goes so far as to say: 'the recommended dosage must remain unchanged.' we can tell you that two capsules twice a day works just as well. It would be too much trouble to petition the FDA for permission to change our ads." Could there be any better indication that even existing laws cannot do the job?

Before I conclude my testimony, I would like to say a few general words about the education of doctors about drugs. It is my opinion that many doctors do not know as much about the drugs they use as they should. As evidence for this statement. I would like to refer to the May, 1969 (*10*:209) issue of THE BULLETIN OF THE AMERICAN COLLEGE OF PHYSICIANS, probably the most

respected professional scientific organization in America today. The Executive Director of this association gave, what he called "startling" statistics about drug reactions as they were discussed by Dr. Leighton E. Cluff, Professor of Medicine at the University of Florida College of Medicine. For one thing, it was stated that about 15% of patients are admitted to hospitals because of adverse drug reactions. He claimed "this represents 1.5 million patients a year." And this does *not* include patients who have a drug reaction after being hospitalized. Virtually every drug reaction could be prevented if the doctor was aware of what the drug can do—in addition to its alleged therapeutic effect. Even excusing undetected idiosyncratic patient allergies, the fact the one doctor claims a million and a half patients a year suffer drug reactions has to indicate a gross failure of doctors to know all they should know about drugs.

Another reported observation was that 20% of all hospitalized patients received antibiotics, but that this number was not compatible with the reported number of infections. In other words, patients were given antibiotics without any evident reason. The Executive Director of The American College of Physicians is not afraid to say that: "It is possible physicians themselves may be overinfluenced by claims made for drug efficacy."

Unfortunately, there are relatively few opportunities, other than medical journals, for practicing physicians to learn about drugs today. Most post-graduate courses stress theory and dwell on diagnosis—with the emphasis on how the medical laboratory (rather than the physician himself) can best make that diagnosis. One reason for this lack of academic courses on drug education is that where such courses do exist, they are more often than not, sponsored by a drug company—and they inevitably include free drinks and dinner for the doctors who attend. Again, you start such a meeting with a built-in bias and it is difficult for human beings—even if they are doctors—not to be influenced under such conditions. Medical schools just cannot compete with drug companies when it comes to offering seminars on drugs.

That physicians want to know more about drugs is quite evident. While on of *JAMA*'s editors, I had the responsibility of running the Queries and Minor Notes Department (now called the Questions and Answers Department). This editorial department handled letters to the editor that asked questions about drugs and diseases. Often, a physician sent in an abbreviated case history of a patient he was treating and asked for specific advice as to what drug to use, or whether it was all right to utilize a certain drug. Several times these questions and their answers were published in book form and sold by the AMA. I recently took another look at one of these books, entitled "Selected Queries and Minor Notes," and found that half of all the questions asked related to drugs, as opposed to diagnostic procedures, surgical techniques, etc.). What was of even greater interest, in reviewing this book, specifically with this testimony in mind, was that 4 out of every 5 questions on drugs asked for information that should have been common knowledge to the medical profession (side effects of drugs, proper dosage, specific rather than general indications for use, etc.) ; these were questions that showed the ads for the drugs had omitted the most important prescribing information.

But doctors only have time to read the "headlines" in a drug ad; not because the doctor does not want to read more, but because he just does not have the time to read all the details—and especially to search out and study the references that really tell about the drug. And he does assume that if the ad is in his "official" association journal, it must be all right. This is because most doctors are quite unaware of the dichotomy between the editorial departments and the business departments of their association. And, it is my opinion that this false trust in advertising in JAMA, and other AMA publications, is what has led to the gross overuse, as well as misuse, of drugs.

It seems obvious that legislation now on the books, has not reduced the incidence of drug reactions—the very best indication of drug use and abuse. To require that certain information be in fine print does not, at the same time require that the doctor read that fine print. But to require that the headlines in a drug ad emphasize—with equal attraction—the bad along with the good could help reduce the drug reaction problem.

Properly evaluated advertising could be the best method of bringing the doctor up-to-date on drugs. But only the medical profession can insist on such standards. I hope the past and future hearings of this committee will bring this fact to the attention of the doctors and that they, in turn, will insist on such standards as a rigid policy in their "official" publication.

But, if the AMA will not take the lead in setting advertising standards, and more so if the doctors of this country will not demand that the AMA assume this responsibility, then I must admit that it becomes an absolute and necessary duty of some legislative body to take over the task that medicine will not do for itself. The dangers of drugs, and the obvious misuse of drugs, are such that it is irresponsible for doctors to obtain distorted education about the products their patients take. The important thing is that the legislation must be strong enough, and adequately enforced, to do some good. Unlike almost any other form of advertising, drug advertising is not directed toward the ultimate consumer—allowing that consumer to make a "free choice" with a full awareness of the dangers involved. Therefore it does not seem wrong to have adequate controls over the education the doctor receives so that his course of action is based on full, rather than inadequate or distorted, information.

And when the doctors of this country fully understand the reasons behind such actions—that the protection intended for the patient is equal protection for them—I feel they will back any modality that offers them better educaion.

Thank you.

I do have other advertisements that illustrate how doctors are deceived (such as the ommission of extremely pertinent data). I will gladly show these ads, if you so desire.

APPENDIX II

STATEMENT OF JOSHUA LEDERBERG

"Lack of knowledge and sophistication in the proper use of drugs is perhaps the greatest deficiency of the average physician today." This indictment is one of the most disturbing conclusions of the task force on prescription drugs, headed by Dr. Philip R. Lee, recently Astsistant Secretary for Health and Scientific Affairs in the Department of HEW, and Chancellor of the University of California Medical Center in San Francisco.

This theme is now also the focus of hearings before the Monopoly Subcommittee being chaired by Senator Gaylord Nelson (D., Wisconsin). Its critical tone is shared by almost all of my own colleagues in academic medicine.

This appraisal of the competence of medical practitioners, at large, to make informed and critical judgments about drugs has ramifications even wider than an obvious concern about the quality of care offered by individual physicians. If the prescribing physician were qualified, he could be relied upon to winnow fact from self-interested fancy among the clatter of claims for new drugs, or old ones in fancy new packages, constantly being promoted by the drug industry. The creative efforts of that industry would then be directed primarily to competent research to find new agents capable of persuading competent and critical judges of their value in medicine. Without that reliability, we need ever more stringent policing of the industry and its propaganda to protect physicians, or rather their patients, from a crime that may be closer to self-delusion than fraud but is no less dangerous.

This kind of policing on the part of a government agency is not only clumsy, contentious and expensive. It also leads to the opposite error, of bureaucratic negativism on the principle that no one is ever applauded for approving a risky application: the lives that might be saved by taking a chance with a new drug will never be counted by comparison with a single unhappy death or malformation. But if the doctors cannot police themselves, what other choice do we have?

The evidence for widespread incompetence in drug prescription is impelling, but mostly anecdotal. Some rather superficial surveys have been made of the sources from which physicians obtain their drug information, and their own views of its reliability. The importance and credibility attached to detailmen's presentations should be alarming on the objective principle that they can hardly be expected to criticize their own products. Chloramphenicol was widely used long after its potential hazard for producing fatal aplastic anemia had been widely publicized. This has been the most instructive case study so far, because one could search out this rather rare disease from death certificate files. In California, between January 1963 and June 1964, there were 60 deaths from aplastic anemia, out of a total of 225,000. Ten out of these 60 were related to chloramphenicol, which had been administered to about 220,000 patients. The risk of drug-induced, fatal anemia is then about one in 22,000, which is thirteen times the general population risk.

Most medical authorities condemn the use of chloramphenicol except for typhoid fever and a few other diseases, and some believe that it is never the drug of choice. Most of the cases where doctors had prescribed it certainly did not meet these needs. Why then did they use it? Were they ignorant of the published hazards? Did they discount them on the grounds of their own experience with the drug, which may have cured many infections without the misfortune of an aplastic anemia case? That is, were they their own experts, or are they incompetent or both? We do not know.

Most of the remedies so far proposed are unlikely to go very far to meet the problem. A government-sponsored drug compendium, free of advertising bias, may be very advantageous for other purposes, but will it be read by busy practitioners for drug information, any more than they now consult the journals? The Medical Letter is a particularly useful, convenient, and critical review of contemporary drugs that deserves to reach far more than the twenty percent of U.S. physicians who now consult it. Above all it is a voluntary, independent evaluation; a principle that suggests that if it is imperfect, others can try to improve on the effort.

If indeed many physicians are incompetent to evaluate drugs, they can hardly justify the monopoly of prescribing them, and we will have to set up special examinations and licenses for the privilege of, say, prescribing drugs less than ten years old, and with the legal obligation to report adverse effects.

The indictment has, however, not been proven by objective, quantitative evidence. According to Medical World News, Dr. Maynard I. Shapiro, president of the American Academy of General Practice, flatly denies it and complains that he has not yet been heard by Senator Nelson's committee. If anything, he also points out, physicians get too much information, with many warnings about isolated cases of possible side-effects whose significance is impossible to evaluate.

Medical centers see (and sometimes produce) too many cases of drug-induced illness for this problem to be hastily discounted. However, before we prescribe drastic remedies for this disease, it needs more research both on efficacy and side-effects. What exactly is the problem—is there an identifiable group of physicians who need to be restricted or re-educated? How much of the issue is within the range of valid medical judgment; and to what extent should "experts" dictate the practice of a conscientious but dissenting practitioner? Does overt promotion of drugs by manufacturers serve any useful social purpose, except as impelled by competition with others? What measures are likely to be effective in improving the drug-prescribing behavior of physicians, and how can we pretest and evaluate them?

APPENDIX III

THE LIBRARY OF CONGRESS
Washington, D.C., January 21, 1969.

To: Senate Select Committee on Small Business, Subcommittee on Monopoly (Attention of Mr. Benjamin Gordon).
From: Education and Public Welfare Division.
Subject: Federal expenditures in support of medical education.

This is in reply to your request for information on the amount of Federal expenditures used to support medical education in the United States.

Since the academic year 1958–59, the Association of American Medical Colleges has conducted a survey of medical school expenditures based upon reports of the financial data submitted from each of the accredited institutions in the country. The results of the survey are published annually in the Education Issue of the *Journal of the American Medical Association* near the end of each year.[1] The data included in this report to the Subcommittee are for the year 1966–67 and are the most recent available.

Total medical school expenditures for 1966–67 amounted to $1,010,327,369 and represents an increase of $128,143,207, or 14 percent more than the amount spent by these schools during 1965–66. Among the four-year schools, total annual expenditures ranged from a minimum of $2,332,264 to a maximum of $43,417,130. Total expenditures, incidentally, for the academic year 1958–59 amounted to

[1] "Medical Education in the United States," *Journal of the American Medical Association*, Vol. 206, No. 9, November 25, 1968; annual report on medical school expenditures.

$319,028,651, so that expenditures for 1966–67 were 217 percent greater than amount expended at the end of the previous decade.

Expenditures reported by the medical schools are generally divided into two categories: sponsored program expenditures and regular operating program expenditures. Sponsored program expenditures are medical school activities that are fostered and supported under special contracts, restricted grants, or restricted gifts, by agencies or organizations interested in special medical school programs. Regular operating program expenditures are those made from funds entirely under the control of the medical school. The overwhelming proportion of Federal funds expended by medical schools are under the category of "sponsored expenditures."

In 1966–67, expenditures for sponsored teaching and training programs amounted to $138,216,973, of which 92 percent came from Federal contracts and grants:[2]

SPONSORED PROGRAMS—TEACHING AND TRAINING

Category	1958–59	1966–67	Percent increase
Federal contracts and grants	$20,772,182	$126,672,337	510
Non-Government contracts, gifts, and grants	4,660,146	11,544,636	148
Total	25,432,328	138,216,973	443

According to the survey report, funds expended in support of this activity are for most of the postdoctoral education programs conducted by medical schools.

In 1966–67, $420,231,585 was spent for sponsored-research programs, of which $344,480,141 was provided by the Federal Government (82 percent of all sponsored research in medical schools). Non-Federal divisions of government provided about 3 percent of the funds, while the remaining 15 percent came from nongovernment sources (industry, foundations, voluntary health agencies, individuals, and others):[3]

SPONSORED RESEARCH EXPENDITURES

Category	1958–59	1966–67
Federal grants and contracts for research	$74,128,157	$344,480,141
Non-Federal divisions of government	2,855,127	12,732,011
Industry	5,800,286	9,001,266
Foundations	8,277,327	16,926,247
Voluntary health agencies	12,935,649	16,823,251
Individuals and others	4,924,173	9,771,507
Total	133,705,625	420,231,585

Approximately 41 percent of all medical school expenditures are for sponsored research, and 52 percent of all medical school expenditures are funded from Federal sources. About 34 percent of all expenditures come from Federal research expenditures. We are enclosing the tables which show the sources of these expenditures for your review. These data do not include capital-outlay expenditure figures nor teaching hospital financial data.

If information on basic medical education programs is required, please let us know.

GLENN R. MARKUS.

[2] See footnote No. 1; table 30.
[3] See footnote No. 1; table 30.

TABLE 30.—SUMMARY OF MEDICAL SCHOOL FINANCIAL REPORTS, 1958–67

	1958–59		1965–66		1966–67		4-year colleges	
	Colleges using source	Amount	Colleges using source	Amount	Colleges using source	Amount	Minimum	Maximum
A. SOURCES OF SUPPORT FOR SPONSORED PROGRAMS								
1. Federal contracts and grants for teaching and training	85	$20,772,182	86	$110,730,028	88	$126,672,337	$100,909	$4,771,836
2. Nongovernment contracts, gifts, and grants for teaching and training	68	4,660,146	74	10,423,085	79	11,544,636	0	812,018
3. Total of sponsored teaching and training grant programs (1 plus 2)	85	(25,432,328)	86	(121,153,113)	88	(138,216,973)	102,278	5,478,090
4. Federal contracts and grants for research	85	74,128,157	87	307,401,572	88	344,480,141	256,473	14,036,153
5. State, city, and county contracts, gifts, and grants for research	43	2,855,127	59	12,081,831	63	12,732,011	0	1,645,429
6. Nongovernment contracts, gifts, and grants for research	(1)	31,937,435	87	48,179,199	88	52,522,271	20,157	2,134,156
7. Endowment income restricted for research	34	3,029,630	42	5,506,157	43	6,405,838	0	1,017,668
8. Other funds restricted for research	17	1,755,276	15	1,947,659	13	4,091,324	0	2,182,772
9. Total of non-Federal support for sponsored research (total, items 5 through 8)	85	(39,577,468)	87	(67,714,846)	88	(75,751,444)	20,157	4,047,475
10. Total expenditures for sponsored research (4 plus 9)	85	(113,705,625)	87	(375,116,418)	88	(420,231,585)	314,281	17,727,818
11. Federal grants and contracts for foreign teaching programs (included in item 12)			10	(1,322,940)	6	(887,212)	0	427,128
12. Miscellaneous sponsored programs (exclusive of research teaching, training, and student aid)	(1)	5,099,963	43	17,936,783	39	22,675,558	0	11,272,523
13. Total expenditures for sponsored programs (items 3, 10, 12)	85	(144,237,916)	87	(514,206,314)	88	(581,124,116)	514,294	34,478,431

[1] Part of combined items; total number not computed.

TABLE 30.—SUMMARY OF MEDICAL SCHOOL FINANCIAL REPORTS, 1958–67—Continued

	1958–59		1965–66		1966–67		4-year colleges	
	Colleges using source	Amount	Colleges using source	Amount	Colleges using source	Amount	Minimum	Maximum
B. SOURCES OF SUPPORT FOR REGULAR OPERATING PROGRAMS								
14. Tuition and fees	85	$24, 368, 278	87	$41, 019, 126	88	$43, 943, 788	$41, 400	$1, 477, 385
15. Overhead on Federal contracts and grants			87	53, 730, 487	84	55, 410, 997	0	2, 809, 703
16. Overhead on non-Federal contracts and grants			85	5, 114, 871	68	4, 628, 760	0	674, 826
17. Total overhead on contracts and grants (15 plus 16)	85	13, 339, 212	87	(58, 845, 358)	84	(60, 039, 757)	0	3, 293, 342
18. Endowment income		17, 576, 918	53	26, 227, 239	51	28, 016, 439	0	3, 163, 530
19. Unrestricted gifts and grants		10, 960, 387	85	13, 771, 283	83	14, 038, 235	0	1, 163, 957
20. Medical college expenses paid by teaching hospitals and clinics	28	13, 727, 308	33	31, 047, 912	37	46, 789, 800	0	11, 986, 593
21. State, city, and county grants-in-aid or subsidies paid to medical college	11	7, 592, 430	6	6, 816, 009	7	8, 265, 103	0	2, 355, 538
22. Medical college expenses paid by medical service funds	22	10, 635, 435	33	25, 203, 185	41	30, 247, 655	0	3, 065, 449
23. Income from college services (medical laboratory, etc.)	45	5, 259, 981	55	14, 112, 449	53	15, 293, 171	0	2, 498, 814
24. State payments or subsidies paid through compacts such as WICHE and SREB	11	573, 342	7	783, 206	8	825, 656	0	275, 000
25. Other income from regular operations		6, 501, 150	59	15, 829, 695	67	27, 157, 669	0	3, 450, 023
26. Miscellaneous income (total of items 23, 24, 25)	45	(12, 334, 473)	79	(30, 725, 350)	81	(43, 276, 496)	0	3, 913, 272
27. State appropriations for defrayal of medical college expenditures	40	49, 778, 410	43	111, 985, 457	47	132, 992, 088	0	7, 346, 619
28. Miscellaneous medical college reserves			3	226, 539	6	779, 774	0	389, 140
29. Miscellaneous university income and reserves	45	14, 477, 884	51	22, 110, 390	49	20, 814, 148	0	2, 400, 915
30. Total expenditures for regular operating programs (exclusive of sponsored programs)		(174, 790, 735)	87	(367, 977, 848)	88	(429, 203, 253)	1, 308, 431	17, 662, 899
31. Total expenditures		319, 028, 651	87	882, 184, 162	88	1, 010, 327, 369	2, 332, 264	43, 417, 130

TABLE 31.—MISCELLANEOUS MEDICAL SCHOOL FINANCIAL DATA, 1958–1967

	1958–59	1965–66	1966–67
EXPENSE ITEMS BY SOURCE OF FUNDS			
1. Expenditures for teaching, training, and research from all Federal grants, contracts, and subsidies	$94,900,339	$474,948,244	$524,685,047
2. Expenditures for research paid by nonfederal divisions of government	2,855,129	12,081,831	12,732,011
3. Expenditures for research from nongovernment gifts, grants, and contracts	31,937,435	48,179,199	52,522,271
(a) Paid by industry	5,800,286	8,779,751	9,001,266
(b) Paid by foundations	8,277,327	15,092,399	16,926,247
(c) Paid by voluntary health agencies	12,935,649	15,908,032	16,823,251
(d) Paid by individuals or other organizations	4,924,173	8,399,017	9,771,507
4. Expenditures for equipment purchased from school funds but not included in "Summary of Medical School Financial Reports"	$4,186,842	$5,627,795	$6,552,600
5. Number of schools in which operating income exceeded operating expenses	(12)	(13)	(11)
6. Total operating surplus funds of colleges referred to in item 5	$941,541	$2,938,933	$2,709,106
7. Disposition of operating surplus of funds referred to in item 6:			
(a) Held for future operations		2,137,850	2,252,895
(b) Held as part of general university funds	941,541	79,052	110,074
(c) Used for purchase of equipment, improvement of facilities, etc		600,000	32,924
(d) Refunded to State treasury or paid to university as reimbursement for services		122,031	313,213
8. Unrestricted university funds used to support medical school operations (exclusive of State appropriations)	10,953,600	25,049,323	23,175,461
9. Source of funds referred to in item 8:			
(a) General university unrestricted gifts and grants		632,390	1,514,519
(b) Profit on auxiliary enterprises (bookstore, snack bar, etc.)		2,244,311	2,491,708
(c) Allocated from miscellaneous university income and reserves		17,235,633	13,718,435
(d) Unrestricted university endowments		4,936,989	5,450,799
10. Percentage of total medical school expenditures applicable to regular operating programs (excluding sponsored programs)	55	42	42
11. Percentage of total medical school expenditures for all sponsored programs	45	58	58
12. Percentage of total medical school expenditures for sponsored research	36	43	41
13. Percentage of total medical school expenditures paid by Federal funds	30	54	52
14. Percentage of sponsored research paid from Federal funds	65	82	82
15. Percentage of sponsored research paid from non-Government funds	35	15	15
16. Percentage of sponsored research paid from state and local government funds		3	3
17. Percentage of total medical school expenditures paid for Federal research	23	35	34

APPENDIX IV

[From Canad. Med. Ass. J., Apr. 6, 1968, vol. 98, pp. 701–705]

A SURVEY OF PHYSICIANS' REACTIONS TO DRUG PROMOTION

(R. W. Fassold, M.D.,* and C. W. Gowdey, D.Phil.† *London, Ontario*)

The purpose of this study was to obtain an objective assessment of how physicians react to current drug promotional methods and whether they feel that they are being provided with enough reliable information on drugs to meet their requirements for prescribing. It was considered possible that the posing of certain questions on drugs might encourage more physicians to greater participation in formal programs of continuing education.

METHOD

To test the reactions to drug promotion, a list of questions was compiled which was revised repeatedly after consultations with several practising physicians, pharmacologists and a pharmacist, and with the aid of Payne's "The Art of Asking Questions". (1) The questionnaire was pretested by two local practition-

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NOTE.—Numbered references at end of article.

ers who suggested several minor changes and estimated the time required for completing the questions. In June 1966 the questionnaire was mailed to the 1584 doctors in the 14 counties of Southwestern Ontario. Included with it were a covering letter from Dr. A. T. Hunter, Director of Continuing Education, encouraging participation in the study, and a stamped self-addressed envelope. No rewards were offered for returns and no reminder letters were sent. The covering letter did state, however, that if the questionnaires were signed, the results would be sent to all participants.

RESULTS AND DISCUSSION

A total of 531 questionnaires (33.5% of those originally sent) were returned completed; 10 more were returned incomplete because the physician was no longer in practice. Of the *completed* returns 253 (48%) were from general prac titioners and 270 (51%) were from specialists, but for eight the type of practice was not indicated and could not be determined. Although the distribution of general practitioners and specialists in the mailing list is not known, it is worth noting that the percentage distribution of the returns was very close to the distribution of all Canadian physicians as reported by Canadian Facts Company Limited (2) (i.e. specialists 48%, general practitioners 52%). The distribution of specialties in our returns is also very similar to that for the Canadian physician population, except that our percentage of returns from psychiatrists was higher, and from surgeons was lower than the actual distribution. This may reflect a great interest by psychiatrists in a study of this type, or probably that psychoactive drugs are being more actively promoted now; the surgeons would not be expected to have as great an interest in drug promotion.

Although the instruction stated that a signature was not required, it is of interest that 91% of all doctors replying did sign the questionnaire. That many of the doctors who replied did so conscientiously can be inferred from the detailed answers to some questions and from the number of unsolicited observations and thoughts expressed on drug promotion. It might be argued that doctors with strong opinions on drug promotion would be more likely to return completed questionnaires. Nevertheless, these were the opinions expressed by a group of over 500 doctors representing a cross-section of the Canadian medical profession.

The answers to questions concerning the size of the community in which the doctors practised and the country and year in which they graduated revealed that, as expected, 95% of the specialists practised in communities with populations exceeding 20,000, and 78% in centres over 50,000. Of the general practitioners, 45% practised in communities under 20,000. Most of the doctors replying graduated between 1940 and 1950: 71% of specialists and 63% of general practitioners. There was little difference between the group as to the country where they became medically qualified. Although 80% of all doctors qualified in Canada, 10% in the United Kingdom and 3% in the United States, a total of 14 countries were represented in the remaining 7%.

In the tabulation of results all respondents indicating a specialty are called "Specialists". The eight returns where the type of practice was not specified are not listed separately but are included in the totals for "All Doctors". The results throughout are given in percentages of *answered questions* with the totals in parentheses. Any discrepancy between the totals shown in the tables and the number of respondents (531), or between "General Practitioners" and "Specialists" replying and the total replies, is accounted for by the eight unspecified returns and by those in which that particular question was unanswered. Because in all tables the percentages shown have been rounded off to the nearest whole number, not all the figures add up to exactly 100%. For questions containing "other" categories, there were not enough of any answer to be considered significant and these are not subdivided.

TABLE I.—PERCENTAGE DISTRIBUTION OF ANSWERS FROM ALL DOCTORS

Choice of answers	Most informative and/or most acceptable: 1st choice or no rank [1]	Least informative and/or least acceptable: 1st choice or no rank [1]
Direct mail advertising	6	67
Drug detailman	46	13
Exhibits at medical meetings, etc	20	8
Advertising in medical journals	19	12
Other	9	0
Total number of doctors replying	521	521

[1] To the question on "Most acceptable" 16 doctors gave more than 1 answer but did not rank them; both answers are included in totals and percentage calculations. Similarly, for "Least acceptable", 39 doctors gave 2 unranked replies and these are included.

The questions can be grouped into three main categories: (a) general, (b) those dealing with the sources of drug information, and (c) those seeking opinions as to the quality of drug information.

Question 1—Which of the following drug promotion methods do you think usually is most informative and/or most acceptable? and Which of the following drug promotion methods do you think is least informative and/or least acceptable?

Analysis showed that 56% of the general practitioners replying to this question considered the drug detailmen most informative and/or acceptable and 76% indicated that direct mail advertising is least informative and/or acceptable. Not so many specialists (37%) appeared to find the drug detailmen most informative or acceptable, and not quite as many (59%) reacted adversely to direct mail.

Fig. 1 summarizes the reactions of all doctors replying and shows clearly that, taken separately, the method of drug promotion most informative and/or acceptable involves the drug detailmen, whereas the least informative and/or acceptable is direct mail advertising.

It is realized, of course, that some of the reactions expressed to this and several other questions may have been coloured by the impressions made on doctors by the drug detailmen and direct mail arriving in the office just before the questionnaire. But the answers given lead us to conclude that in many cases these opinions are held strongly and were not prompted by the questions themselves.

Question 2—Which of the following do you think most influences you to use a drug for the first time?

From these results it would appear that most doctors like to obtain information on new drugs from their colleagues (Table II). Continuing education programs dealing with pharmacology and therapeutics could supply at least some of this information.

TABLE II.—PREFERRED SOURCE OF INFORMATION ON NEW DRUGS

Choice of answers	Distribution of answers	Percent
Manufacturer's written advertising (direct mail, advertisements in Journals, etc.).	Specialists	6
	General practitioners	3
	All doctors	4
Manufacturer's spoken advertising (detailman, exhibits, etc.)	Specialists	18
	General practitioners	31
	All doctors	24
Colleague or consultant recommendation	Specialists	57
	General practitioners	54
	All doctors	56
Patient request	Specalists	
	General practitioners	2
	All doctors	1
Other	Specialists	19
	General practitioners	11
	All doctors	15

Note: Total number of doctors replying, 521.

Question 3.—Do you think the methods of promoting and advertising drugs in general are: ethical? beneficial? economical?

Of the doctors who answered either "yes" or "no" to this question a total of 92% thought that they were not "economical" but more than half considered them "ethical" (Table III).

TABLE III.—OPINION ON METHOD OF PROMOTION

	Choice of answers			
	Yes (percent)	No (percent)	Don't know (percent)	Total answers
Ethical	62	23	16	498
Beneficial	48	32	20	484
Economical	6	77	17	492

Question 4—Do you think that drug advertising found in medical journals is subject to stricter, more impartial censorship than most other forms of written drug advertising, and therefore contains more accurate and less biased information?

Of the 518 doctors who answered this question, 44% said "no" and of the 363 who said either "yes" or "no", 64% believed that drug advertisements in medical journals were not that different from other written advertising. This was the feeling in spite of the fact that a number of the leading journals have in the past few years made their criteria for accepting journal advertising much more rigorous.

Question 5—What happens to the drug advertising you receive in the mail?

The answers given to this question correlate well with those to questions 1 and 2: only 34% try to read all or some of the direct mail advertising; 20% never or rarely see the material, and 45% sort through but rarely read any of it (Table IV).

TABLE IV.—FATE OF MAILED ADVERTISING

[In percent]

Choice of answers	Specialists	General practitioners	All doctors
Do you:			
Try to read all of it?	5	3	4
Try to read some of it?	33	26	30
Sort through but rarely read any of it?	48	43	45
Rarely see any of it, i.e. your nurse or receptionist disposes of the material as she sees fit?	5	10	8
Immediately discard without looking at any of it?	8	15	12
Other	2	2	2
Total answers	266	250	523

Question 6—"Briefly, what are your thoughts on direct mail drug advertising?"

After reading through many of the answers to this question, it was decided to group the replies as shown in Table V. Some doctors gave answers which fitted into more than one category (e.g. they said "waste of time and of little value"); hence in this question the sum of the percentage of distribution of answers exceeds 100.

TABLE V.—ASSESSMENT OF DIRECT MAIL ADVERTISING

Quotations from replies	Distribution of answers percent
Waste of time and/or money	38
Useless; of little value; can do without	36
Too much volume; too much repetition; too long	27
Sometimes useful	19
Annoying	15
Inadequate; inaccurate; misleading	12
Too promotional; gaudy	5
Of little interest to practice, or no interest to practice	4
Wants reprints or reviews only	3
Wants file cards or standard brochure once	3
To announce new drug only	2
Total number of doctors answering	518

Using these and other quotations it was found possible to classify the answers into three groups: (a) mostly favourable, (b) mixed or indifferent, and (c) negative or hostile (Table VI). In some cases when the answer was mostly negative or hostile but the reply to the preceding question indicated that the physician tried to read some or all of this mail, the reply was classified as "mixed". It is noteworthy that only 3% of the specialists and 1% of the general practitioners did not express an opinion in reply to this question.

TABLE VI.—REACTION TO DIRECT MAIL ADVERTISING

[In percent]

Category of reply	Specialists	General practitioners
Negative or hostile	68	67
Mixed or indifferent	23	27
Mostly favorable	9	6
Total answers	259	250

Canadian doctors may have been influenced in their reactions to drug advertising by the 1960 report of the Committee on Pharmacy to The Canadian Medical Association (3). After the appearance of this report, Kelly (4) summarized what believed to be the attitude of most doctors to the "flood of direct mail advertising" by pointing out that: "it is so voluminous that only the most conscientious recipient opens each piece before consigning it all to the waste basket . . . most of it constitutes outstanding examples of the printer's and lithographer's art which conveys the impression of great expense and consequent wastefulness . . . it appears so expensive that doctors feel that it may contribute materially to the cost of prescribed drugs to the patients . . . it produces in the minds of many doctors an unfavourable image of the firm which sponsors it."

Since that report, efforts to improve this medium were certainly made by some of the pharmaceutical companies and the total volume has been reduced. The fact remains, however, that in 1966 over two-thirds of 509 doctors still reacted in a negative or hostile manner to direct mail advertising and a total of 65% stated that they rarely read, rarely saw, or immediately discarded mailed drug advertising. These reactions to our questionnaire are different from those reported by the Canadian Facts Company who claimed from their survey (2) that "only 16% of doctors allowed anyone else to discard any of their pharmaceutical mail before they themselves saw it . . . as many as 70% gave an affirmative answer to the question 'Do you make a point of trying at least to look at all your advertising mail? . . . only 36% expressed any dissatisfaction with the selection of mail sent to them".

Question 7. How would you grade most detailmen with regard to the following attributes?

Table VII shows that the majority of doctors rated most detailmen favourably (i.e., "good" or "excellent") as to personality (86%), reliability (65%) and honesty (69%); not so favourably (i.e., "fair" or "poor") in the categories of general knowledge (67%), knowledge of drugs (63%) and usefulness (59%).

TABLE VII.—ASSESSMENT OF DETAILMEN

Attribute	Poor (percent)	Fair (percent)	Good (percent)	Excellent (percent)	Total answers
Personality		14	74	12	519
Reliability	5	30	56	9	504
Honesty	2	30	60	9	503
General knowledge	11	56	32	2	506
Knowledge of drugs	13	50	34	3	513
Usefulness	18	41	38	3	509

Question 8—Have you ever reduced or stopped your use of a drug manufacturer's products because of what you believe to be misleading or objectionable advertising in any form (i.e. include impressions made by drug detailman)?

In their answers to this question there was a marked divergence between specialists and general practitioners, but the reasons for this are not known (Table VIII). In any case, it is significant that almost one-half of all doctors replying stated that they had reacted in this way to misleading or objectionable advertising.

TABLE VIII.—INFLUENCE ON PRESCRIBING PRACTICES OF OBJECTIONABLE ADVERTISING

Choice of answers	Yes (percent)	No (percent)	Total answers
Specialists	39	61	263
General practitioners	59	41	248
All doctors	49	51	518

Question 9.—Do you think there should be a regular publication by an independent medical body, giving practical and unbiased guidance on new drugs?

An overwhelming majority (94%) of doctors replying thought that there should be such a publication (Table IX).

TABLE IX.—DESIRE FOR INDEPENDENT OPINION ON NEW DRUGS

Choice of answers	Yes (percent)	No (percent)	No opinion (percent)	Total answers
Specialists	94	4	2	269
General practitioners	92	6	1	249
All doctors	94	5	2	524

The need for such information was recognized by the Royal Commission on Health Services. (5) One of their recommendations (No. 62) was that a National Drug Formulary be prepared, issued and maintained on a current basis. "This Formulary would include only those drugs which meet the specifications of the [Food and Drug] Directorate. . . ." "There should be established . . . an Information Service which would issue periodic bulletins providing the latest information on drugs and drug therapy to physicians, pharmacists and hospittals." Whether a Canadian Drug Formulary can be produced and kept up to date is questionable, but there are several currently available publications which do give information on the newer drugs. (6–10)

Question 10.—Are you familiar with The Medical Letter?

It appears that somewhat more general practitioners than specialists are familiar with and use this publication (Table X). Analysis showed that of the 79 specialists who stated that they read it "regularly" or "often," 28 were specialists in medicine, 11 in psychiatry and 8 in obstetrics. The proportion of psychiatrists who said that they read this publication is relatively high and may be another reflection of their current interest in drugs.

TABLE X.—FAMILIARITY WITH "THE MEDICAL LETTER"

[In percent]

Choice of answers	Specialists	General practitioners	All doctors
Yes, I use it regularly	20	25	22
Yes, I use it often	10	20	15
Yes, but I rarely use it	36	25	30
Yes, but I have never used it	7	10	8
No	28	20	24
Total answers			523

Question 11.—Do you consider The Medical Letter an adequately authoritative, unbiased, and thereof useful source of information on new drugs?

Although the doctors were directed to omit this and the following question if their answer to Question 10 was "No", it was realized during the analysis of results that this was an error in instruction (Table XI). Therefore we recorded answers to these questions *only* if the preceding answer was either "Yes, I use it regularly" or "Yes, I use it often."

TABLE XI.—OPINION OF "THE MEDICAL LETTER"

[In percent]

Choice of answers	Specialists	General practitioners	All doctors
Yes	56	42	47
No, but it is the best source of information of this type presently available	39	56	49
No	2	1	2
No opinion	2	2	2
Total answers [1]	79	113	195

[1] See text for explanation.

Question 12—If the Medical Letter presented a clearly adverse report on either the safety or effectiveness of a new drug you were using, or anticipated using, what influence do you think this might have on your treatment plans? (Assume the drug in question could not generally be considered a 'life-saving drug', and that there are older, more widely used drugs available, and recommended for the condition.)

Of the 195 doctors who answered this question, and had stated earlier they read this publication regularly or often, 89% stated that they would heed the adverse report. Several suggested that if the adverse report had to do with safety, they would not use the drug until they had more information, but if the report concerned efficacy, they would use their own judgment as to continuing it.

SUMMARY

A total of 531 physicians from Southwestern Ontario responded to a questionnaire that sought their reactions to current methods of drug promotion—a response rate of 33.5%. The distribution of general practitioners and various specialists was comparable to the Canadian average. Most physicians had graduated in the 1940's; 80% had qualified in Canada, 10% in the United Kingdom. Direct mail drug advertising was reported to be the least informative and/or acceptable to 67% of all doctors, and the same number gave negative or hostil answers when asked for their thoughts on this type of promotion; it was sorted through but rarely read by 45%, and rarely seen by another 20%. Drug detailmen were reported to be most informative and/or acceptable by 46% of the doctors and most of them were rated favourably as to personality, reliability and honesty, but not so favourably as to drug and general information, and usefulness to doctors. The majority of doctors declared that recommendations from colleagues (or consultants) were the greatest influence to use a new drug. On the promotion of drugs in general, a majority thought it ethical and 77% thought it was not economical. Of the respondents, 94% thought there should be a regular publication

giving practical, unbiased guidance on new drugs; 49% reported that they had reduced or stopped using a manufacturer's products because they believed the advertising to be misleading or objectionable.

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REFERENCES

1. PAYNE, S. L.: The art of asking questions, Princeton University Press, Princeton, N.J., 1951.
2. Canadian Facts Co. Ltd.: A study of Canadian physicians' attitudes to medical mail advertising and pharmaceutical literature, Seccombe House Canada Ltd., Toronto, September 1966.
3. Canadian Medical Association, Committee on Pharmacy: *Canad. Med. Ass. J.*, 83: 505, 1960.
4. KELLY, A. D.: *Ibid.*, 83: 553, 1960.
5. Canada, Royal Commission on Health Services: Report, vol. 1, Queen's Printer, Ottawa, 1964, p. 42.
6. American Medical Association, Council on Drugs: New drugs evaluated by the A.M.A. Council on Drugs, Chicago, 1967.
7. HUGHES, F. N., editor: Compendium of pharmaceuticals and specialties (Canada), 3rd ed., Canadian Pharmaceutical Association, Toronto, 1967.
8. American Society for Pharmacology and Experimental Therapeutics: Pharmacology for physicians, vol. 1, Philadelphia, 1967.
9. Consumers' Association: Drugs and therapeutics bulletin, vol. 1, London, May 3, 1963.
10. AARON, H., editor: Medical letter on drugs and therapeutics, vol. 1, Drug and Therepeutic Information, Inc., New York, 1959.

APPENDIX V

ARTICLES FROM VARIOUS SOURCES ON DRUG TESTING

[From the Washington (D.C.) Post, Jan. 9, 1969]

THE IMMUNIZATION OF DRUG TESTERS

(By Morton Mintz)

The quality of testing of prescription drugs is one of those problems whose complexities elude the grasp of most of us but whose implications are of life and death importance. For if poor testing is allowed to conceal from a physician that a medicine is useless, inferior of even positively harmful, it is not the doctor but the patient (or hundreds, thousands or even millions of patients) who may be exposed to needless exploitation, delay in obtaining effectve therapy and even injury or death.

Periodically something happens to make the problem surface. There were, for example, congressional investigations by the late Sen. Estes Kefauver, Rep. L. H. Fountain and former Sen. Hubert H. Humphrey. Some testing was "superb," Humphrey once said. He found other instances of outright fraud. But much more often, he said, "mediocre and substandard testing was . . . conducted on good, bad, or indifferent drugs."

Humphrey's inquiry ended in 1964, when he ran for Vice Presidet. Then, just three years ago, a tired industry-oriented Food and Drug Administration got a new Commissioner with a rock 'em sock 'em style. A mere 11 weeks after Dr. James L. Goddard was sworn in he told the Pharmaceutical Manufacturers Association that he was "shocked at the quality" of much of the test data PMA members had submitted to the agency. "The hand of the amateur is evident too often for my comfort," he said.

Last July 1, Dr. Herbert L. Ley, Jr. succeeded Dr. Goddard. Dr. Ley's style is anything but rock 'em, sock 'em. For five months he made no public speeches

at all. But when he did, Last Dec. 3, he, too, focused on unsatisfactory testing of drugs.

"I must tell you frankly that we have not seen the degree of improvement in the quality of clinical data from drug investigations that we would like," Dr. Ley told an educational conference sponsored by the FDA and the Food and Drug Law Institute.

He documented his point with a capsule review of the 406 drug-marketing applications received by the agency in the fiscal year ended last June 30. Only 59 were approved—about one-fifth as many as were so low in quality as to be "not approvable." Of the rejected applications, Dr. Ley said, more than half "suffered from deficiencies in clinical studies and inadequacies in efficacy data."

"I intend to give this matter renewed attention * * * and possibly call upon experts outside the agency as well to see if we cannot find means to correct existing shortcomings," he said.

As if to underscore his point, the FDA soon thereafter disclosed that it intends to halt the sale of six antibiotic-containing combination drugs for which investigation showed there was little if any scientific evidence of efficacy—but which nonethless were widely advertised and, over the years, prescribed for millions of patients.

Two days after Dr. Ley spoke, support came from an unexpected quarter. In the Dec. 5 *Medical Tribune*, spokesmen for two major pharmaceutical houses were reported to have made a joint statement in Geneva, Switzerland, that despite improvement in recent years, "the vast bulk of clinical work with new drugs that is published is of abysmally low quality."

This fact often is held against the drug industry, Drs. H. Bloch of CIBA, Ltd., in Basel and G. E. Paget of Smith Kline & French Laboratories, Ltd., acknowledged at a meeting sponsored by the Council for International Organizations of Medical Sciences in cooperation with the World Health Organization and the United Nations Educational, Scientific and Cultural Organization. But, the two doctors said, "it is as much to industry's disadvantage as to medicine's that this situation exists. This unsatisfactory state of affairs does not come about because industry seeks third-rate investigators to carry out these [drug testing] trials in the hope that they will thereby obtain an unreasonably favorable outcome . . . It arises because of the dearth of investigative facilities and first-class investigators throughout the world." As they saw it, the answer lies in "a complete revolution in the attitude of medical schools and teaching hospitals to the clinical investigation of drugs and the training of investigators."

Their advice is not out of proportion to the seriousness of the problem. But alone it is not enough. The Government might well look upon the training of drug investigators as a public health necessity and pay the bill. Apart from that, as witnesses have told the continuing drug hearings led by Sen. Gaylord Nelson, steps must be taken to eliminate the possibiltiy of bias in testing. As it is, manufacturers commission testing. Those who do it know what company is paying the bill, whether a gift to a favored medical school may somehow be in the balance, whether there will be such forms of ego massage as honorariums for speaking at a conference in a distant city, whether a favorable result will cause a rise on the stock market from which personal advantage may be derived.

One way or another, testing should be done by specialists who do *not* know the identity of the manufacturers, who *cannot* benefit financially from the result, who are *not* motivated even subconsciously by a desire to get anything but the truth. If war is too important to be left to the generals, so is drug testing too important to be left to manufacturers and to investigators who have not been immunized against possible bias.

[From the Bulletin of the Atomic Scientists, January 1969]

DRUG TESTING: IS TIME RUNNING OUT

(By William M. O'Brien)

(NOTE.—Dr. O'Brien, who is associate professor of preventive and internal medicine at the University of Virginia, Charlottesville, discusses the hazard of drug testing in the diseased human being. He contends that the FDA should be strengthened by improving its scientific status and upgrading the quality of its scientists; that drug testing should be taken out of the hands of the pharamaceutical industry, which he criticizes for showing unwarranted optimism about drugs.)

The vast majority of physicians feel that the best way to test drugs is to use the "art of medicine"—every doctor should be allowed to try out a new drug and see how it works, and the doctors' testimonial should be sufficient evidence. After all, shouldn't a drug be tested and judged just as it is used—by the physician in his office?

A second approach considers medicine to be a science and not an art, and demands rigorous experiments in drug testing. Since the course of most diseases is highly variable, a control period is essential. Testing a new drug implies a comparison with a standard established remedy or, if there is no evidence that drugs in any way benefit the disease being studied, a comparison with an inert dummy medication, usually referred to as a placebo. The drug and placebo treatments are randomly assigned to comparable patients and, to avoid any possible bias, the physician evaluating the response and the patient are unaware of which medications are active. The second approach is rarely used. Most clinicians are skeptical of controlled trials, and particularly distrust the final statistical analysis which is required to insure that the investigator has not been misled by chance or deceived by natural fluctuations in disease activity. Drug companies prefer the first approach; uncontrolled trials are easier, and the resulting testimonials are apt to be favorable. A famous physician once remarked: "Drug trials can be divided into two groups; enthusiastic trial with no controls and controlled trials with no enthusiasm."

The uncontrolled trial—the "art" of testing new drugs—is, however, full of logical traps. Caring for disease is depressing, and both physician and patient may become wildly enthusiastic about new remedies. Sir William Osler is reputed to have remarked: "We must use drugs quickly before they lose their power to heal." A new drug is introduced, has its fling, and then is discovered to be of little value or comes to be associated with severe toxic reactions. This pattern has repeated itself over and over again.

FLIPPING THE COIN

Another trap concerns the widely used technique of placebo substitution. Consider a disease with a highly variable course. Let us suppose that a patient has just experienced a severe exacerbation of disease activity. The physician, confronted with a patient who is doing poorly, decides to start a promising new drug. He gradually increases the dose of the drug, and eventually the patient has a remission of the disease process. Now the physician substitutes an inert dummy medication, a placebo, and the patient soon gets worse. He repeats the process several times, and each time obtains a verdict in favor of the drug. But has the favorable effect been due to the drug, or is it due to the cyclical nature of the disease? This is the same fallacy as a coin-flipping game with the rules which require that if it's heads I win; but if it's tails, you don't win, we flip again. Under these circumstances, it is hardly a fair game; if the game goes on for a number of coin tosses, the chances of your winning becomes virtually nil. Placebo substitution is an example of just such a logical fallacy, since the physician can decide to substitute the dummy whenever he wishes. The rules of the game must be determined before the game begins, not during the play.

In a recent congressional hearing on the adequacy of drug testing, when the fallacy in the placebo substitution technique was pointed out, a vice president in charge of research at one of the largest drug companies defended it: "To imply that these clinical investigators purposely chose to institute placebo at the point in the patient's disease when the patient is about to experience an exasperation of his illness, is sheer nonsense, and is a reflection on the scientific integrity of the observer and also on his moral character." Most physicians would agree, and would still prefer the "art" approach, in spite of this and many other fallacies in the use of these uncontrolled techniques.

A final problem in the art of drug testing revolves around payment for the tests. The companies must have favorable reports in order to market new products. If a physician constantly produced scientifically sound but unfavorable reports, would he continue to receive support from the drug industry? My experience would indicate that he would not. If a physician consistently produced favorable testimonials, would he receive generous support? One physician is known to have received considerably more than $32,000 for results of drug tests praising new remedies over a two-year period. The Food and Drug Administratiton (FDA) later produced evidence that these trials involved gross fraud and the physician was convicted in Federal Court. This is hardly an isolated example. Marketing of the pain killer Norgesic was based on tainted data, and

numerous other instances could be cited. One wag suggested a second way to classify tests: "Drug trials can be divided into two groups: fraud and gross fraud."

DRUG PROMOTION

I am a specialist in rheumatic diseases, and through my career I have watched the development of a series of new drugs for the treatment of rheumatoid arthritis. I, and many other rheumatologists, have considerable doubt that any drug is really effective in arresting the course of rheumatoid arthritis, so surely our first concern should be *primum non nocere:* first not to injure the patient. Often it seems, however, that for the long-suffering arthritic the purported cure is worse that the disease.

Early in my career, corticosteroids were being widely acclaimed. Unfortunately, they cause a variety of severe and even fatal side reactions including psychoses, peptic ulcers, osteoporosis, fractures, cataracts, diabetes, and so forth. Another great hope was phenylbutazone, which was moderately effective, but which unfortunately caused peptic ulcers, and even worse caused severe depression of the bone marrow and occasionally resulted in leukemia. Next was chloroquine, which was relatively weak, but seemed almost free of side effects.

Unfortunately, after a few years of therapy, some patients became totally blind. Then came indomethacin, another rather weak drug, which had numerous serious side effects. More recently dimethylsulfoxide (DMSO) was proposed as a panacea. This drug probably has no effect at all, but acts as a classical counter irritant. When rubbed on the skin, it causes redness, scaling, burning, and pain—the skin hurts so badly that the patient forgets his arthritis. Some patients developed ocular changes, and a few died of shock after receiving DMSO; human use of the drug is now prohibited. Today, we are beginning the era of the immunosuppressives, which can cause total depression of the blood-forming elements in the bone marrow. These are the most dangerous agents ever used in treating rheumatoid arthritis, and we can only wait to see what will result.

THE INDOMETHACIN STORY

Indomethacin is a good example of how a drug is tested and promoted. The drug was developed at the research laboratories of Merck, Sharpe and Dohme, and the basic studies represented careful pharmaceutical research. By 1964, extensive clinical testing of the drug was underway. The only requirement of present U.S. law is that a drug be safe and effective as labeled. Advertising is legally defined as labeling. By June 1965, the FDA felt that the drug met these requirements and that it was relatively safe if used as labeled, so they allowed the drug to be marketed.

Merck immediately embarked on an ambitious advertising campaign. By early 1966, most medical journals contained eight-page color advertisements with headlines stating that indomethacin was "the most promising antirheumatic agent that has been made available for clinical investigation since the introduction of cortisone." Many physicians might misinterpret this statement as meaning the drug could be used in any rheumatic disease. In fact, it has been tested and approved in only four specific diseases. The advertisements also stated in large type that the drug "extends the margin of safety in long-term management of arthritic disorders." Again, this implied that the drug was safer than other drugs and it could be used in any form of arthritis. Unfortunately, it did not specify what indomethacin was safer than.

The advertisements also contained four testimonial statements by eminent pratitioners, two of which stated indomethacin was "the drug of choice," implying this drug in comparisons had been found more effective than other drugs when in fact such comparisons had not been made. One physician claimed that he had found the drug "extremely helpful in over 500 patients." Later, FDA officials indicated Merck's own records revealed the physician had never treated anywhere near 500 patients. The claim was also made that the drug did not increase susceptibility to infection. They omitted mentioning that these claims were based on experiments in a few rats with a system involving bacterial endotoxins, evidence which certainly could not be projected to claim that all infections in human beings would behave in a similar fashion. In fact, the drug increases human susceptibility to infection. Further, the advertisements stated periodic blood counts were not necessary, implying that the drug did not depress the bone marrow: the drug is known to cause total fatal marrow depression.

The direct promotion of the drug to physicians seemed even more distorted than the advertising. One regional sales manager instructed detail men under his supervision: "It is obvious that Indocin will work in that whole host of crocks and cruds which every general practitioner . . . sees everyday in his practice." (The drug is too toxic for routine use in minor complaints, and the "crocks and cruds" indicates considerable contempt for the public.) Further, the salesmen were told to play down side effects.

A SEMANTIC PROBLEM

In the summer of 1966, officials of the FDA demanded that Merck drastically alter its advertising. Officials felt that the advertising did not contain sufficient information on toxicity and overstated the usefulness of the drug, particularly in implying that it could be safely used in any form of rheumatic disease or arthritis. Merck complied for a brief period, but in November 1966 the firm began an even more objectionable campaign, resulting in a second crackdown, and a request by the FDA to the Justice Department that the company be criminally prosecuted for the November advertisements. At the Senate hearings on indomethacin, the president of Merck and Company pleaded:

"Language is not a perfect method of communication, and it may well be that words and phrases that we used in the belief that they mean one thing may have been interpreted by some physicians to mean something else. Such are the complexities of semantics."

This company's advertising converted the legally approved labeling of "Indocin itself may cause peptic ulceration . . ." unto "Ulceration of the stomach . . . has been reported." The difference is hardly semantic, since the second statement implies doubt as to causality, while the first does not. Even worse "semantic" difficulties were arising over the use of the drug in children.

In late 1964, the FDA had recommended to Merck that the prescribing directions for the drug state that this drug should not be used in children. No experiences in children had accumulated and children often react differently to drugs than do adults. Unfortunately, in the prescribing directions issued with the drug, this warning was altered to read "not recommended for use in children," rather than an absolute prohibition. In the fine print in the advertising, this was further changed to "Safety in pediatric age groups . . . has not been established," implying that the drug was safe in children, but little experience had accumulated as yet.

This language was, indeed, not a perfect method of communication, and physicians did use the drug in children. By July 15, 1966, the FDA had learned of sudden deaths due to overwhelming infection in several children receiving indomethacin. The officials requested that Merck immediately warn all American physicians by letter against the use of this drug in children. In addition, the FDA required that the labeling include additional warnings, contraindications, and clear indications of adverse reaction and precautions.

By November 1966, the Canadian Food and Drug Directorate became increasingly concerned about deaths in children. Rather than rely on the company to warn physicians, the Directorate sent letters directly to every Canadian physician, stating:

"Several deaths have been reported in children with severe forms of rheumatoid arthritis, dermatomyositis, and rheumatic fever who were receiving indomethacin. Some of these children succumbed to an intercurrent infection, the severity of which may have gone unrecognized during treatment. The exact relationship to indomethacin was difficult to determine in these reports. However we recommend that indomethacin should not be used in children until the results of further studies become available."

A PILL PER ILL

In early 1967, further disquieting news appeared. Previous evidence of the effectiveness of indomethacin had been based almost solely on testimonials by physicians and much of this information had never been fully published in reputable scientific journals. In early 1967, for independent, careful, double-blind trials were published in leading medical journals. In these trials two groups were used, one receiving indomethacin and another receiving some contrast medication (either a standard drug such as aspirin or an inert dummy). Neither the physician nor the patients knew which capsules were active. All four of these independent scientific trials (none of which relied on art or clinical opinion) failed to show that indomethacin had any more potency than simple aspirin.

The trials could not substantiate any of the claims made in previous reports, which had indicated that 60 per cent of patients had improved.

The company declared some of these trials were totally invalid and in later testimony urged that drugs be evaluated in an uncontrolled fashion by physicians who were expert in the treatment of rheumatic diseases. While no one could question that many of the company-sponsored physicians were expert clinicians, the question of whether they were performing scientific experiments remains unresolved. The company also implied in later testimony that the controlled trial is something new in medicine. An excellent controlled trial was performed in 1747 on board the British warship *Salisbury* by Dr. James Lind. Twelve seamen with scurvy were divided into six groups of two. He tried different therapeutic regimens on the similar groups and found that only the two sailors who received citrus fruits were cured. The technique of controlled experimentation is hardly anything new in either science or medicine and the issues in drug testing really boil down to art versus science and testimonials of "experts" versus numerical evidence.

Certainly the public desperately hopes that the medical profession will provide a pill for every ill. The public realizes that pharmaceuticals are important and represent a potential cure for any disease. But the public is also coming to realize that they may be killed by drugs, and particularly, that they may receive new and untested drugs without even being informed of the potential dangers. Even worse, the physician himself may be unaware of the potential dangers of the drug. The medical profession responds that every physician should use new drugs and get acquired with them and that it is only in this way that the public will receive instant benefit from latest advances. Doctors certainly like to try the newest remedies. About one third of American thalidomide babies were born to wives of physicians who had received free samples of the drug.

SPEND $900 MILLION ON ADS

The average physician's utilization of drugs is at best disturbing. In a study of 408 cases of bone marrow depression due to chloramphenicol, of which one half resulted in death, the drug was prescribed for a valid reason in only six per cent of the cases, and was given for common colds in 12 per cent. The drugs industry spends about $3,500 per physician on salesmen who personally "detail" the doctor on the latest breakthroughs. A total of $900 million is spent on advertising, about three times the amount spent on medical education. And the advertising is successful. A recent survey of drugs dispensed by the mail order drug service of the American Association of Retired Persons revealed that Peritrate, an expensive, long-acting dilator of the coronary arteries, was the most commonly prescribed drug in old persons. This is indeed a triumph for the hard sell Madison Avenue campaign which modestly billed the drug as "life sustaining," for several careful scientific trials have shown the drug has no pharmacologic effects of any kind on coronary artery disease. Of the 12 top drugs prescribed for these retired persons, two were expensive substitutes for aspirin, and four were expensive substitutes for phenobarbital. The use by physicians of fancy, dangerous, and expensive substitutes for old standard remedies undoubtedly contributes to the staggering costs of medical care.

In a survey of 1,014 consecutive medical admissions at Yale University's teaching hospital, 10.3 per cent of patients had a drug reaction; in 1.4 per cent the reaction threatened the patient's life; and in 0.4 per cent the patient died as a result of the reaction. A similar survey at Johns Hopkins of 714 medical patients revealed 17.1 per cent had reactions and 1.55 per cent were fatal. Even if only one-tenth of one per cent of all hospital admissions died of drug reactions, the deaths would approach 29,000 per year. Deaths due to drugs would be a major public health problem comparable in importance to infectious disease, cancer of the breast, and nephritis as a cause of mortality. I would be the first to admit we have no idea what the magnitude of the problem is, but I would violently disagree that no problem exists.

Physicians are not legally required to report drug reactions to the FDA. In fact, it is to their advantage not to report reactions since it might involve them in a possible lawsuit on the part of the injured patient. Just what percentage of drug reactions are not actually reported is unknown, but most informed sources feel that it is less than one per cent. Lowinger recently reported in Science magazine that only 10 of 26 reports on drug safety which he had submitted to 19 pharmaceutical manufacturers had ever been forwarded to the FDA. He further

stated that 14 companies which failed to submit toxicity reports included some of the largest and most scientifically capable pharmaceutical houses. We do not know the extent to which adverse reactions to drugs are a problem in American society, and probably we will never know since the physician and the drug company both attempt to conceal evidence of toxicity.

NATIONAL TESTING POLICIES

The medical profession has generally felt that the practitioner should be allowed to use any drug in any way he sees fit. Attempts to control his use of drugs or to prevent him from using new compounds would be interpreted as an infringement of his basic right to practice medicine and to prescribe in a way in which he sees fit. The FDA does not actually prevent doctors from experimenting with new drugs, but does request the physician to register with the agency, keep accurate records, and that either he or his sponsor promptly informs the agency of adverse reactions. The American Medical Association, which receives over half its income from drug industry advertising, has not been vigorous, in fact not even feeble, in demanding careful clinical testing, honest advertising, or the control of highly toxic drugs.

The pharmaceutical industry itself has demanded a hands-off attitude and has vigorously fought every attempt at any inquiry into drug testing or drug toxicity and has opposed all legislation aimed at controlling drugs in any way. It has done little to police itself and undoubtedly will do little in the future. The industry has established warm and cordial relationships with, and donates funds to, medical organizations. In return, the pharmaceutical industry has an undue influence over the policies of these organizations.

America's great disease-oriented foundations, that rely on public contributions to study cancer, heart disease, arthritis, and so forth, have not made any major attempt to protect the public against drug reactions. This is perhaps understandable, since most of the fund-raising abilities of these organizations is based on promising the public a cure, usually by drugs, and scary stories about toxic reactions to drugs will hardly help fund raising. Furthermore, these foundations have strong ties with the drug industry.

The nation's medical schools are too poor financially to do much to promote either better trials or good postgraduate education on the use of drugs. The faculty of medical schools probably represents the only major source of physicians with the talent and skill required to scientifically test and evaluate new drugs. Contrary to what most people believe, the drug industry is not pumping money into medical schools to support research on drugs. During 1965–66 the medical schools' total expenditures for sponsored research was $375 million. Of this, they received $3 million from nongovernment sources for unrestricted research. If one assumed half of this came from the drug industry, this would amount to about half of one per cent of the total research budget of the schools. The widely publicized Pharmaceutical Manufacturer's Association Foundation, which devotes itself to the "betterment of public health," had awarded only $55,000 in faculty development awards in clinical pharmacology up to the end of 1967. A few companies—notably Burroughs Welcome—provide excellent faculty fellowships, but these are few and far between—about 20 in the entire country. Considering the numbers of MDs and PhDs which the drug industry consumes annually, they may actually make no net contribution and may even represent a drain on the resources of the schools.

NIH SUPPORT

The only substantial source of support for good testing and research on drugs comes from the National Institute of Health (NIH). The total expenditures for support of research on drugs are about $50 million, of which $3.5 million is specifically earmarked for drug testing. This amount, less than five percent of the total NIH budget, is hardly enough to support all the work that needs to be done. Because of the difficulties in obtaining funds for clinical pharmacology, most departments have drifted to where the money is: basic molecular biology. The result has been good, but medical pharmacology has become lopsided. Most departments are headed by molecular biologists, and emphasize basic research. Only two or three real departments of clinical pharmacology are to be found in the entire country. The bright young clinical investigator finds support difficult to obtain for testing drugs, and tends to gravitate into other areas where funding is easier to obtain.

Unfortunately, many medical school investigators whose research programs are funded by NIH also receive personal honoraria from the drug industry. While federal funds are paid only to the medical school and can be used as prescribed in strict budgets, the industry funds may be received as personal income outside the framework of medical school salary scales. Some of these investigators seem far more concerned about the welfare of the pharmaceutical industry than they do about the tax-paying public, even though the public actually provides most of their support. The industry has every right to pay their consultants as they see fit, but publicly-supported investigators should not be permitted to be involved in serious conflict of interest.

The FDA is the only real organization solely devoted to protecting the American public. This agency is the stepchild of two great drug catastrophes: the Food, Drug and Cosmetic Act of 1938 was passed as a result of the elixir of sulfanilamide catastrophe in which 108 children died, and the 1962 Harris-Kefauver amendments were enacted because of the thalidomide catastrophe. The powers of this agency are limited by law and the officials are subject to political pressure. If anyone in the medical profession wishes to criticize or belittle the FDA, he can find an immediate audience in almost any medical journal and his efforts will bring him rich rewards from the pharmaceutical industry. Claims are continually being made that the agency is interfering with research and depriving the public of life-saving drugs. The truth, more likely than not, is that the agency has prevented doctors from poisoning patients with some new, expensive drug of questionable merit.

This agency has a long way to go. Under Commissioner James Goddard many improvements came about. Officials gradually began to insist on better quality trials, and a crackdown on false advertising was begun. Although Goddard was overly frank, and the drug industry capitalized by both misquoting him and exploiting his candor, the public owes him a great debt for improving the Administration. There is every expectation that his successor, Dr. Herbert Ley, will continue to serve the public interest, and see that the FDA becomes even more effective in its mission.

FUTURE THERAPEUTIC CATASTROPHES

Over the past 30 years, this country has experienced several major therapeutic disasters. Many patients were needlessly killed or badly injured by indiscriminate use of certain new drugs. It is said that this is a price we must pay for progress. If a good scientist examined the records of these disasters, he would have to conclude that if testing were conducted in a totally impartial, highly scientific manner, all of these catastrophes could have been avoided. But the Pollyannas of the drug industry assure us that new disasters are impossible.

A few Cassandras, however, prophesy even worse calamities. Pharmaceutical companies are producing new and highly toxic compounds at a startling rate and the number of new drugs being introduced for clinical testing is rapidly increasing. What are the possibilities of another major drug disaster? Dr. H. Friedman, in a letter to Science magazine, stated:

"Let us assume that a drug (such as a combination psychic energizer and diuretic) with no known side effects is aggressively promoted and very widely used throughout North America and Europe. Some 16 years after its adoption, the first hints of unexpected side effects begin to appear and several more years are required before they are confirmed. All children born to mothers using this drug during the first three months of pregnancy (effective as it is for morning sickness) are found to be sterile. The use of the drug for 20 years has affected the larger proportion of an entire generation so that populations of countries effected will drop sharply for several decades and require several additional decades to recover if given the opportunity.

"The effects of thalidomide were relatively easy to discover and limit, but how readily can we detect more subtle effects in time to prevent the possibility of a history-changing catastrophe? In contrast to such a situation, the individual tragedies attributed to past and present drugs would seem rather tolerable."

All the elements for vast future catastrophes are present: lots of new, highly toxic drugs, sloppy and dishonest testing, and hard-sell, dishonest advertising campaigns, to which the average doctor is highly susceptible.

WHAT CAN BE DONE?

I think we can expect little stimulus for correcting the inadequacies of our present system from organized medicine. Physicians' organizations and our disease-oriented foundations have been sweethearts and financial dependents of the drug industry too long to desire any effective change: drug testing must be cleaned up.

Tests are not getting any better. In 1960, McMahon and Daniel, reporting in the Canadian Medical Association Journal, found only five per cent of published trials met even the crudest scientific standards. The trials I reviewed in 1967 were not any better. The doctrine that other parts of medicine are science, but that drug testing is a mystic art which can be performed by only uncontrolled dabblings of so-called experienced clinicians is a sham. Further, it is ethically unacceptable to subject human beings to dangerous drugs unless the experiments are scientifically excellent. The FDA has made some feeble beginnings, but society must demand that only scientific experiments which produce meaningful numerical results be acceptable. Drug testing should be taken completely out of the hands of the pharmaceutical industry. They have repeatedly been guilty of irresponsible optimism about drugs, and their use of paid testimonials is a shallow substitute for good scientific trials.

The distorted Madison Avenue approach used in the promotion and advertising of drugs must be completely eliminated. How can society, which spends only $250 million on medical education, idly stand by and watch the drug industry spend $900 million annually on the post-graduate miseducation of physicians? The public eventually foots not only the bill for the advertising, but also the bill for the new, dangerous, fancy substitutes for the old established remedies. The annual $5 billion drug bill could easily be reduced by $2 billion. Claims that advertising is necessary, and that promotional efforts serve a useful purpose are a joke. The physicist would hardly think of announcing the discovery of a new particle by an aggressive advertising campaign. Why can't physicians get information on new drugs from scientific journals? This is exactly the manner in which they learn about the latest observations on complications of pneumonia, or electrocardiographic changes in heat block.

New legislation is needed. The present laws require only that a drug be safe and effective as labeled. A drug must meet no pressing need, and a more toxic substitute for a standard drug can be marketed. The penalties for violations of the present laws should be increased. Convictions for serious fraud in advertising may carry only a maximum penalty of $1,000 under the present legislation. The penalties are so trivial and prosecution so infrequent, that huge settlements in personal liability suits resulting from drug injuries have a much greater influence on controlling the drug companies' advertising than does federal legislation. A lawsuit to attempt to collect damage for a death is a very poor substitute for preventing the death.

A STRONGER FDA

NIH should surely expand its work in clinical pharmacology, making every effort to upgrade it as a precise science. But simply providing more support is not enough. The public must be assured that investigators who receive public grants are loyal to the public cause, and are not involved in any financial conflicts of interest.

The FDA likewise should be further strengthened. FDA officers receive a constant diet of abuse and rarely if ever congratulation for the vital public service they perform. All of us have a role to perform in refuting frequent unfounded attacks on officials of this agency. At the same time, every scientist should in any way possible prod the FDA to improve its scientific status and the quality of its staff.

Scientists must urge the public not to accept excuses for drug catastrophies or for excessive medical costs due to drugs. The scientist must particularly guard against the jargon games used by the pharmaceutical industry in obscuring any problem. Endless demands for proof positive, suggestions for long-term studies, and frightening announcements that any action will destroy the entire pharmaceutical industry are all part of this game. Dr. I. D. J. Bross, in *Science*, has particularly warned against the fallacies:

"The only way to close the credibility gap is for the spokesmen for science to speak plainly, honestly, and bluntly—without minimizing mistakes, evading responsibility, rewriting history, or otherwise trying to cover up unpleasant facts. Language games in technical jargons have long been a favorite academic sport, but this is too dangerous a game to play when human lives and well-being are at stake."

Finally, the physicist or other scientist who is totally removed from the sphere of medicine and drugs should not ignore this area. Obviously the medical profession itself has been remiss in demanding the highest ethical and quality standards. Nowhere is the American public more exposed to the fruits of good scientific research than when it benefits from drugs which are useful in combatting disease. Likewise, the public is never more conscious of bad scientific research than when it is the victim of a therapeutic catastrophe. We must all face the unpleasant fact that adverse reactions to drugs are major public problems. Surely all scientists should do everything possible in their public roles to see that the quality of scientific research in drug testing is upgraded, and that the public interest is always first.

[From the New York Times, July 29, 1969]

PRISON DRUG AND PLASMA PROJECTS LEAVE FATAL TRAIL

(By Walter Rugaber)

WASHINGTON, July 28.— The Federal Government has watched without interference while many people sickened and some died in an extended series of drug tests and blood plasma projects.

The profits generated by these activities have gone to an enterprising contractor for the nation's biggest pharmaceutical manufacturers.

The immediate damage has been done in the penitentiary systems of three states. Hundreds of inmates in voluntary programs have been stricken with illness and serious disease. An undetermined number of the victims have died.

In a broader sense, countless millions of American consumers have been involved.

Potentially fatal new compounds have been tested on prisoners with little or no direct medical observation of the results.

Prisoners failed to swallow pills, failed to report serious reactions to those they did swallow, and failed to receive careful laboratory tests.

These studies have generated data that have in turn been used to justify the sale of drugs at prescription counters across the country.

This forbidding trail has been marked out by an Oklahoma-born physician named Austin R. Stough and corporations in which he owns a substantial interest. Despite his importance in two vital fields, he is practically unregulated in either.

As a general practitioner who reports no formal training or education in pharmacology, he is said to have conducted between 25 per cent and 50 per cent of the initial drug tests in the United States.

The 59-year-old doctor, whose companies have been blamed for the repeated use of dangerous methods and inadequate equipment, is estimated to have produced the plasma for about a fourth of an important byproduct that is widely used to protect people exposed to infectious diseases.

These prison-based enterprises have regularly incurred local disfavor. Dr. Stough was evicted from one prison by the Oklahoma authorities in 1964. He was forced out of an Arkansas prison by officials there in 1967. One of his corporations is now under orders to close down prison operations in Alabama.

But Dr. Stough (rhymes with How) is said to retain financial interests in some private blood banks in Birmingham and Dallas, and he is known to be seeking connections with prison systems in new areas.

He can do so freely. He has incurred no penalties, and dissatisfaction with his performance in one state has not prevented a repetition of it in another.

The Federal Government and the pharmaceutical industry—the two forces with enough broad power to compel safe practices from state to state—have maintained a general indifference at every turn.

Several agencies within the Department of Health, Education and Welfare have known the details of Dr. Stough's plasma collections and drug tests for years. They have not curtailed them.

Some officials in Washington have attributed their inaction to gaps in the law and in the regulations under which they work, and a shortage of specific Federal standards is occasionally apparent.

But critics in Congress and elsewhere have blamed bureaucratic inertia and timidity for the failure to regulate drug and plasma operations, and a lapse in enforcement is also occasionally apparent.

For example, the Food and Drug Administration employs only a single physician to conduct field investigations of all the studies underway in the United States, and the Agency's inquiries rarely go behind the dry scientific data.

METHODS CALLED DANGEROUS

The Division of Biologics Standards, a unit of the National Institutes of Health that is responsible for the regulation of blood products, recently asserted that the safety of plasma donors was not its concern.

Several major pharmaceutical manufacturers have recognized that some of the methods employed by Dr. Stough were extremely dangerous. They continued to support him with large sums of money.

An executive of Cutter Laboratories once acknowledged, for instance, that gross contamination was apparent in the areas where the largest blood plasma operations were conducted. The rooms were "sloppy," he observed.

When a Government doctor asked why Cutter continued to reward such an enterprise with hundreds of thousands of dollars' worth of business, the executive explained that the Stough group enjoyed crucial "contacts" with well-placed officials.

FEES AND PARTNERS

These contacts involved, among other things, the payment of sizable retainers to influential lawyer-legislators and the establishment of "partnerships" for a number of prison physicians who remained on the public payrolls.

With neither Government nor industry intruding, with most of their records held in secret, with officials passing the problem on to someone else, Dr. Stough prospered at his work throughout the nineteen-sixties.

He has generally declined to talk with local newspapermen about the controversies involving him. And he recently refused to grant an interview with a reporter for The Times.

"We've taken the position of no comment," Dr. Stough said during a recent telephone conversation with a reporter who had asked to see him. "I don't think we're interested in airing anything in the newspaper."

"We think some people have made a mistake," he remarked, referring to the medical observers, editorial writers and state officials who have assailed him. But, he added, "I'm not looking for revenge on anybody."

Efforts to photograph Dr. Stough were unsuccessful, and an extensive search of newspaper files and other sources turned up the pictures of the physician.

STARTED IN OKLAHOMA

Dr. Stough graduated from the University of Tennessee Medical College, spent a one-year internship in Oklahoma City, and opened a private practice in McAlester, site of the Oklahoma State Penitentiary, late in 1937.

He soon began to serve, on a part-time basis, as the prison physician. With direct access to more than 2,000 inmates, his drug tests began to grow extensively. In the meantime, he started a new endeavor.

On March 25, 1962, the inmates at McAlester began lining up to participate in a medical procedure called plasma-pheresis. Under it, a unit of whole blood is drawn and the plasma, a fluid that makes up about 55 per cent of the blood, is taken out.

The remaining cells are reinjected. That was the critical step on Sept. 19, 1962, when one of Dr. Stough's technicians processed an inmate named Tommy Lee Knott, 47, an illiterate prisoner with a long criminal record.

Knott's blood type was O-positive, but he subsequently charged in a lawsuit that after the plasma had been drawn off, the technician pumped another man's cells, which happened to A-negative back into his veins.

ORGANS DIAGNOSED

Unfortunately for Knott, his liver, lungs, brain, kidneys and other organs were injured, his nervous system underwent shock, and his weight dropped 58 pounds in 17 days.

In suing Dr. Stough and two associates for $270,000 in damages, Knott also reported that the incompatible blood had caused a double hernia, permanent secondary anemia and a 10 per cent reduction in life expectancy.

The defendants managed to settle out of court for $2,000 after Knott, who had been removed from the penitentiary for treatment, went off on a crime spree that landed him in a small town jail.

Only three months after this inauspicious episode, Dr. Stough embarked on an ambitious expansion effort. The financial rewards inherent in his initial plasmapheresis program would now be greatly multiplied.

He brought his plasma operation to Kilby Prison, a drab institution near Montgomery, Ala., in December, 1962, and in the following year he began drawing blood in two more of the state's prisons, Draper and Atmore.

In October, 1963, he started a plasma program at the Cummins Farm, a sprawling unit of the Arkansas state penitentiary that was quietly going through an era of general brutality and neglect.

PROTEINS EXTRACTED

Plasma itself can be used in the treatment of shock, but it also contains a number of proteins, including gamma globulin, that can be extracted and employed to counteract a variety of medical difficulties.

The gamma globulin from most donors contains enough antibodies against such diseases as measles and hepatitis to be effective when it is reinjected into a person who has been exposed to those diseases.

This is not the case, however, with diseases such as mumps, whooping cough, tetanus and smallpox. Groups of donors receive vaccinations to build up the antibodies in the gamma globulin intended to treat these illnesses.

The result is know as hyperimmune gamma globulin, and much of the plasma Dr. Stough extracted was used by manufacturers to produce this serum. It can be a hazardous process.

Dr. Stough demonstrated this immediately upon his arrival in Arkansas. Andrew Buddy Crawford, a 45-year-old inmate at the Cummins Farm, received the first in a series of whooping cough shots on Nov. 23, 1963.

DIED AFTER 8TH SHOT

More amounts of the vaccine were injected weekly for a time, and on March 7, 1964, after a two-month lapse, Crawford received his eighth shot. He became ill about a week afterward.

Crawford died slowly and in very painful fashion, and three Little Rock physicians, who reported the process with the lack of patients' names often encountered in medical journals, said it was probably the result of the repeated vaccinations.

It was left to The Pine Bluff (Ark.) Commercial to report, only last January, that the man who died on June 13, 1964, was Andrew Buddy Crawford, and that the program involved was directed by Austin R. Stough.

As a measure of his grip on the market at about this time, a Government source calculated that Dr. Stough's plasma would produce 193,970 cubic centimeters of hyperimmune gamma globulin solution monthly.

Since only about 800,000 cubic centimeters of this type of plasma product were distributed each month throughout the United States, Dr. Stough's output was the source of practically a fourth of the entire national supply.

OTHER PRISONS EYED

"With demand exceeding supply," a Government doctor wrote of the boom, "inquiries were made in other states concerning the possibility of opening plasmapheresis centers in other . . . prisons."

A certain style had developed. In Oklahoma, Dr. Stough himself was the prison physician. The salary of $13,200 a year was inconsequential by his standards, but the standing it gave him within the prison was invaluable.

So, in Alabama, he awarded Dr. Irl R. Long, the senior prison physician, a financial interest in the program. Until a few weeks ago, Dr. Long simultaneously received a salary of $942 a month from the state.

A committee of the Alabama Medical Association remarked in a report issued earlier this year that "this unconscionable situation, regardless of reason, should never have been permitted to come into existence."

The prison physician in Arkansas, Dr. Gwyn Atnip, was paid $20,000 a year for his work in the plasma program there. As a desperately needed doctor among the inmates, he received $8,000 annually from the state.

GOT POLICIAL AID

Dr. Stough also lined up political support outside the prisons, a tactic that demonstrated its importance when members of the Oklahoma Legislature began to ask wether his penitentary operations were sanctioned by law.

One of Dr. Stough's most vehement opponents was Gene Stipe, then a State Senator. But early in 1963 Senator Stipe changed sides and successfully pushed a bill that firmly established the physician's standing in the prison.

Later it was discovered that at about the time this change of direction occurred and the saving law was enacted, Mr. Stipe, a lawyer, began to receive a $1,000-a-month retainer from the concern headed by Dr. Stough.

A spokesman for the organization asserted that the money was for legal services only. Mr. Stipe agreed. Henry Bellmon, then Governor, expressed displeasure but noted that the state had no applicable conflict-of-interest law.

The political nature of the matter was usually most apparent when Dr. Stough moved to enter the penitentiary system in a new state. His drive on the major prison at Reidsville, Ga., was an example of the technique.

CHECKED WITH CENTER

Dr. Joseph Arrendale, the institution's medical director, one day telephoned Dr. Ronald F. Johnson, then on the staff of the National Communicable Disease Center in Atlanta.

Dr. Johnson had followed Dr. Stough's plasmapheresis operations for some time, and Dr. Arrendale wanted advice. In a memorandum of the conversation, Dr. Johnson reported as follows:

"It was clear that Dr. Arrendale did not favor [a plasma program]. However, he felt that Dr. Stough might be 'bringing political pressures to bear through the state legislature' which could clear the way for such a program."

The Georgia campaign ultimately failed, and a similar move on the state prison at Parchman, Miss., was also turned back. But by then Dr. Stough had encountered serious difficulties in his existing programs.

The five prisons in which he was operating by the end of 1963 all were drastically in need of operating funds, and all exhibited obvious signs of longstanding general neglect.

NO RECORDS

The factors pertinent to Dr. Stough's activities included a lack of medical attention (it bordered on the nonexistent in Arkansas), an absence of records, and an atmosphere of isolation and secrecy.

Still, Dr. Stough's trail remains vivid at each significant turn, and its progress behind the high walls of Kilby Prison serves to illustrate the type of infection that was spread through four other institutions.

By April, 1963, five months after Dr. Stough had opened his plasmapheresis center at Kilby, the incidence of viral hepatitis, an often fatal disease of the liver, was climbing sharply.

From none or one or two cases a month, the disease now rose to more than 20 in a single period. Moreover, the outbreaks held generally firm between 10 and 15 a month through the following November.

The rates then soared again. There were 29 cases in December, 22 in January, 1964, 23 in February, 27 in March, and 27 in April. A tenth of the prison population had been admitted to the Kilby hospital.

Joe Willie Tifton, 46, died on March 18. Emzie B. Hasty, 42, died on April 14. Charlie C. Chandler Jr., 31 died on April 16. David McCloud, 27, died on May 22. Each death was attributed to infectious hepatitis.

Little bits and pieces then began to leak to the outside world. A penciled note from one inmate said, "They're dropping like flies out here."

But a prison spokesman said:

"The doctors are quite confident that there is no connection between the plasma program and the cause of hepatitis and jaundice."

Dr. Stough's partner, Dr. Long, spoke as the senior prison physician.

"That same program is being carried on at Draper and Atmore," he declared, "and there have been no cases reported there."

This assurance was published in The Montgomery Advertiser on May 24.

INMATES AFFLICTED

Actually, the records show that by the end of May, at the time he spoke, 37 inmates had been hospitalized at Atmore and six sent to the infirmary at Draper, all with the same symptoms.

It was not then mandatory in Alabama to report hepatitis cases to the public health authorities, and in that respect Dr. Long overlooked not only the cases at Atmore and Draper but also those at Kilby.

Dr. Ira Myers, the state's public health officer, told the National Communicable Disease Center as late as June 5 that an epidemic "apparently" was under way in the prisons. There was, he said, "no direct confirmation."

The exact number of hepatitis cases in the five prisons was never established and is never likely to be. Too many medical histories vanished, too many were never completed, and too many were improperly kept by "inmate doctors."

Some 544 cases were firmly established, and that conservative figure is the one most often used. But the communicable disease center records also contain estimates of more than 800 and evidence that the figure could run to more than 1,000.

The number of deaths is similarly undetermined. In addition to at least the four in Alabama, there were reports of at least one in Arkansas and at least one in Oklahoma.

The dimensions of the disease were more clearly and precisely stated in sets of percentages, or "attack rates," that measured the incidence of hepatitis among those who gave plasma and those who did not.

At Kilby, for example, 28 per cent of the men who participated in Dr. Stough's program came down with the disease. For those who did not take part, the rate was only 1 per cent.

The rate for participants in one of the barracks at Kilby was 39.1 per cent. At the four other centers, the illness struck between 20 per cent and 26 per cent of the donors and from 0.9 per cent to 1.8 per cent of the nondonors.

FIRST ALLIED TO JAUNDICE

The Federal investigators, reflecting scientific caution, initially referred to the prison cases as "illnesses associated with jaundice." A number of their records employed this phrase.

Jaundice means a yellowish skin, and while it is a symptom of hepatitis, its presence is not conclusive. After extensive testing and study, however, the Government doctors concluded:

"The illnesses seen in these prisons seemed to be indistinguishable with viral hepatitis. It is not felt that any serious question of the nature of the illnesses need be entertained."

Hepatitis is a threat in every blood and plasma program, but the careful use of properly designed equipment can reduce the danger virtually to zero. Dr. Stough managed a double play: technique and apparatus both were cited in the epidemics.

The details are complicated, but the general picture drawn by the experts was reflected by K. T. Kimball, an executive of Fenwal Laboratories who had observed some of the plasma operations and who reported to Dr. Johnson of the Atlanta center, according to a written memorandum, as follows:

"Mr. Kimball directed the conversation to the general level of care exercised by Dr. Stough's technicians. He felt that collection of large amounts of plasma in a rapid operation using equipment of simpler design that Dr. Stough approved might easily lend itself to a high level of contamination of technicians' hands and surfaces of tables, equipment, and the actual bags and tubing used in the procedure.

"He felt that contamination of these objects by the plasma of all donors could have occurred, and that absence of strict medical supervision could easily have led to short cuts in and inadequacies of sterile technique."

SAYS HE WAS "APPALLED"

This was equally apparent to Byron Emery, an official of Cutter Laboratories who also visited some of Dr. Stough's operations and who also talked with Dr. Johnson. Another Federal memorandum reported:

"Mr. Emery stated that when he visited Alabama in April, 1964, he was 'appalled at the situation' he found. He said the plasmapheresis rooms were 'sloppy' and that gross contamination of the rooms with donors' plasma was evident.

"Mr. Emery stated that [Dr. Stough and an associate] . . . could not be trusted to carefully supervise such a plasmapheresis program.

"I then asked Mr. Emery why Cutter did not choose to operate such plasmapheresis programs by themselves without using Dr. Stough's group as an intermediate company . . .

"Mr. Emery replied that Dr. Stough had contacts at the prison and it was through him the permission was obtained from the prison officials to operate the program."

REMAINED BIG CUSTOMER

Cutter nevertheless remained one of Dr. Stough's biggest customers.

Alabama shut down the plasmapheresis centers in the middle of the epidemics and blocked Dr. Stough's efforts to start them up again. Oklahoma had taken over the plasma and drug-testing programs almost simultaneously just before the Federal investigation.

In Arkansas, where he had never tested drugs, Dr. Stough was permitted to continue his plasma operations for three years before a quasi-public foundation successfully replaced him.

And although the Alabama authorities had stopped the traffic in plasma, they permitted him to continue his drug tests without interruption. The enterprise was quickly stepped up.

A pharmaceutical manufacturer generally develops a new product in the laboratory, tests it on animals, and then notifies the Food and Drug Administration that a three-phase tryout on human beings is ready to begin.

Phase one is in many ways the most delicate step of the three because it is designed to establish basic factors such as toxicity, safe-dosage rates, metabolism, absorption, and elimination.

Because of their critical nature, the first-phase tests are usually carried out on healthy subjects. The drug is tried on people who suffer from the target disease only after the phase one hurdle is cleared.

Phase two involves limited administration of the drug to "carefully supervised patients," and phase three embraces "extensive clinical trials" that can include studies by doctors in private practice.

COMPANY JUDGES DOCTOR

The Food and Drug Administration is responsible for * * * the advance from phase to phase. The role of the individual manufacturer is substantial, however.

It is basically the company, for example, that judges a doctor's qualifications as a drug investigator, chooses him to do the job, directs the testing, assembles the results and pays the fee.

Healthy prisoners who by definition exist in closely controlled circumstances are perfect for phase one studies, and Dr. Stough remained in heavy demand by pharmaceutical concerns.

The Food and Drug Administration, citing regulations of the Department of Health, Education and Welfare, refused requests by The Times to examine its records on Dr. Stough.

A spokesman for the agency said, however, that since 1963 the physician has carried out some 130 investigational studies for 37 drug companies. Other types of tests and work by an associate involved 45 additional programs.

The F.D.A. declined to disclose the names of the drugs that Dr. Stough examined or the names of the companies for which he worked. Some of the information has been obtained from other sources, however.

BIG COMPANIES

The companies included the Wyeth Laboratories Division of American Home Products Corporation; the Lederle Laboratories Division of American Cyanamid Company; the Bristol-Myers Company; the E. R. Squibb & Sons Division of Squibb Beech-Nut Inc.; the Merck, Sharp & Dohme Division of Merck & Co. and the Upjohn Company. These concerns, according to the current directory published by Fortune Magazine, are among the 300 largest corporations in the United States.

An investigation of Dr. Stough's work for these and other concerns began earlier this year after Harold E. Martin, editor and publisher of The Montgomery Advertiser, wrote a series of highly critical stories about the drug studies.

The State Board of Corrections asked the Alabama Medical Association to name a committee of inquiry, and Dr. Tinsley R. Harrison of Birmingham, a nationally known cardiologist, was selected as chairman.

Even when the committee dealt with the welfare of the inmates its investigation inevitably raised broader issues, for Dr. Stough's "findings" became data and the data helped to justify public sale.

The medical association investigators concluded not only that Dr. Stough's work had been "bluntly unacceptable" but also that as one result, "the validity of the drug trials themselves must occasionally be seriously in doubt."

Because of the Food and Drug Administration's refusal to permit an inspection of its files, it is impossible to determine conclusively whether Dr. Stough ever reported unfavorably on the drugs he was paid to test.

However, he has published a number of scientific articles on his findings, and a review of those cited in the comprehensive Cumulated Index Medicus since 1960 discloses not a single critical appraisal.

It was learned from independent sources that one of the drugs Dr. Stough had tested was Indocin, a best-selling product of Merck, Sharp & Dohme that is used in the treatment of rheumatoid arthritis.

Dr. Stough's findings on Indocin are unavailable, but it went on the market after largely favorable data had been generated by company-paid investigators, and the subsequent controversy points up the broad significance of testing.

Indocin was assailed * * * the Senate Subcommittee on Monopoly. Contrary to findings of the initial data, witnesses said, careful tests had found the drug no more effective than aspirin, and it produced serious effects as well.

A careful medical examination in advance of a drug test is regarded as essential to insure that the prisoners involved do not show signs of subtle disabilities that would make the study invalid.

A member of Dr. Harrison's committee recalled during an interview that one day he and another investigator turned up at Kilby Prison to discover that 80 inmates had been examined for a new program in just four hours.

Since that meant an examination every three minutes, the investigators asked to see the records. None were found on the premises—not for a single prisoner. The records that existed were said to be at Dr. Stough's headquarters.

The committee noted in its report that prisoners about to embark on a new test had "received a rapid explanation of the purpose" that left "considerable variation in the understanding of what had been said."

NO DOCTOR PRESENT

The committee continued:

"All this had seemingly been done by technicians with no physician being present as far as could be determined. Two of the four prisoners who were interviewed indicated that they had never been examined by a physician while they were in the prison although they had been on several drug trials."

The fundamental purpose of a drug test is to spot any adverse effect and report it. There were breakdowns in Dr. Stough's operation, and Dr. Harrison's committee cited a number of examples.

First, it encountered a Mr. Howell, "a man with very little previous medical training whose experience before entering his present position had been that of a venereal disease inspector."

"It was stated with pride by this individual who functions as hospital director, that he himself was able to deal with nine out of every 10 patients who came to him so that the doctor was not bothered."

A number of qualified medical sources said that without a physician regularly on hand to look over the inmates who took drugs, it would have been "totally impossible" to gauge reactions.

PRISONER FEES VARIED

Dr. Harrison's committee took up the question of fees paid by Dr. Stough to inmates who participated in drug tests. These varied widely, but a man could usually make at least $1 a day for taking a series of pills.

This was big money for people who otherwise received only 50 cents every three weeks for incidental spending, and it created what one investigator called "a built-in negative feedback."

Prisoners often covered up severe reactions in order to keep on with the tests, and several told The Montgomery Advertiser that they shammed taking pills and later spit them out. The medical group said of one inmate:

"He had hung on to the end [of a test] although he had been feeling very ill and had not complained of this illness because it would have meant his losing the pay which he was hoping to receive for his participation."

One conscientious experimenter who has gone deeply into the question of fees believes that a prospective subject should be offered no more than two or three times the amount he would receive without taking part.

NUREMBERG CODE CITED

The medical investigators underlined the importance of the fees and inadequate explanations of the tests by attaching to their report the Nuremberg Code, developed after the concentration camp excesses of Nazi doctors.

The code calls for "free power of choice" and holds that a subject "should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision."

The Alabama committee also inspected Dr. Stough's laboratory. Its role in analysis samples taken from the inmates was especially important since the direct medical observation was rated low.

In one instance the group found an error of about 40 per cent in the control agent against which laboratory samples from about 20 prisoners were being measured. The investigators said:

"This was pointed out to the laboratory director and he excused it [on grounds that the committee rejected]. His attitude to us was unacceptable and reflected poor technique."

The operation "probably compares favorably with many small hospital laboratories in Alabama," the group concluded. But it "lacks the better qualified personnel and more careful quality control seen in better run laboratories."

The committee reported that on top of the other problems, both Dr. Stough and Dr. Long had "limited training in basic pharmacology." The available biographical information shows they had no formal education in the field at all.

"You might say they have had a lot of on-the-job training and background," one clinical pharmacologist said. "But this is a weak argument. Nowadays, with the sophistication of modern drugs, you need more than this."

Last May, after the State Board of Corrections had a look at the committee's report, Dr. Stough received another eviction notice and started to close down the drug studies in Alabama.

Thus, Dr. Stough suffered another setback. As before, a state saved its prisons from any further trouble. But as usual, the Federal authorities and the pharmaceutical companies remained silent.

ONLY ONE PHYSICIAN

The single physician employed by the Food and Drug Administration to investigate drugs tests throughout the United States has visited Dr. Stough's operations twice, an agency spokesman said.

Some citizens tend to think of the agency as an eternally vigilant organization, and in his dealings with local officials and newspapermen Dr. Stough has turned this misapprehension to advantage.

"They [F.D.A. officials] love to close people down," he said in the brief telephone conversation in which he refused to grant an interview. "So if I was off-color, they'd be on me like a hawk."

"That's one of the reasons the [Alabama Corrections] Board wasn't concerned," explained Frank Lee, the state's commissioner. "We knew they [F.D.A. officials] came in here and looked into the operation."

Dr. Herbert L. Ley, Jr., the F.D.A. Commissioner, branded Dr. Stough's assertion "a non sequitur."

The Food and Drug Administration's lone medical inspector is alert to "flagrant" dishonesty, and there have been men who tested drugs on nonexistent people and who produced imaginary results.

But an inspection is limited mostly to checking data that have been submitted to the sponsoring drug company to insure that it agrees with data sent to the agency. There is little or no effort to look behind the figures.

"Our responsibility is not the direct supervision of the [drug] investigators," Dr. Ley said in an interview. "Our responsibility is to evaluate the data that come in to us. We can't be omnipotent or omniscient."

While the agency has never found occasion to reprimand Dr. Stough, its inspector, Dr. Alan B. Lisook, did make some "suggestions" earlier this year about "the lack of medical supervision of patients."

NOT ENOUGH SUPERVISION

"We told him we thought there should be more supervision," Dr. Lisook said, "and he admitted there was not as much as he would like because of the volume of drugs being tested."

This was virtually an acknowledgement by Dr. Stough that more tests had been undertaken than could be adequately overseen, but the F.D.A. did not require change.

The agency "frowns" on insufficient supervision, Dr. Ley said, but under present policies there are no specific minimum standards. In the gray area that results, frowning is about the limit.

Since between 25 per cent and 50 per cent of the phase one studies have been concentrated in Dr. Stough's hands, Dr. Ley was asked whether volume alone—quality aside—concerned his agecny.

"It's a red flag, there's no question about that," he replied. But the commissioner explained that neither law nor regulation permitted the agency to force a cut back in the number of studies assigned to a single man.

There is no step short of outright disqualification for obvious misconduct, Dr. Ley said. That is an action the F.D.A. has taken no more than a dozen times in its history.

SHORTAGE CHARGED

The drug companies contend there is a shortage of investigators, and Dr. Ley said that while he believed there were enough to study the "really new drugs," he wanted to avoid charges that the agency blocked progress.

"It's harder to get a driver's license in the United States than it is to get fatal drugs," complained Dr. William M. O'Brien, an associate professor of preventive and internal medicine at the University of Virginia. He added:

"To get a driver's license you have to take tests, show you know how to drive, and so on. For drugs, you just walk in the door and say, 'I'm an M.D. I want to test drugs.' It's fantastic. It's unbelievable."

It is difficult to measure the precise sums of money that the pharmaceutical industry has poured into Dr. Stough's operations, but a number of reliable clues are available.

Operating within at least nine separate corporations, the major one of which is Southern Food and Drug Research, Inc., Dr. Stough has a gross income in a good year probably approaching $1 million.

SMALL OVERHEAD

He has not carried a high overhead. His net income in Alabama in 1967 was nearly $300,000 (on a $500,000 gross), and his profit before taxes in Arkansas in 1966 was about $150,000.

The Alabama Medical Association's committee treated the drug manufacturers with circumspection in its report, suggesting that the companies could hardly police the state's prisons.

But it pointed out that the makers, as well as the Food and Drug Administration, had engaged in monitoring of the drug tests that might have been "too superficial and too remote to provide maximum safety."

The committee also found that in sponsoring Dr. Stough's tests the drug concerns had given "tacit approval" to his research. In this, it reported, the companies had "demonstrated some lack of discretion."

"Our companies are usually pretty careful about who they have doing phase one work," said Dr. C. Joseph Stetler, president of the Pharmaceutical Manufacturers Association. "They aren't interested in guys who aren't doing a first-class job."

Mr. Stetler said that some concerns might make more rigorous over-all studies of potential investigations than others and that in some instances the day-to-day supervision "gets to be seemingly routine."

DOUBTS NEED FOR BARS

Heavy demand for phase one work may also be a factor in quality, Dr. Stetler added. But he said he was not sure the Government should restrict an investigator's work for high volume if the "end product" was satisfactory.

Each of the pharmaceutical companies that could be identified as having retained Dr. Stough was asked to comment on his drug testing, and each defended the validity of the data he submitted.

For example, Merck, Sharp & Dohme said in a prepared statement that Dr. Stough's "facilities, staff, volunteer group, and prior experience were particularly suited" for the studies it required.

The physician has conducted 14 projects for the concern since January, 1968, and, the company's statement concluded, "in our opinion the studies were properly conducted and the data provided have been sound."

Merck, Sharp & Dohme asserted that practically all of the studies carried out by Dr. Stough had been "extensively studied and clinically used" by others and that some of the drugs had already been approved for marketing.

LACK OF CRITICISM

A spokeman for Lederle Laboratories pointed out that Dr. Stough's testing operations at the Oklahoma State Penitentiary had not been criticized publicly by qualified medical observers.

Wyeth Laboratories said it had retained Dr. Stough for only a single study. The company said he was hired in 1964 to test an experimental drug that was never placed on the market and has not been used since.

One company official, who asked not to be identified, remarked: "How he [Dr. Stough] operated, how he had his machinery set up—they didn't even know at the prisons."

To ship blood products in interstate commerce requires a license from the Division of Biologics Standards, and when a manufacturer obtains one he must face and continue to face regular inspections.

DOCTOR NOT LICENSED

Dr. Stough does not have and never has had a license from the division. Under the so-called "short supply provision" of the agency's regulations, a licensed company can pick up the scarce plasma at Dr. Stough's door and ship it to its laboratories without violation.

Serious things can happen if the slightest thing goes wrong once the plasma reaches the hands of a licensed company. Nothing can happen, so far as the standards division is concerned, if everything goes wrong before that time.

Dr. Stough incurred no Federal disfavor for the hepatitis epidemic in three states because the disease apparently was routinely killed out in the manufacturing process that turned his plasma into gamma globulin.

"The conclusion that we came to was that the quality of the product was not affected," recalled Dr. Roderick Murray, the division's director, "and therefore we had no backing to tell them (the companies) not to use plasma that came from Stough."

INVITATION REJECTED

This is felt so keenly at the division that Dr. John Ashworth, then an agency official, refused an invitation from Dr. Johnson just to go and look at a plasmapheresis operation.

"He said that his appearance at the plasmapheresis center would not be consistent with the policy of D.B.S.," Dr. Johnson wrote, because the policy did not include "direct supervision or policing of the actual procedures."

"Any time that we've attempted to write into the regulations elements that are designed to protect the donor," Dr. Murray said, "this has been disallowed because there's no statutory authority."

What about the communicable disease center, which traced the hepatitis epidemic directly to Dr. Stough's programs? That agency, a spokesman said, is only a consultant to the states. Enforcement is up to the state authorities.

The question thus is put to the Alabama public health officer, Dr. Myers. He answers that the State Health Department has "no specific jurisdiction in the prisons."

APPENDIX VI

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., July 7, 1969.

Hon. GAYLORD NELSON,
U.S. Senate,
Washington, D.C.

DEAR GAYLORD: I am writing as the ranking Minority Member of the Monopoly Subcommittee and at the request of the other Minority Members. I understand that the staff of the Monopoly Subcommittee has submitted a list of questions to Dr. A. Dale Console regarding his testimony submitted to your Subcommittee on Thursday, March 13, 1969. These questions and their answers, I understand, are to be included in the record.

Because Dr. Console was unable to attend the hearing due to illness, the Subcommittee Members and their staffs did not have an opportunity to question him in person. The Minority Senators would like to request at this time the opportunity to submit certain questions to be included, with Dr. Console's answers to them, in the hearing record, along with those of the Majority staff.

I have reviewed Dr. Console's March statement, together with his prior testimony before the Kefauver Committee in 1960 and his answers to the questions submitted by the Subcommittee staff and feel that the following questions would be appropriate.

1. In your opening statement before the Kefauver hearings, Wednesday, April 13, 1960, you stated: "Since I destroyed the records in my private file when I resigned from the industry, I can offer nothing which can construed as proof. I can offer a distillate of my experience and the opinions I have formed as a result of the experience." (Hearings Before the Subcommittee on Antitrust and Monopoly of the Committee on the Judiciary, U.S. Senate, Eighty-Sixth Congress. Second Session, p. 10368.) In your opening statement submitted to the Subcommittee on Monopoly of the Senate Select Committee on Small Business, March 13, 1969, you wrote that "for almost ten years I have devoted 90% of my time to the private practice of psychiatry and my contact with the so-called 'white towers of medicine' has been minimal." You continued, "the primary justification for my appearance here derives from a degree of expertise I gained during six and one-half years I spent as Associate Medical Director and Medical Director of E. R. Squibb & Sons." Could you outline what contact you have had with the drug industry since the time you left Squibb twelve years ago that has enabled you to keep your information and conclusions current and updated, especially in light of the statements just quoted.

2. On page 8 of your question and answer pages you were asked a question on the "role of testimonials in the advertising and promotion of drugs with respect to efficacy and safety" by the Subcommittee staff. In answering this question you referred to examples from your experiences which occurred while you were at Squibb. You also requested part of your testimony before the Kefauver hearings in 1960 be included in the record as part of your answer. Would you have any more recent information that would be relevant to this question.

3. While at Squibb did you have a great deal of contact with Medical Directors from other companies? Further, since the time you left Squibb twelve years ago have you had any subsequent contact with Medical Directors of either Squibb or any other company. If so, how extensive has this been?

4. In response to a question by the Subcommittee staff on overseas promotion, advertising and marketing of drugs, you referred almost exclusively to experiences you had while you were at Squibb. Over the past twelve years with the exception of the Marsalid example you found in Mexico "about four years ago," have you had any contact with the drug industry so as to be aware of the policies it is currently pursuing in overseas sales? And, if so, how extensive has this been?

5. In answering a question by the Subcommittee staff referring to estimates by Dr. Frederick Wolff and Dr. George Baehr of New York on drug expenditures you stated: "I know of no way to make an accurate estimate of the percentage of drugs that patients pay for unnecessarily." You then went on to estimate that 50% of prescription drugs are worthless. Could you give us some idea of the basis which supports your belief that 50% of prescription drugs are worthless.

6. Throughout your testimony and the answers you submitted to the Subcommittee staff, you have made numerous references to your experiences at Squibb. In reading through the testimony, however, one frequently has the

impression that you are speaking of the drug industry as a whole. Could you clarify for us whether you intended to discuss the entire industry, or whether you intended your testimony to refer to Squibb.

I would appreciate your submitting the above questions to Dr. Console and inserting his answers, together with these questions, at the proper place in the record.

With best wishes,

Sincerely,

JACOB K. JAVITS.

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., July 17, 1969.

Hon. JACOB K. JAVITS,
U.S. Senate,
Washington, D.C.

DEAR SENATOR JAVITS: In accordance with your request, I am submitting your questions to Dr. Console.

Since Dr. Console's original statement and his answers to my questions have already been printed in Part 11, of our hearings, I have asked the Committee staff to include your questions and Dr. Console's answers—when received—at the appropriate place in the printed record of the hearings.

The questions sent to Dr. Console were submitted by me as Chairman of the Subcommittee in accordance with my opening statement of March 13, at which time I said: "The questions I had planned to ask will be sent to Dr. Console, and his answers will be placed in the record immediately following his statement." (P. 4477, Vol. II of our hearings.)

Naturally, as is always the Subcommittee's policy, had any other member or members indicated an interest in submitting questions, I would have been more than happy to accommodate them and this material would have been placed in the record with Dr. Console's statement, which, incidentally, was available to all the Subcommittee members in advance of his scheduled appearance.

Sincerely,

GAYLORD NELSON,
Chairman, Monopoly Subcommittee.

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., July 17, 1969.

Dr. DALE CONSOLE,
Princeton, N.J.

DEAR DR. CONSOLE: I am attaching a letter which I received from Senator Javits, in which he asked that certain questions be submitted to you for your consideration.

Senator Javits' questions and your answers will be inserted in the printed record of our hearings at an appropriate place.

Sincerely,

GAYLORD NELSON, *Chairman,*
Monopoly Subcommittee.

A. DALE CONSOLE, M.D.,
Princeton, N.J., July 20, 1969.

Hon. GAYLORD NELSON,
U.S. Senate,
Washington, D.C.

DEAR SENATOR NELSON: I enclose my answers to Senator Javits' question. I agree that the Minority Senators have an equal right to submit questions and that the answers to those questions should be made a part of the record.

Sincerely,

A. DALE CONSOLE, M.D.

The major thrust of most of Senator Javits' questions appears to be based on the assumption that the practises I observed 12 years ago are no longer pertinent and that the industry has changed. This is a valid point and I believe it deserves serious consideration. In my opinion, however, the conclusion that the drug

industry has changed must be based on the assumption that the basic nature of man has changed in 12 years. I know of no evidence that supports such an assumption.

When I went into the drug industry a door opened and exposed drug industry practices that are unknown to any one who is not in, or has not been in the industry. Similarly, when I left the industry, that door closed and I have had only one reliable guide that permits me to draw conclusions about changes in the drug industry. That guide is the advertising and promotion practices that always have been and still are exposed to public view. The manner in which a drug firm advertises and promotes its products is a reliable index of the firm's philosophy. Since I have seen no change in these practises since I left the industry I find little reason to conclude that other practises have changed.

Yet it is possible that improvements have occurred and that I have been unaware of that improvement. It is equally possible that the situation has deteriorated and I have no knowledge of that either. The practises I have described and criticized arise out of a basic conflict between the profit incentive that motivates any big business and the ethical considerations of medical practice. The practises derive from human frailty which always has been, and still is with us.

Quoting from the individual views of Senator Wiley in the Kefauver Subcommittee report to the parent Judiciary Committee he said, "Still there is often a tendency, both on the part of individuals and of business, to become preoccupied with their own point of view and their own narrow outlook in a manner which is contrary to the best public interest". I find no reason to believe that this fundamental observation on the nature of man and of business has changed in the past 12 years. Poor research, poor designs in clinical studies, the use of testimonials, and shabby methods of advertising and promoting drugs derive from this fundamental conflict and from the nature of man. The few improvements that have occurred are those that were forced by the 1962 legislation. The drug industry opposed those changes and still uses every trick in the book to evade the law.

Answering Senator Javits' question specifically:

1. Since I left the industry 12 years ago I have had no direct contact with the industry. My only reliable guide has been a continuing study of advertising and promotion practices. Drug industry practices are similar to an iceberg. Only a small portion of the practices are exposed. Until the portion that is exposed shows significant changes there is no good reason to conclude that the unexposed portion has changed. There has been no significant change for the better in the advertising and promotion practices over the past 20 years. If there has been any change it has been for the worse.

2. Even superficial perusal of advertising and promotion will demonstrate that the testimonial still plays the same significant role it played during the time I was in the industry. Examples can be found in the record of these hearings. Probably 90% or more of the letters the FDA has received relative to the proposed ban on fixed antibiotic combinations have been testimonials and I have yet to see evidence of any attempt to supply data which would satisfy the definition of efficacy contained in the Kefauver-Harris Amendments. Testimonials were used when I was in the industry. They were used in 1963 in the proposed ban on antibiotic-cold preparations that I described in my testimony. They were used in 1968 and are still being used in 1969.

3. The last experience I had with the contradictory practices used in the domestic versus the overseas markets was the Marsalid episode I described. I believe that we must strain reasoning more to conclude that those practices have changed than to conclude that they have not changed. I am quite certain that chloramphenicol is still marketed in other countries without adequate warnings. If I am wrong about this I would appreciate it if evidence that I am wrong is brought to my attention.

4. During the time I was in the industry I had close contact with physicians employed by other drug companies. Since I left I have maintained some contact with some of these physicians who became friends. Nevertheless I would not want to leave the impression that this contact has been significant or that it has furnished me with a pipe-line into the inner workings of the industry; it has not.

5. My 50% figure was an estimate and I called it such. I also said, "I know of no accurate way to arrive at such an estimate." My response was a reasonably informed guess and was made relative to higher percentages estimated by other witnesses.

After all I am still a practicing physician and I maintain contact with other physicians as well as with patients who have been treated by other physicians or are being treated for non-psychiatric problems. I am impressed by the fact that the American Psychiatric Association is considering a closer look at its own advertising pages because drugs are being advertised and promoted for use in any and all human problems which are essentially normal stresses of every day living and in which no drug therapy is required or indicated. This is a recent decision which appeared not 12 years ago, but in the last issue of the Psychiatric News.

Since drug advertising that does not sell drugs does not survive it follows that the advertising that does survive is effective. A study of advertising that has survived is amply evidence that many drugs are being abused. In addition it has been estimated that 40% of all drugs are fixed combinations. With very few exceptions these are deplored by the majority of experts because they are considered irrational. To this estimate of about 40% we need only add 10% misuse of single drug entities. While my estimate is a guess it is also my guess that it errs on the low side of the true incidence of irrational prescribing. I still believe that the "chances that a patient will get the right drug in the right amount at the right time is in the order of 50%".

6. It has never been my intention to single out and to criticize Squibb. The practices I have described are drug industry practices and apply across the board. As I have pointed out on several occasions, I was aware of practices used by other companies that Squibb would not stoop to. While I was one of the executives who played poker with Dr. Henry Welch, I know of no evidence that Squibb supported his very profitable business in selling reprints or that Squibb tried to introduce a sales slogan into a supposedly objective symposium on antibiotics.

The conclusions I have drawn are based on an inside knowledge of the practices that were used, on a knowledge of why they existed and still exist, and on the information derived from a continuing study of advertising and promotion practices. So long as the profit motive is considered a legitimate part of medical and para-medical practices and drugs are advertised and promoted by "Madison Ave. tricks" that sell soap, cigarettes and toothpaste we will continue to have abuse.

Finally let me point out that my criticism of advertising and promotion practices included exhibits of advertisements printed in March 1969.

APPENDIX VII

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., September 2, 1969.

Mr. EDWARD D. MARTIN,
National President,
Student American Medical Association,
Flossmoor, Ill.

DEAR MR. MARTIN: I am attaching a letter which I received from Senator Javits, in which he asked that certain questions be submitted to you for your consideration.

Senator Javits' questions and your answers will be inserted in the printed record of our hearings at an appropriate place.

Sincerely,

GAYLORD NELSON,
Chairman, Monopoly Subcommittee.

U.S. SENATE,
SELECT COMMITTEE ON SMALL BUSINESS,
Washington, D.C., June 24, 1969.

Hon. GAYLORD NELSON,
U.S. Senate,
Washington, D.C.

DEAR GAYLORD: At the conclusion of the hearings on the promotional activities of drug manufacturers which were held before your Monopoly Subcommittee on June 19, 1969, you granted the Minority Counsel's request to submit written questions to the witnesses, specifically to Messrs Henry Brodkin, Charles Payton, Edward Martin and Richard Pohl.

I have reviewed the matter and feel that the following questions would be appropriate:

1. In your opinion have the drug manufacturers, in engaging in the type of promotional activities described in your testimony engaged in conduct which is actionable criminally or civilly, or which violates any existing government regulations.

2. Should drug manufacturers have the right to engage in promotional activity, except to the extent restricted by existing law?

3. If you believe that a drug manufacturer's right to engage in promotional activity should be restricted beyond the limitations presently imposed by existing law and regulations, please state the manner in which such activities should be limited and the objectives sought to be achieved by such limitations.

4. Who should have the responsibility for determining the precise nature and extent of such limitations and for their enforcement?

5. Would such further limitations on the right of a drug manufacturer to engage in promotional activity result in a significant reduction in health care costs, and if so, how much of a reduction?

I would appreciate your submitting the above questions to each of the witnesses who testified on June 19, and inserting their answers, together with these questions at the proper place in the record.

With best wishes,

Sincerely,

JACOB K. JAVITS.

STUDENT AMERICAN MEDICAL ASSOCIATION,
PUBLISHERS OF THE NEW PHYSICIAN,
Flossmoor, Ill., September 23, 1969.

Senator GAYLORD NELSON,
Chairman, Monopoly Subcommittee,
U.S. Senate,
Washington, D.C.

DEAR SENATOR NELSON: This letter is in response to your letter of September 2, 1969, in which you requested answers for questions submitted to us by Senator Javits.

The following are our responses to the questions enclosed in your letter.

1. In your opinion have the drug manufacturers, in engaging in the type of promotional activities described in your testimony engaged in conduct which is actionable criminally or civilly, or which violates any existing government regulations.

We are in no position to judge whether drug manufacturers have engaged in activities which violate existing government regulations or conduct which is actionable criminally or civilly. It was our feeling, however, that we must take a close look at the professional standards which the profession sets in accepting promotional material or advertising. It is the government and the courts that should give opinions as to the legal considerations and how they are adhered to, not medical students.

2. Should drug manufacturers have the right to engage in promotional activity, except to the extent restricted by existing law?

The drug manufacturers should have the same rights and responsibilities to engage in promotional activity as does any industry related to the health of the people in the free enterprise system. If these privileges are adjudged to have been violated, as in the case of misleading advertising, price-fixing, etc., one would assume that extensions of the existing laws would be made by Congress, as with any other industry or business.

3. If you believe that a drug manufacturer's right to engage in promotional activity should be restricted beyond the limitations presently imposed by existing law and regulations, please state the manner in which such activities should be limited and the objectives sought to be achieved by such limitations.

Our testimony clearly defined areas such as increased support for FDA investigative and regulatory work, the development of a drug compendium, etc. The question whether extensive promotional activity is detrimental to the American people should be answered by Congress in the form of legislation. It is our feeling that while we perceive inconsistencies in the present promotional efforts with the best interests of educating the profession, we, as medical students, are not able to propose limitations on the scope of promotional activity. We can say that

all advertising should be factual, not misleading, and should not confuse or seek to influence the physician about the actual efficacy or indications of a drug in a way not consistent with objective research and clinical trials. Means to objectively evaluate these criteria are needed by the FDA and regulatory powers should be given to them so as to control misleading promotional activity.

4. Who should have the responsibility for determining the precise nature and extent of such limitations and for their enforcement?

The Food and Drug Administration as directed by Congress. Professional organizations, the drug industry, pharmacologists, etc., should have their professional advice available on specific cases for the FDA, who should be responsible for evaluation and enforcement. One great weakness in the present system is that the FDA does not have the facilities and personnel available for evaluation, and must depend upon the drug industry. This should be changed by legislation and increased appropriations.

5. Would such further limitations on the right of a drug manufacturer to engage in promotional activity result in a signicant reduction in health care costs, and if so, how much of a reduction?

This is a difficult question to answer. It is now clear that a great deal of money goes for promotion and advertising, and limitations theoretically could reduce this and divert savings to the consumer through decreased costs. However, the greater questions of quality control, generic equivalency, competition to develop superior pharmaceuticals, the differences in price after retail mark-up, and the educational value of detail men to physicians make this a question that I, in good faith, cannot answer with a simplistic statement. The development of an objective drug compendium, available to all physicians, with wholesale prices included will do a great deal more to save the consumer money than arbitary limitations on the amount of advertising dollars a company can spend.

I hope this is a satisfactory response to your question. Thank you again for the opportunity for us to let our feelings on this very important issue be known.

With best regards, I am,

Very sincerely yours,

EDWARD D. MARTIN,
National President.

APPENDIX VIII

REPORT ON A STUDY OF ADVERTISING AND THE AMERICAN PHYSICIAN

PART I. THE ADVERTISERS' VIEWPOINT

AN OPINION SURVEY MADE FOR THE AMERICAN MEDICAL ASSOCIATION

BY BEN GAFFIN & ASSOCIATES, BOARD OF TRADE BUILDING, CHICAGO 4, ILLINOIS, MARCH 6, 1953

FOREWORD

This report covers "The Advertisers' Viewpoint", the first part of the *Study of Advertising and the American Physician*, made by Ben Gaffin and Associates for the American Medical Association. The second part, "The Physicians' Viewpoint", will be submitted in April, 1953.

In our proposal to Mr. Thomas Gardiner dated September 3, 1952, we defined the objectives of the study: "To uncover fundamental thinking of advertisers and physicians regarding basic advertising problems in general, and the peculiar problems of medical advertising in particular. This information will enable the American Medical Association, through its publication advertising, to better serve its readers and advertisers and by so doing, to increase its advertising revenue".

This first report on "The Advertisers' Viewpoint" is based upon extensive informal personal interviews with 92 executives of 78 representative companies. These companies, all interested in medical advertising, range from ethical drug manufacturers, medical equipment manufacturers, and their advertising agencies, to large consumer product manufacturers with only slight interest in medical fields, and large consumer-account advertising agencies. The firms represented are located in New York and Chicago, and the areas in between. A list of the companies and the individuals interviewed is contained in the appendix. These interviews were conducted between October 20th and December 12th, 1952.

We would like to include in this foreword what is probably an unnecessary word of caution. In reading over this report one will find a number of unflattering comments regarding the AMA, the Councils and the AMA space-selling methods. In context, these critical comments were aimed at AMA policies and practices as interpreted or misinterpreted by the advertisers, and not at any individuals in the AMA administration.

A number of the advertisers, as a matter of fact, stated specifically that the present AMA administrative, editorial, and advertising department personnel were the most cooperative and the most efficient that they had ever dealt with at the AMA. Almost universally, too, the fact that they were being invited to express their opinions and make suggestions in the survey was taken by the advertisers as an indication of the progressiveness and desire for improvement of advertiser relations of the current AMA personnel.

This report is divided into three parts: recommendations based on what the advertisers told us, the advertisers' attitudes toward their own problems, and the advertisers' views of how the AMA can sell more space in its publications.

CONTENTS

RECOMMENDATIONS

The AMA has two strong motives for improving its relations with medical advertisers. The AMA is the logical agency to exercise leadership in medical advertising. This leadership will enable the AMA to raise the standards of medical advertising and to help convert the $130 million now being spent each year on medical advertising from an annoyance to the average physician into a constructive source of useful information on new developments in the fields of drug and other medical products.

The second motive for improving its relations with medical advertisers is the possibility of increasing its advertising revenue by several million dollars per year.

The following recommendations, based on the comments and suggestions of advertisers, constitute a program for the AMA which will help to accomplish these objectives.

These recommendations are offered with the realization that the official nature of JAMA and the overall policies of the AMA involved may militate against their complete adoption as given.

1. Improve AMA-advertiser relations

The advertisers should be made to feel that the AMA personnel believe in the honesty of the advertisers, and that they feel that medical advertising has a worthwhile place in AMA publications.

The advertisers, in general, feel that the AMA, especially through the Councils, distrusts them and views them as potential crooks who would become actively unethical if not constantly watched.

This feeling of the advertisers may or may not have foundation. If it does, then the AMA should review its attitude and attempt to correct it.

In any case, whether true or not, this mutual feeling of distrust must be eliminated as the first step in improving AMA-advertiser relations. The basis for cooperation and for a really successful sales campaign on the part of JAMA must rest on the establishment in the minds of the advertisers of a feeling of mutual respect and a belief in the willingness of the AMA to go half-way in working out mutual understanding between the AMA and the advertisers.

The professional advertisers must be made to feel that their advertising is wanted by the AMA. At present, they have the feeling that the AMA looks on space-selling as a favor to the advertisers, and merely as a source of some additional revenue which it can very well do without. The fact that in 1952 the AMA derived $3,137,000 from advertising, most of it from JAMA, is an indication of the importance of advertising to the AMA.

The manufacturers of drugs and other medical supplies are no longer in the position where they have to bow down to the AMA. They can circumvent direct control of their advertising and products by the AMA by refraining from submitting products to the Councils and by channeling their advertising and promotion efforts through non-AMA journals or through detailing and direct mail. The fact that since 1948 advertising space in *Medical Economics* and *Modern Medicine* has increased 40% while AMA space sold has decreased 3% during the same period, is proof that advertisers are tending more toward non-AMA media.

The fact that the AMA gets as much advertising income as it does, the majority of advertisers state, is because of the unique position of JAMA, and in spite of the feeling toward the AMA, and the AMA's relatively ineffective space-selling methods.

The report will show that a number of advertisers question the need for getting Council Acceptance for the ordinary product, and question whether or not JAMA is well-read by physicians. It seems likely that more than a little of this feeling is an attempt to rationalize the advertisers' resentment at AMA "aloofness."

The industry expresses a desire for working with the AMA in maintaining high standards in the medical field, rather than in working independently of it. It feels, however, that the AMA should give some concrete evidence of willingness to cooperate on the other side.

Good advertiser relations can be built if the AMA will make a systematic effort, thorugh editorials, through speeches, and through personal contact with manufacturers and their trade associations, to explain its point of view to the industry, and to attempt to understand the industry's problems and point of view.

2. Set up a joint AMA-advertiser board

One of the best ways for the AMA to learn the advertisers' problems and explain its own problems to the advertisers would be through the establishment of a joint AMA-industry board, the purpose of which would be to work out mutually satisfactory solutions to various problems. This could be done through one or more of the already existing trade associations, such as the American Pharmaceutical Manufacturers' Association and the American Drug Manufacturers' Association. Such an offer of cooperation on the part of the AMA would indicate positively to the industry the desire of the AMA for greater mutual understanding.

3. Aim at higher advertising standards for AMA publications

The majority of medical advertisers definitely prefer the AMA to accept for advertising in its publications only products of professional interest presented in a professional way. They furthermore express the belief that if the AMA would adopt this policy, additional revenue from increased medical accounts would more than make up for the loss of the non-medical income.

It would probably be unwise to make this change suddenly. A gradual change, however, could be achieved by concentrating selling effort exclusively on professional advertisers, and by gradually tightening the restrictions on the non-medical product copy.

As a first step, the advertisers almost universally suggest that the advertising of non-Council products be made to conform to the "honesty in advertising" rules to which the Council products are subject. They would apply this restriction particularly to advertising by cigarette manufacturers who make pseudo-scientific claims in their copy.

4. Expand direct-mail promotion

The advertisers, practically without exception, agree that if they were presented with more evidence of the value of AMA space, if they were shown how they could increase their results proportionately more by devoting their budgets to AMA publication space rather than to non-AMA space, they would increase their space purchases in AMA publications.

The direct-mail promotion program should be carefully set up to tie in with the personal sales calls of the space representatives. It should be designed so as to cover continuously the various areas which need to be covered. It should allow for the continuous turnover of personnel on the mailing list, so that new people are informed of points which they should know and that old hands are periodically reminded of these points. Throughout, a systematic effort should be made to build up the prestige of the AMA and to increase the good-will of the recipient toward the AMA.

The direct-mail pieces would fall roughly, according to purpose, into three classes: public information, which would aim at giving information on how specific AMA publications serve the medical industry; service pieces, which would aim at giving the manufacturer helpful statistical compilations, information on how to write more effective ads, survey results on attitudes of physicians, etc.; and public relations pieces, aiming at creating favorable attitudes toward the AMA and its publications, and practical esteem for Council Acceptance, reprints of ads, editorials and articles about how the AMA is trying to improve the attitudes of physicians toward using medical advertising, etc.

5. Improve personal selling

The advertisers universally comment that the AMA is doing a poor job of promoting and selling publication space. All but the larger accounts state the space representatives call on them infrequently, that their presentations are non-existent or poor, and that the representatives are poorly informed on AMA policy.

The advertisers say that if more selling effort is made by the AMA, the AMA will sell more space. From a purely business point of view, it would seem that the possibility of increasing advertising revenue by several million dollars per year would justify increasing the expenditures made for promotion and selling of space.

The first step, it appears to us, would be the establishment of a system of remuneration of all AMA personnel connected with sales, which reflects directly their productiveness. This would enable the AMA to get and hold top caliber personnel who would do the kind of promotion and selling job which the AMA publications as leaders in the field, deserve. Secondly, establishing a centralized

systematic method for prospecting and contacting clients. And thirdly, developing good presentation materials, and training representatives in the proper use of these materials.

6. Standardize Council procedures insofar as possible

The subject of Council rulings is a difficult one for many of the advertisers. If the objectives of the Councils could be re-evaluated and logically justified in the light of current conditions, and if standardized procedures could be worked out so that manufacturers could know what to expect from the Councils in advance, much of the present apathy and ill-feeling toward Council Acceptance could probably be eliminated.

The manufacturer frequently has a large investment tied up in a new product. He feels that the Councils do not understand nor appreciate his problems and his need for prompt action. He also feels that the slowness in publishing the notice of acceptance in the Journal is a result of the AMA's lack of understanding and interest in his problem.

7. Review the Council stand on trade names and mixtures

The chief and almost universal criticism of the Council is on its stand on the use of trade names in advertising, and on compounds and mixtures. Even the companies most favorably disposed toward the AMA feel that on these two points the AMA is often arbitrary and unrealistic.

This feeling is intensified by the admission into JAMA of general products which are not subject to similar restrictions.

If changes in circumstances since the adoption of these two rules are such as to enable the AMA to reconsider and modify them on a professional basis, considerable additional advertising revenue would accrue to the AMA with little or no additional effort.

8. Sell Council acceptance to the physician

The advertisers place little value on the Council Seal for the ordinary product because they feel that the average physician does not understand it, and does not usually value it.

The AMA could improve its position both with its members and with the advertisers by setting up a definite program to educate the physician on the meaning and value of the Council Seal.

As part of this program, it might be worthwhile to include as one of the privileges of membership in the AMA a free copy of the "New and Non-Official Remedies".

9. Publish an index of advertisers

Include in a prominent spot in the AMA publications an "Index of Advertisers", and differentiate in it between Council Accepted and non-Council advertisements. Indicate there, for the physician, a brief outline of what standards the accepted products have met.

Include along with the Index of Advertisers a "reader request for information" check-list. This would tend to eliminate the measurability-by-coupon-return advantage which direct mail and detailing possess in the eyes of a great many of the advertisers. It would also help physicians to get more direct information on new product developments from reading JAMA advertisements.

10. Review policies on inserts

Much of the criticism of the Pfizer insert in JAMA might be eliminated by more clearly labeling the editorial matter as an advertisement. Many of the advertisers who resent the Pfizer insert state that they feel that in the editorial matter, the company has usurped the editorial funcion of the AMA. Unmistakable labelling of it as advertising might help to eliminate some of the criticism

The AMA would also improve its advertiser relations if it would clearly define its policy on inserts, and make this information available to all the advertisers through a release. This would do much to eliminate the feeling (unwarranted though it may be) that the AMA plays favorites with certain advertisers.

11. Make AMA publications as attractive as possible to the readers

The more physicians read the AMA publications, and the more they value them, the greater will be the value which the advertisers attach to them.

In general, JAMA is rated very highly by the advertisers. There is some feeling expressed, however, that JAMA is frequently inclined to be over the heads of the majority of the readers. There are several requests for a clearer definition of the function of JAMA.

The feeling is also expressed that JAMA, in attempting to be so complete as to satisfy the one or two percent of the readers at the high extreme, tends to overawe the great majority of readers, who are interested in greater simplicity and less completeness. Most of the 135,000 AMA members, several advertisers point out, will never take any refresher courses, and the AMA Journal should do its best to take their place.

FINDINGS

In the "Recommendations", we have listed specific methods whereby the AMA can improve medical advertising and increase its advertising revenue. The majority of these recommendations were made explicitly by the manufacturer and advertising agency personnel with whom we talked.

It has been estimated that medical advertisers spend around $130 million a year for advertising and promotion: $100 million for detailing, $22½ million for direct mail, $7½ million for journal advertising. In 1952, the AMA received $3,137,000 of this, of which $3,009,000 was for space in the Journal of the AMA. The AMA received an additional $270,000 for convention exhibits. The dollar increase over previous years is the result of rate increases, not of increases in the amount of space sold. This has decreased slightly since 1948, during the period when *Modern Medicine* and *Medical Economics* have increased their amount of space sold by about 40%.

The total amount of expenditures for advertising and promotion of medical products is very large. Much of it, as we shall see in our physician survey on advertising, is wasted.

The AMA has a serious responsibility to the medical profession to raise the level of medical advertising, and to make it as useful as possible to physicians.

Especially today, with so many new developments in the field of medicine it is extremely difficult for the average physician to keep current. Of the 150,000 physicians who are practicing in the U.S., only a very small proportion get any additional formal medical training after completing their internship. Keeping them up on new developments, insofar as it is done, is accomplished not only through professional journals and meetings, but in probably a larger degree than the medical profession has ever admitted to itself, through the efforts and expenditures of the advertisers—through detailing, direct mail, and journal advertising.

The advertisers, as we shall see, have the feeling that physicians, and even more so the AMA as an organization, view them as greedy, selfish promoters who are interested in exploiting the medical profession and the ignorant general public. Unquestionably, there are a small number of fly-by-night operators who would take every advantage possible, if not controlled.

The reputable, large drug and equipment manufacturers, however, who account for the great majority of sales, have long ago realized that, from the point of view of self-interest, if for no other reason, they must maintain high standards and go in for a high degree of self-policing.

For the AMA to raise the standards and effectiveness of medical advertising, there must be mutual understanding and respect between itself and the medical suppliers. If the AMA fails to be more understanding of the real problems of the medical suppliers, if the Council requirements are unnecessarily exacting and the administrative processes unnecessarily involved and time-consuming, then the medical manufacturers will circumvent direct control by the AMA.

This is not a vague or remote possibility. It is happening today to an increasingly large degree.

The only direct control which the AMA can exercise on the medical manufacturers is through the Councils, and the acceptance or rejection of advertising in the AMA publications. Medical manufacturers do not have to work through the AMA. Failure to get Council Acceptance on products will not hurt sales in most instances. Advertising of their products is eagerly and aggressively sought by a large number of medical publications which have wide circulation and readership among physicians, and who do not require Council Acceptance.

The AMA is the logical organization to maintain high standards, both in medical products and in medical advertising. The manufacturers would rather that

it be the one to do so. But the AMA must make an effort to maintain this leadership.

The first part of this report will present, from the advertisers' point of view, the problems facing the manufacturer. In it we will attempt to give the manufacturers' point of view on the promotion of his products.

The second part of the report will give the advertisers' views on how the AMA can strengthen its leadership in maintaining high standards in medical products, and can raise and maintain higher standards in medical advertising, and increase its usefulness to the physician.

PART I. PROBLEMS FACING THE MEDICAL MANUFACTURER

The medical manufacturer, like any business man in the U.S. today, operates under what is called the "free enterprise system." As an individual, he is in the business of manufacturing medical supplies to gain financial profit and to gain the personal satisfaction which comes from doing a good job.

He is usually satisfied with an overall profit from his operations. Quite often, he will manufacture one or more items knowingly at a loss as a "service", or for prestige, or for some other reason which will in the long run work for the long-term profitability of his operations.

He is generally much more interested in long-term than in short-term profit. He realizes that shoddy products on which he might make an excessive profit during the short time it would take for his buyers to catch on, would hurt him in the long run much more than it would help him. As a result, he conscientiously tries to turn out only products of unquestionable value.

Because he is interested in the long term, he plows back a good proportion of his profits each year for research and for the development of new products.

After he has developed and started manufacturing a new product, he must find someone who will buy it. In the medical field, he is faced with the unique problem of having his products bought to a large extent by people who do not make the decision themselves on buying, but have this decision usually made for them by their physicians or druggists.

Accordingly, the reputable medical manufacturer puts the emphasis in his efforts to make known and "sell" his product, not on the ultimate consumer, but on the druggist, and to a greater degree, the physician.

1. Purpose of advertising

The medical manufacturer, then, is faced with the problem of informing the physician that there is in existence such a firm as his own, that there is in existence such a product as he has to offer, that his product is useful for certain purposes, and that his product is better, or at least as good, as any product offered for the same purpose by any other firm.

Many advertisers have never formally thought this through. Many of them operate only on precedents, and do what they do merely because all their competitors do it. Some of them are entirely selfish in their viewpoint, some are much more far-sighted.

In our interviews with advertisers, one of the topics on which we tried to get them to express an opinion was on what they considered to be the purpose of their advertising. An eastern advertising agency man offered the following:

"The sole end use of advertising is the promotion and sale of products, and the establishment of the good name of the manufacturer before the audience he seeks to impress."

An X-ray manufacturer offered this:

"The purpose of advertising is to make the selling job easier for the salesman, to keep our name in front of the doctor, to do the selling job on the doctor on an institutional basis. We must put out excellent equipment and service continuously, because our good name is very important. We are consciously aiming our advertising at this point."

A small east-coast chemical manufacturer put it this way:

"The purpose of advertising is two-fold—educating the physician and selling our drugs."

The head of one of the large ethical drug manufacturers expressed it as follows:

"The doctor has problems in the form of patients. Our job is to assist him in the solution of these problems by providing useful medicine which he can use. In order to get him to use our product, we must tell him what it is, what it will do, where and how it is to be used and how it is available."

A middle-western ad agency president expressed it more specifically in terms of the Journal of the AMA:

"The pharmaceutical world never pays enough attention to one fact: when physicians leave school and go into practice, only a small percentage ever go back for refresher courses; only a small percentage follow all the advances in the medical journals. Much information *must* come from advertising. Advertising in the JAMA is screened and sound, and physicians can place confidence in what is stated there."

The AMA can help considerably both the profession and the advertiser by helping the advertiser understand more clearly the purpose of his advertising.

The level of medical advertising would be raised considerably if the advertisers and their agencies viewed their advertising as a mutual service to the medical profession and to themselves.

2. Budgeting

Most decisions about advertising are based on precedents and hunch. This applies to medical advertising as well as general advertising.

The large majority of advertisers told us that they determined their advertising budgets as a percentage of anticipated sales, which practically speaking means on past sales. Accordingly, when sales are high, advertising budgets are high. When sales fall off, and advertising is needed most, advertising budgets are cut.

Although this is patently lacking in rationality, it is the accepted practice in advertising and will probably continue to be so.

An X-ray manufacturer's advertising manager told us this:

"About the budget—we get the total amount of money to be spent from a percentage of sales. Of the total appropriation, media of all kinds (journals, etc.) get about 25%, conventions get about 40%, and direct mail, sales literature and other miscellaneous activities get the rest."

A medical equipment manufacturer states:

"About the budget—we try to stay between 5% and 10% of gross sales. We work with our advertising agency in setting up a budget for the following year. They do the art work, and we do the copy. To us, advertising budget means only magazine advertising and conventions. We do not include direct mail as part of the advertising budget. As far as proportions into which the budget is split; conventions come first and then journals. Of the journals, first comes the Bone and Joint book, then SAMA. We wouldn't miss these. They are important because they are the specialized books. They are the first channels for new information."

A drug firm which publishes a full-line catalog told us this:

"On the older products, we use a percentage of sales in setting up the budget. On the new products, we try to determine what we will do with it the first year, then estimate how much we would like to invest in it. Mostly, we use sampling and direct mail because in these we can see our results. For example, on Vitamin B–12, we made two mailings, got a 12% and a 15% response respectively. This gave us leads to follow up."

Another drug manufacturer said:

"First, we get our advertising appropriation for the operating period. This is determined in part as a percentage of sales. We then decide the job to be done, and determine what we can spend on this job. We then split up the appropriation between the various methods. The best combination is then used. We need all of the advertising methods. About all I can say on that score is that we split up our appropriation according to our best judgment. We don't have any fixed method. The importance of the various means changes from time to time."

A large ethical drug manufacturer who uses the "task" method of figuring budget put it this way:

"Our budget is not based on sales, our proposals are based on the job to be done, on the need for selling the product. We look at each product individually. Each product stands on a budget of its own. We consider what is needed to carry this product for the next fiscal year. We use one advertising means to accomplish one objective. Certain products have characteristics which make them more susceptible to specialty advertising. Everything goes back to exactly what is needed to advertise each individual product. We then dovetail all media together for the good of an individual product.

"To take a specific case, let's take JAMA. We set a schedule for so many pages among the products that are Council-Accepted. This is based on the cost and frequency of the ads. It is not much of a problem with JAMA. We have

only certain products which are Council-Accepted which we want to advertise in JAMA. There are some products on which we can do a better selling job without suffering the restrictions on claims by the Council. There are times when regulations are so restrictive that a better job can be done without Council Acceptance."

Of the firms we interviewed, the large majority got up their budgets as a percentage of past sales, modified on the basis of hunch. A few used the "task" method, whereby they determined what they wanted to accomplish in the way of sales, and then guessed how large the appropriations would need to be to accomplish these objectives.

If the AMA, through research, could arrive at some more scientific method of budget determination, it would render a real service to its advertisers.

It might also be well to point out that using the relatively flexible methods that they do in determining their budgets, advertisers are very open to selling on the part of JAMA. If convinced of the value to them of JAMA or special journal spaced compared to other media, advertisers can fairly easily change their minds—and their budgets.

3. Selection of advertising channels

A medical advertiser has three main methods whereby he can tell his story to the physician: through detail men, through direct mail, and through journal advertising. Each of these methods has advantages and disadvantages which vary in weight, depending: on the type of product to be advertised; the age, size and reputation of the advertisers; and the period of development of the product at the particular time.

Each method supplements the other and usually the manufacturer ties them together as much as seems effective.

There is no hard and fast rule in media selection and the emphasis put upon each of these three methods varies considerably with the individual advertiser. Because of this fact, JAMA's potential sources of advertising revenue include not only advertising now going to other journals, but also what is now going into direct mail, and possibly even to some extent, what is now going into detailing.

For JAMA to develop fully these potential markets for its space, it must not only do considerably more and better selling and promotion of its wares, but it must also develop more fully the usefulness of journal advertising in general, and its own in particular. It must work both with the advertiser and with the physician-reader to accomplish this. It must help the advertiser develop the type of journal ads which are of maximum usefulness and interest to the physician. And it must change the physicians' attitude toward advertising, and help him to learn how to get the most benefits from advertising.

The following comments, selected from interviews with advertisers, are typical of the attitudes of advertisers toward their problem of advertising-channel selection. As one of the large medical ad agency people expressed it:

"It is generally agreed that the order of effectiveness is, first, detailing; second, direct mail; third, journal advertising. The emphasis, however, varies from one advertiser to another."

A physician connected with a large ethical drug manufacturer stated:

"The three basic media complement each other. A detail man does more than a journal ad—provided he can see the doctor. If he can't, a journal ad is obviously more effective. Similarly with direct mail."

The double problem of first deciding how much emphasis is to be put on each of the three basic advertising channels, and then secondly, how much of the journal advertising is to be run in a specific journal was expressed by the head of an ethical drug manufacturing firm as follows:

"We first decide whether to use direct mail or journal ads, and then we consider which journal is best for the particular product under consideration."

The idea of the different contributions which are made in varying degrees by the different journals was added by a medical supply manufacturer:

"Because we manufacture medical supplies, which are also advertised directly to the consumer, we consider the purpose of our advertising to be institutional, both to the medical profession and the consumer. We want to keep our name before the audience in JAMA, and we push our special products in the other journals.

"JAMA has the best coverage, but we spread out into the other journals, particularly because of our specialty products, like baby products. JAMA is the best for CP's. We use other journals for pediatricians, etc. Other journals are useful because they help keep our products before the public.

"Direct mail is also good for us, and we use it a lot."

A medical ad agency executive gave this statement on media:

"Media are selected on the basis of the objectives sought in the promotion of a product. JAMA is good to keep the name of the House before the physician-public, and to advertise Council-Accepted products, particularly new or specialized ones. We use other journals particularly for specialty products or for proprietary drugs. Direct mail is used to push specific products."

A manufacturer of industrial chemicals and pharmaceuticals outlined his formula:

"For a new product that requires presentation to the medical profession, a company should get Council Acceptance if possible. It should then run an insert or series of inserts in JAMA announcing the product. But it won't get the desired interest or distribution unless it also announces it to wholesalers and hospitals, and the JAMA ads should therefore be tied in with detailing. The next step should be a follow-up by direct mail, and by ads in the specialty journals if appropriate. Direct mail is the costliest of the three media, but it is the most selective."

The same man said elsewhere:

"There has been a lot of money spent on pharmaceuticals recently, but this year there has been a falling off. I guess all advertising budgets will be cut next year.

"Our policy, in a depression, would be to cut down on detailing, direct mail, and ads in specialty journals. We would concentrate on ads in JAMA and other top-circulation journals."

As we mentioned earlier, the amount of emphasis put on the various advertising channels varies considerably from company to company, and in the same company from product to product.

One of the main reasons advanced by advertisers for preferring detailing and direct mail over journal advertising is that in the first two the advertiser has a measure (if crude) of its effectiveness, through inquiries and returns:

"Pharmaceutical houses prefer detailing to all other advertising and selling methods. They know how much they are paying out and how much they are getting in return. This is also true of direct mail, to a great extent—you have some check on its profitability. Journal advertising is the least attractive to them because its profitability is impossible to check. It would be helpful, in this connection if advertisers could be informed of the extent to which doctors read JAMA."

The president of an X-ray equipment company stated:

"Our journal advertising is purely prestige and institutional advertising. Direct mail is used for specific products. However, we intend to get prospects from journal ads also, because most ads have coupons attached. Both means of advertising are important. We would not have one without the other."

A large ethical drug manufacturer mentioned that they split their advertising budget among the three channels:

"Generally we advertise in JAMA for institutional purposes and other non-specialty journals for broad coverage. The journals get about 20 percent of our advertising and promotion budget, direct mail gets about 30 percent and detailing about 50 percent."

Another ethical drug manufacturer, in summarizing their position on media selection, said:

"This depends on many factors. With a new product, direct mail is usually preferable; with an established one, journal advertising. However, in the case of a new product that has received Council Acceptance, JAMA advertising is a 'must'."

The advertising manager of a chemical and pharmaceutical house emphasizes the interdependence of the various media:

"We look on JAMA advertising as a means for building our reputation and for activating our direct mail at low cost. Direct mail *sells* our products, but it has to follow *journal* advertising and would be useless without it. We spend comparatively little on detailing at present, since we are a new firm with a small sales staff."

This same idea was expressed by a drug manufacturer, most of whose products are not eligible for Council Acceptance:

"Direct mail and journal advertising complement each other. We do not use one for one purpose and the other for another."

A consultant stated:

"Direct mail is the most effective medium for a *new* product. You can aim more effectively at the specific group you want to read; for example, specialists

or regional groups. Also, the response for samples is better from direct mail than from journal advertising. After the product has gained acceptance, however, institutional advertising in the journals acts as a necessary reminder."

To summarize, journal advertising seems to be used most widely for reminder advertising, direct mail to introduce a new product. Usually, the two of them are tied together. Detailing is generally considered the most effective of the three and is used both for new products and for reminding.

If JAMA would set up a reader service, where the physician could return a postcard or list to the AMA on which he had checked off literature or samples of products advertised in JAMA which he would like to get, JAMA would be rendering a very useful service both to the reader and to the advertiser. The inquiries could then be turned over to the advertisers for follow-up.

This service would also do much to counteract the feeling of the advertiser that direct mail and detailing are more effective because their results can be measured.

4. Deciding For or Against Applying For Council Acceptance

One of the problems which plays a large part in determining which journals in which to advertise is the question of Council Acceptance.

If the product is by its very nature one which is ineligible for acceptance by the Council, there is no problem—the product will not be submitted to the Council and only non-AMA publications can be used for advertising.

If the product is of such a nature that it has a possibility of being accepted, then the manufacturer must decide whether or not the disadvantage of having his advertising claims reviewed and approved by the Council outweighs the advantage of having the product carry the Seal of Acceptance. His decision will depend on how great he considers the disadvantage to be in the particular case, as against how valuable in the particular case having the Seal will be.

The value of the Seal will vary in his eyes in proportion to the value which he thinks the physicians place upon the Seal in connection with this specific product.

In the case of an unknown firm, whose name is no recommendation to the physician, its product will be more able to compete with similar products of well-known firms if it has the Seal. Or even in the case of well-known firms, if the product is one which is dangerous or unknown, and the physician may be fearful of using the product, then the Seal enables the physician to pass responsibility for the results back on the Association, and in that case, may attach importance to the Seal.

In the case of well-tried and well-known products put out by firms whose names are highly respected, the physician will usually evince no interest in whether or not it is accepted, and therefore the advertiser will also attach little or no importance to getting the Seal. In this case, it is highly likely that the bother of submitting the product and the requirement of limiting advertising claims to those acceptable to the Council, will outweigh whatever slight and questionable value there might be to having the Seal. The only real advantage the Seal would have in this case would be that it would enable the advertiser to run his copy in AMA publications.

There is, as we shall see later, considerable resentment on the part of advertisers toward the Councils, especially the Council on Pharmacy and Chemistry. The two main sources of ill-will are the rules of the Council on trade names, and its refusal to accept certain compounds and mixtures, even though they are widely used and accepted by the medical profession, and even though the firm putting them out has top standing.

The manufacturers in general are favorable toward the *idea* of having Councils. They feel that since its founding in 1905, the Council on Pharmacy and Chemistry has served a valuable purpose, especially in the years prior to the tightening up of federal legislation regarding food and drug standards.

Practically all of the manufacturers feel that the Council still serves a worthwhile purpose in maintaining high standards both in products and in advertising. Much of its influence, however, they feel is being lost because of what they consider unreasonableness in its stand on trade names and mixtures and compounds.

About half the advertisers we talked to stated that they considered Council Acceptance as being useful in selling and stated that they would get the Seal "if it wasn't too much trouble." About a quarter said they considered it of value only in the case of new or controversial drugs, or in the case of an unknown firm. On established products, they would not bother to get it. Another quarter stated

that they practically never bothered getting Council Acceptance, except on one or two products so they could carry institutional advertising in AMA publications.

A small drug manufacturer stated:

"Council Acceptance has value in the case of new or toxic drugs, and with people in teaching institutions. Council Acceptance is easier to get when researchers in medical schools have tested it extensively. We always send them our stuff if we want Council Acceptance on it. On routine drugs, Council Acceptance means nothing at all. As far as actually insuring the quality of the drug, it is useless; F&DA does the interstate job pretty well."

A consultant in medical advertising pointed out:

"The main value of Council Acceptance is that it increases the prestige of a firm. The average drug firm is selling the *firm*, rather than the product; its *integrity*, rather than its manufactures. Anything that helps establish the integrity of the firm is therefore important. By obtaining Council Acceptance, even for one product only, a firm can advertise in JAMA and thus get institutional entree and build up its prestige."

One of the large medical ad agency people had considerable to say on Council Acceptance. His comments are fairly representative of the feelings of the reputable medical advertisers:

"Council Acceptance means practically nothing to today's MD. If the drug is new and toxic, it is helpful to have it, but not a hindrance if you don't. In the case of a small house, it is probably always of some value. On routine preparations, and on the products of an established firm, it is meaningless. Very few MD's ever inquire and most of these are not much impressed by it.

"The Council is much too slow. It often takes a year or more to get a product through. Meanwhile, your whole investment is tied up. * * *

"A reputable house today must test its products far beyond the limits of any Council requirements, for it risks its entire reputation if it puts out one bad drug. Yet the Council doesn't even trust its own colleagues and the evidence which is presented to it from certified sources.

"The policies of the Councils are sometimes ludicrous. They refuse to allow but one company to have a trade name advertised for a given drug. When a market has been established for a drug, no manufacturer is going to change the name. Yet he can't advertise in JAMA or have it accepted unless he uses only the generic name.

"Another instance is the rule on mixtures, many of which are commonly accepted by the profession today. Vitamins are the best example of this. Even standard techniques are not accepted under these rules. The profession has long accepted the combination of pencillin and sulfaniamides in certain combinations. Not only won't the Council accept that product for advertising, but it won't even allow any abstract of the article in JAMA to be printed as an ad, though no ad copy was to be included.

"Competitors do not trust the Council and are continually disappointed by it. It seems to play favorites a lot of the time, and what applies to one doesn't apply to another in what seems to be identical circumstances. Big advertisers, Chicago firms, and oldest advertisers seem to get away with things that no one else could.

"Since a company cannot depend on getting Council Acceptance, even if it meets all the requirements and submits the evidence, and since the Council has no sense whatever of the time involved in these things, many advertisers must cut their schedules, or just leave JAMA out to a large extent.

"Let me give you one example. Although a folder was submitted based on the papers written on a drug by three of the country's recognized leaders in pharmacology, the Council refused to allow their statements as advertising, though these were statements of pharmacologists, in no way connected with the company.

"Essentially, medical advertising is the most honest of all advertising today. The Councils had a lot to do with making it that way. But this isn't 1910, and the first-class firms are beyond reproach today. Besides that, the F&DA is always watching them.

"Yet the Council behaves as though the industry were still full of barbarians.

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"On the other hand, it allows the most extraordinary claims on products the AMA accepts which are not subject to scrutiny. Respect of advertisers and readers is gone when they see cigarette ads and ethical ads side by side and assume both have been approved by the AMA."

Another smaller medical ad agency head made some of the same points:

"The value of Council Acceptance is greater for the small advertisers because it makes their products more valuable in the eyes of the physician. It is lessened, though, because of the trade name restrictions. This antagonizes many manufacturers, especially where several have been working on the same sort of drug over the same period of time.

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"More publicity should be given on Council Acceptance, directed at physicians, who generally know little or nothing about its meaning. This would increase the value of the Seal. Also, what Council Acceptance involves should be re-stated to the manufacturers, and consistent treatment should be given to all comers.

"There is too much discrimination and waiving of the rules for the bigger companies. Manufacturers never know where they stand on Council Acceptance on their products. Also, there is too much delay and too many refusals without giving constructive criticisms on products or copy."

A New York ethical drug manufacturer, who certainly would not be considered an opportunist, made the following rather typical comment:

"Since the new F&DA, Council Acceptance doesn't mean nearly as much as it used to. The AMA restrictions don't carry the same weight on new products as they did in the past. It's a good thing to have the Seal if you can get it without too much heartache. But it isn't necessary to have.

"JAMA is frequently left out on our schedules for new products because of Council delays. The F&DA *must* act in six weeks if your case is good. With the Council, it is two or three months at best.

"They want to quibble over copy—have a regular schoolteacher attitude. The Council's attitude is that the industry is a crook. The industry resents this attitude—that the Council is always trying to catch it doing something that is crooked. The biggest bone of contention is that they figure you are guilty till you prove yourself innocent."

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The criticisms of the Councils were practically never that the Council standards for products were too high.

Practically universally, however, the manufacturers and agencies were critical of what they considered the *attitude* of the Councils, their lack of standardization, and the two points which the advertisers considered pointless and archaic, the prohibition of the use of trade names and the refusal to accept any mixtures.

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Several of the manufacturers actually felt that the standards for products were not high enough. One of them put it this way:

"The Council Acceptance Seal is of no more value than the Good Housekeeping Seal. They are getting lax in their standards. It lowers my opinion of the Journal."

Another one said:

"Some doctors feel that the Seal has become too easy to get. For example, we have a good but very potent drug that has to be used very carefully. The specialists resent the fact that it has been okayed for GP's."

Sometimes the value of the Seal lies in the fact that if the manufacturer doesn't have it, his competitors use this fact against him with the doctors.

The larger ethical drug firms, for the most part, attach little or no value to Council Acceptance as a selling aid. One of the country's top drug firms had this to say:

"Being able to tell the doctor that a product is Council Accepted doesn't make much difference to us. The doctor doesn't place any particular value on the Seal. Our detail men do not even bother to tell the doctor that a product is Council Accepted. The fact that (NAME OF MANUFACTURER) makes it, carries more weight than the fact that the Council has approved it.

"In general, most doctors do not know whether a product is accepted or not. over 90% of the dotcors are in this category. If they did pay any attention to the Seal, they would ask about it. I do not recall a single instance where the doctor has asked whether or not our product was Council Accepted."

Three more comments, each following the pattern indicated above, but with slight variance, will suffice to give the sentiments of the firms and people with whom we talked. A New York medical ad agency head:

"The average MD doesn't rely on Council Acceptance, and knows little about it. He relies primarily on the company's reputation. Because it takes so long

A small drug manufacturer had something slightly different to say:

"JAMA is used for prestige purposes. It gets about half of our ad budget. We use other journals and throw-aways for the same purpose for which we use direct mail—for product selling. The non-JAMA media combined get the other half of our budget."

The advertising head of one of the top drug firms had this to say:

"Actually, we would never advertise a good product in only one journal. We want to get better coverage. We know every doctor doesn't read every ad. Therefore, with multi-journal coverage, we know we improve our chances of contact with any one doctor."

The three following statements represent the opinions of those who are most favorable to JAMA. Here is what a medical advertising agency head said:

"JAMA is by far a better publication than the throw-aways. We advertise in the throw-aways because we find it difficult to get some products Council Accepted. We use throw-aways for Council Accepted products only for the additional coverage we get. That is the only reason."

A small catalog-pharmaceutical manufacturer said:

"JAMA is the best medium. There is no question at all in our minds about it. It is the most widely read of the journals, if journals are read at all. I am not too familiar with distribution figures, but I know that when a doctor is busy, he will flip through JAMA whereas he may not in other journals he gets. I base this on my own experience."

Another manufacturer of drugs stated:

"JAMA is best for new, highly experimental or toxic drugs. We use other journals mostly for non-Council Accepted drugs, and direct mail for all-out product pushing. This year we are experimenting, giving Modern Medicine and JAMA each 45 percent of our ad budget and 10 percent to other journals."

This ethical drug manufacturer favored JAMA for GP's, other medical society publications for specialty products:

"Journals that are the official journals of the various medical societies (for example, the American College of Surgeons) have greater standing than the AMA special journals, but JAMA is the most effective for GP's."

Some advertisers decide how their budget will be spent by the worthiness of the cause which expenditures will help support. For example, this ethical drug manufacturer:

"Our primary objective in journal advertising is circulation. But we also advertise in every state medical journal, most of which have small circulation, on the theory that our success depends on the good will of the doctors and that we owe them support in their work. We feel that it is our duty to contribute to the support of the state journals. In the same way, we contribute directly to the revenue of the AMA special journals by buying space in them, and indirectly by buying space in JAMA, whose profits help support the special journals."

Less philanthropic, at least toward JAMA, are these two ethical drug manufacturers:

"We do not advertise in JAMA as a contribution toward anything. We take a hard, cold look and consider what we can get out of it. If our money could be spent better somewhere else, we would pull out of JAMA without any compunction."

"We feel a certain obligation to help support some organizations, such as state medical groups and state pharmaceutical groups. About the AMA, we approach it more strictly as a business proposition."

Most of the advertisers feel that JAMA is particularly good for certain purposes, and that others are better for other purposes. For example, this large ethical drug manufacturer:

"We select media on the basis of purpose. JAMA is best for new and Council Accepted drugs, but other journals are better for intensive selling when coupled with detailing and direct mail. Personally, we like JAMA best because it is highly thought of, and has the best coverage both across the board and in several specialties."

An eastern medical ad agency head views the situation somewhat differently:

"We use JAMA for intensive promotional work in the first phase of sales campaigns whenever the product has the Seal. Other journals take it from there and we tie detailing in with the ad campaign. JAMA gets about 20%, other journals about 80% of our ad budget. With non-Council Accepted drugs, we advertise heaviest in the throw-aways."

to get acceptance on many products, many manufacturers wait until the market has been built before applying for it. The entire investment of expensive research and expensive production may otherwise be tied up while awaiting Council Acceptance.

"Since the penicillin episode, when the F&DA stepped in and set standards for manufacture, value of Council Acceptance has lessened even more. The Councils are too slow, too conservative, prejudiced in favor of the large companies, and too whimsical. They allow some companies to do things which they forbid other companies to do."

A large drug house head of high reputation in the field:

"Council Acceptance on a drug does no harm, and might even do some good. It certainly is not a great asset, however.

"The top men in the pharmaceutical manufacturing houses are still suspicious of the Council. Although it has improved in the past years, there is still the great grief of the years gone by. The pressures on the AMA are great, and their ways are devious.

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"The AMA has kept itself out of contact with management in the drug field, and as a result operates in a vacuum as to the actual conditions which management people face.

"Because so many good drugs are readily accepted by physicians without having gotten Council Acceptance, and because of the great trouble required to get acceptance, as well as because the Council seems to adopt the rules its wants to apply to a case as it goes along, there doesn't generally seem much sense to getting Council Acceptance. At least, until the market is established anyway."

Another large drug manufacturing head:

"Many pharmaceutical houses consider it a definite disadvantage to have Council Acceptance on a product. The Council is so hypercritical of the ads, so 'holier-than-thou', that it's really painful. An advertiser necessarily doesn't want to say merely that his product is 'good'; he wants to say that it's 'better'. This is the very essence of competition.

"The limitations on the wording of ads for Council Accepted products in many cases actually prevent the doctors from getting the real facts about a product. For this reason, too, many of the best drug houses wouldn't dream of applying for the Seal as a regular procedure.

"It is undoubtedly true that the Seal has a very definite advantage as a selling point. However, its advantages are considerably outweighed by these disadvantages I've mentioned.

"After all, the AMA is no more honest than the reputable pharmaceutical firms, and no more interested in maintaining the quality of their products."

5. Selection of specific journal media

In the case of those products which the advertiser decides will not benefit sufficiently from having the Council Seal as to make it worthwhile to go to the trouble of getting it, the advertiser merely has to decide which of the non-AMA publications he wishes to use.

Where Council Acceptance has been applied for and received, the advertiser decides whether to use AMA publications or non-AMA publications, or a combination of both, for his journal advertising budget.

In general, the majority of the advertisers consider JAMA tops for institutional and prestige ads. Most of them also consider it the top publication for the GP and the mass physician market.

Where the product is accepted, the big majority of the advertisers will use JAMA. About a third state that they also run the same ads in the controlled-circulation publications, as well as in some of the other general journals.

For specialty products, accepted or not, the majority of the advertisers choose specialty publications because JAMA is too expensive for the average selected market advertisement.

Better than half of the advertisers who were interested in discussing special journals as media volunteered the comments that they considered some or meet of the non-AMA specialty journals superior to their AMA equivalents. One of the book publishers stated:

"We do our media selection on the basis of purpose of the ad under consideration. We use JAMA where we want wide coverage and prestige, use other journals for specific markets. Actually, we use direct mail most of all. This is used continuously to push the firm's wares."

A contraceptive manufacturer stated his policy as follows:

"JAMA provides us with a measure of prestige. We use other books to push our sales."

Another ethical drug manufacturer offered a more explicit statement:

"We use JAMA particularly for prestige purposes and as a reminder of the product. But the other publications are more profitable because JAMA is too crowded with its concentrated ads. For this reason, we have built up a big representation in state and county medical journals, which are more local and personal, and which are less competitive, and give better visibility. I have a high regard for *Modern Medicine* and *Medical Economics*. We need their mass circulation to reach the GP's, who are our chief market. We use the specialist journals chiefly for our endocrine products."

This same idea was mentioned by another small ethical drug manufacturer:

"My feeling is that each of the three general journals—JAMA, *Medical Economics* and *Modern Medicine*—all play a part in the medical field. I personally prefer *Modern Medicine* and *Medical Economics* because their advertising, being interspersed with copy, has a better chance of being seen."

Medical Economics and *Modern Medicine* both have some strong supporters. It is interesting to note that most of these are also most bitter in their comments about the Councils. It seems more than likely that their favorable attitude toward the throw-aways is a rationalization of their dislike of the AMA.

An advertiser, head of a small drug firm, bitter toward the Council, stated:

"For selling, we use *Medical Economics* and *Modern Medicine*. Our detail men have noticed that these books are widely read by physicians, much more so than JAMA, which just seems to pile up in offices."

A specialty drug manufacturer who fits into the above-mentioned category expressed a different slant:

"With other firms who use JAMA, there is no doubt that JAMA is used for prestige. JAMA is, however, the kiss of death for product selling. Principally, this is because of lack of readership. The JAMA editors expect too much of the JAMA readers. The articles are too advanced, too obstruse for the general practitioner. JAMA is too much of an intellectual affair, not at all practical. Furthermore, its frequency of publication is too great."

A physician connected with a large drug firm who has had considerable trouble with the Council stated:

"This question of the relative effectiveness between *Medical Economics*, *Modern Medicine* and JAMA is a very moot one. No two people in our organization agree. I think it is the consensus that both *Medical Economics* and *Modern Medicine* are better read by doctors than is JAMA—but this does *not* mean that they are more influential."

The fact that Council Acceptance is the key to the selling of JAMA space appears again and again. Witness this eastern ad agency man:

"JAMA is used for mass circulation and wide coverage. It is the best possible organ for this, but it is only half as valuable as it could be, because of unrealistic and shopworn methods and restrictions that have no application today. Because of this fussiness, and in many cases inconsistency, JAMA loses lots more advertising which it could otherwise have.

"We use JAMA to get acceptance of new products by the profession. The ad budgets for established products are very low, and therefore we can't afford to use JAMA for them. Besides this, the value of JAMA for an established drug is questionable.

"We use other journals to push new specific products or for non-Council Accepted products. We can conduct a heavy campaign in them, even though the coverage is not as wide as JAMA's, because the readership is considerably higher."

Another ethical drug manufacturer mentioned a different variation of the effect of Council Acceptance on JAMA space selling:

"Of course, we have to advertise our non-Accepted products in non-AMA journals. We accordingly feel that we must also support these non-AMA journals with Council Accepted products as well."

As indicated above, most of the advertisers who use detail men and journal advertising usually make an effort to tie them together. This also applies to JAMA advertising, possibly to a higher degree than with the others.

About a third of the advertisers who discussed the subject of tying in JAMA advertising with detailing stated that their detail men regularly carry the JAMA ads. Another third state that they usually carry the ads but generally use them only in the case of certain products. Another third mentioned that they had no

particular tie-in plan because the Council Seal was not considered of any particular help with the physicians.

Two variations of tie-in are given in the following comments. The first by the head of an ad agency, the second by an ethical drug manufacturer:

"Our detail men make the fullest use of our JAMA ads on their visits to doctors. They do not use them with druggists, though they should. All our distribution points are kept informed of our JAMA advertising, and are sent copies of the ads. Our detail men who visit doctors must not only carry copies of our JAMA ads with them, but they are also supposed to *read* the Journal."

"Our main tie-in between detailing and journal advertising is in the matter of timing. We place our greatest weight of ads when our detailing is heaviest. On the other hand, we sometimes deliberately withhold our ads until after our detailing is completed, using the ads as a follow-up. It all depends on the product."

PART II. ADVERTISERS' VIEWS ON HOW THE AMA CAN SELL MORE SPACE

This survey of advertisers, and the one with physicians which is currently in the field, were undertaken to discover how the AMA could increase its advertising revenue.

It seems to us that while the possibility of increasing advertising revenue by several million dollars per year is a good motive for putting into effect the information gained from these two studies, there is an even more important reason for so doing.

By undertaking the betterment of advertiser relations, the AMA has an opportunity to assume leadership in improving some $130 million worth of medical advertising per year.

Through its leadership, the AMA can show advertisers the way to make advertising a much more positive force for helping the practicing MD keep current on developments which have occurred after he has completed his formal medical training. By accomplishing this, the advertiser will get more value for his money spent, and will receive better reception for all his advertising efforts.

By failing to improve its relations with the medical manufacturers and advertising agencies, the AMA is going to find itself losing its present none-too-strong direct control.

This direct control is exercised by the AMA only through the Councils and through the limitations it puts upon the advertising space it sells. As we pointed out earlier, the AMA is not in a monopolist's position: the manufacturers and agencies have alternative choices. As the facts show, and the comments of the advertisers given herein re-state, the manufacturers can and are achieving excellent sales results with products which have never been submitted to the Councils. The advertisers can and are getting their advertising messages to the physicians without using AMA media.

The manufacturers, at least most of them, prefer that a spirit of mutual understanding and trust and cooperation exist between themselves and the AMA. They are willing to go at least half way to accomplish this. They feel that if the AMA would also go half way, then AMA-industry cooperation can be a reality.

In this part of the report, we are going to show how, in the opinion of the advertisers, a common ground can be found. This will mean not only the raising of standards for medical advertising, but it also can mean an increased advertising revenue to the AMA of several million dollars which are now being spent on advertising in other medical publications, in direct mail, and to some extent, possibly even in detailing.

The four main changes which will be indicated in this section are: the change needed in the attitude of the AMA toward advertisers; the modernizations and improvements needed in the Council rules and procedures; the need for the AMA actively to sell and promote the Journal and its other publications as advertising media; and the fact that the AMA should continue to improve the Journal so as to make it of increasingly greater value to its readers.

1. The AMA should change its attitude toward advertisers

Though we are repeating what has already been said, we feel it necessary to mention again the fact that the advertisers resent being treated as irresponsible or incompetent opportunists.

In our interviews with the advertisers, we got the definite impression that the AMA, while widely respected as the strongest single political factor in the medical field, was liked or understood by practically none. The new and marginal manufacturers were fairly subtle in their stating of these attitudes. The strong, established, leading ethical drug manufacturers, on the other hand, were very explicit in their statements. The theme runs continuously through the interviews and through the comments reproduced in this report.

At least a large part of these unfavorable attitudes are based on misunderstandings of the AMA, or even on definitely false beliefs.

Public relations experts say that good relations with the public are never achieved by accident. They are the result of a definite, organized and continuous program of telling the public the favorable things about oneself, and admitting one's past faults and telling the public about the efforts that are being made to correct them.

The AMA has a two-fold job: that of understanding the problems of the advertisers, and making the advertisers understand the problems of the AMA.

A comment of a small drug manufacturer indicates the consciousness on the part of the advertisers of a need for closer cooperation:

"The ironing out of the difficulties and disagreements between the manufacturers and the AMA is of tremendous importance. JAMA could and should be a made-to-order, natural medium for advertisers of medical products. It has *everything*, or it could have, if it would clean itself up and become a real professional journal. I should like to be able to use JAMA to the exclusion of all other medical journals."

Another drug manufacturer made a similar statement:

"We would like to see the industry get closer to the AMA from the marketing standpoint. There has been a step in that direction here. For a while, this company has been a bit standoffish. The trend is going in the other direction now. We actually submitted more products in the last six months than in the previous two years."

One of the large ethical drug firms issued this plea for cooperation:

"Wet get along very well with the AMA, but they could do a better job with their advertisers if they found out what problems those people have to face, and cooperated with them. A committee of the pharmaceutical industry might be jointly set up with one from the AMA to work out some of these problems in an across-the-board fashion."

There were a number of advertisers interviewed who expressed the opinion that the AMA today is considerably better off than it has been in the past. We quote the following large drug manufacturer as typical of this group:

"There have been improvements. Dealings with the AMA are easier now, but still hard, although Storment personally is wonderful. His predecessors, however, will not easily be forgotten. The damage Leach did will rankle for many years to come. The AMA cannot go ahead on the policy that everyone is out to get the better of it. It must know that most of the manufacturers respect and want its approval, but by making it impossible to deal with them, they antagonize the very people who are doing their best to uphold the AMA's standards."

Here is one medical advertising agency head's comment on the AMA's need for better public relations:

"I do think that the AMA ought to do a better public relations job. No one, for example, knows the new editor of JAMA; and in some areas, such as New England, the doctors are anti-AMA, which means, among other things, that Council Acceptance carries little weight. Something should be done about this."

The aloofness of the AMA was expressed by one contraceptive manufacturer as follows:

"The journal is too far away. Many of us would do more in JAMA if the AMA acted like they wanted us to. They act like they don't want to sell space. If they offered to help us get approval, we would undoubtedly advertise more in the Journal. Our only contacts with the AMA are through our agency."

One of the bluntest statements was made by a small eastern ethical drug manufacturer:

"The public relations of the AMA are lousy. They have no thought of dealing with anyone in any but a high-handed manner, including the people who support them."

A softer-spoken manufacturer said:

"Our biggest gripe is the old-fashionedness of the AMA, and their apparent lack of interest in the advertisers' products or markets."

A manufacturer of professional equipment interpreted this disinterest in a different fashion:

"The legitimate manufacturers feel that the AMA is not interested in them. It is only interested in selling space—both at the conventions and in JAMA."

Three final comments, the first by an agency man, the second an ethical drug manufacturer, and the third another manufacturer of contraceptives, tie in their feelings with the old bugaboo, Council Acceptance:

"JAMA could get lots more ads by applying a little common sense, and 1952 thinking. Reasonableness on requirements, on time, etc., in the case of Council-Accepted drugs; acceptance of advertising on non-acceptable drugs from Grade A houses; dropping the rule on mixtures and combinations; and working with, rather than against, the industry—would make things much better for all concerned."

"The whole problem of JAMA advertising turns on the Council. We went through lots of trouble needlessly to get acceptance on drugs, and then found out that we didn't need it. Other journals do just as well for us as media as does JAMA, and we don't have to break our necks to meet the incomprehensible and in many cases ridiculously arbitrary demands of Council people. Combinations should be allowed in JAMA. But again, acceptance should be easier and less like a schoolboy's history examination. The AMA doesn't trust its own colleagues or anyone else. It is too arbitrary and prejudiced."

"For advertisers, meet time scheduled on Council Acceptance, and give them the consideration that any magazine does. Work with them, and be reasonable about policies. Don't treat them as if you are doing them a favor to let them into the book. Modernize JAMA, also. Modify the format and the page layout. Make the book more attractive to the physicians and it will be more attractive to the advertisers. The type is good, but use better stock, this present stuff offsets and shows through too much."

2. The AMA should improve the councils and sell the value of the seals

The complaints of the advertisers about the Councils follow fairly definite patterns. They criticize the Council for the stand on trade names and mixtures. They complain that it takes too long to get decisions, and that the basis for decisions oftentimes seem arbitrary and contradictory. The following comment by a highly respected drug manufacturer is typical:

"Certain things about the Councils are silly to the point of annoyance. It is most difficult to get reasonably fast answers from the AMA on most questions. Once the AMA has made a decision which they later may acknowledge as wrong, it is still almost impossible to get it changed. A case in point is the trade name (BLANK). The Council gave the drug a name completely different from the common one. We prepared a long brief on the history of medical nomenclature and on this drug in particular. There was no objection from them, but they wouldn't change it for a year and a half.

"Combinations, too, must be allowed. It is silly not to allow combinations of accepted drugs, and to ban combinations of drugs that are commonly in use. The Council is so hidebound in many affairs that they simply refuse to accept what has been a fact for a long time.

"Council procedure should be standardized, speeded up, and constructive—not just yes or no. The same rules should apply to everyone.

"But most of all, the AMA should show it respects the pharmaceutical manufacturers as they respect it; and it should work *with* them, not against them."

A man with one of the big international consumer ad agencies expressed his feelings as follows:

"The business of Council Acceptance is a constant source of irritation. I used to think it was Fishbein, but the same kind of thing still goes on. It's just handled in a most unbusinesslike way.

"For example, when one of the JAMA representatives in New York said that they would consider liquor ads of an institutional nature, we asked him how we could get consideration for (BLANK). He was completely vague—just said he wanted a specimen of the ad, etc.

"What the JAMA representatives need is a printed form for applicants specifically stating all conditions and requirements.

"Another trouble is the *difficulty* of getting Council Acceptance. There is always too much delay. You can't get decisions on anything, which means that

you can't allocate or prepare your ads. We were once told we couldn't get an answer because several of the Council doctors were away in Europe.

"The New York representatives do their best. They make frequent calls to Chicago for us, but they don't seem to be able to get any information. They are kept in the dark. Among other things, all this mystery and delay makes space-buyers and agencies wonder whether they are being discriminated against. A more businesslike policy is needed to convince us that we are getting fair and equal treatment."

The apparent arbitrariness on decisions about copy is another source of misunderstanding. Witness the comment of this ethical drug manufacturer:

"Council Acceptance is valuable to us as a selling point, and we tie it in with our direct mail and detailing whenever it is appropriate, but its value could be increased if the difficulties it presents to advertisers could be removed.

"There are too many objections to valid statements in the copy—statements which are supported by the best research in the best houses. I appreciate that JAMA must maintain a high standard. But when clinical investigations prove certain things about a product, why can't the ads say so?

"The AMA and the manufacturer *should* work together to inform the doctors, but the limitations imposed by the AMA prevent this. We have also found that there is unnecessary delay in granting Council Acceptance."

This comment on the same subject was offered by the head of a large medical ad agency:

"The Councils are inconsistent. They want a statement of facts as *they* see them, regardless of the truth or the requirements of good advertising. They even edit doctors' direct quotes.

"No one wants JAMA to accept junk, but reputable firms know what they are doing and self-policing is general. The fact that an advertiser naturally plays up the *best features* of his product doesn't mean that his claims are *untrue*. But the Council frequently objects to the emphasis in ads.

"For this reason, many manufacturers will establish a new product, making all the claims they want to make, before applying for Council Acceptance. Or sometimes they deliberately refrain from getting Council Acceptance at all because of the way it restricts their advertising."

Another complaint on trade names was offered by an executive of one of the large ethical drug firms:

"The policy on advertising of trade names is ridiculous. The product is actually sold under the trade name by every other method of selling."

Another large ethical drug firm offered this comment on mixtures and combinations:

"From an advertiser's standpoint, combination drugs should be given Council Acceptance if at all possible. We are terrifically restricted by not being able to get Council Acceptance on combinations. The rules of the Council definitely limit the amount of advertising which is allowed to appear in JAMA. There is no question about the fact that space we use would increase if it were not for these restrictions."

This double-barrelled comment came from an X-ray manufacturer:

"About acceptance of the Seal, *speed it up*. If the Seal meant anything, we would definitely hold up an advertising campaign, but it doesn't mean anything now, so we don't."

An otherwise happy ethical drug ad manager offered this comment:

"The time taken to grant acceptance is not bad, considering the problems involved. We got quick action on our last three applications.

"However, JAMA does take far too long to publish the official notices of acceptance. For instance, we had a product accepted last May and the announcement of acceptance has *still* not been published, even though this is December. Considering the number of ad pages they cover, JAMA should devote more space to these official notices, if lack of space is the reason for this delay."

The foregoing comments were criticisms of the Council as far as its standards or its operations are concerned.

A number of manufacturers felt that the AMA was remiss in not doing a better job in selling the value of the Council Seal to the physician. They felt that the advertisers placed comparatively little value on the Seal, because physicians place little value on and know little about, what the Seal stands for.

A medical equipment manufacturer gave as his opinion:

"If I had anything to do with the promotion and direction of the formation of policy of the Council, I would promote the Seal to the doctors. Don't make a commercial venture of it. Think of it in the light of protection to the doctor."

A contraceptive manufacturer stated it this way:

"The principal drawback to Council Acceptance is that most physicians are not aware of the meaning of Council Acceptance. They should be made more conscious of the Council purposes and their methods. NNR should be more widely distributed, and the value of it should be stressed. Druggists don't care one way or another about Council Acceptance. The AMA should not have given up publishing NNR. It would be better if they published it, rather than Lippincott."

A medical and agency head said:

"The AMA should develop material showing the purposes and methods of the Councils, and should re-emphasize the value of Council Acceptance. They should educate MD's as to the real meaning of Council Acceptance.

"They should also speed up processing of drugs which have been submitted, and loosen up their policy on trade names."

Another medical ad agency man, himself a physician, offered the following:

"Its value could be increased if the laity knew more about it, and if the Seal could be put on the package. The doctors, too, should be better educated about what the Seal is and means. Many of them seem to think you can *buy* it. Druggists are even more ignorant and cynical about it."

A manufacturer of commercial chemicals expressed the same thought somewhat differently:

"The value of the Seal could be greatly increased if the AMA would take steps to explain its real meaning to doctors. Most of them don't appreciate its importance, especially in the case of new drugs. And there are lots of things they don't realize, such as the fact that if a firm has some Council Accepted products, it can't advertise its full line in direct mail, but has to keep its Seal products separate."

One of the large ethical drug manufacturers, motivated by self-interest, made this unusual comment:

"From the standpoint of the AMA, the AMA should promote the Seal with the druggists. Such promotion would do no good with the doctors. In fact, promoting the Seal would bring the smaller companies with Council accepted products to a par with the larger, established companies—that would be the trend."

3. The AMA should sell the Journal as a medium

One of the commonest reactions to our interviews with the advertisers was surprise that the AMA was interested in the opinions of the advertisers. More than one of the interviewees, when we explained the purpose of the survey, expressed amazement and said something like, "Do you mean the AMA is *really* interested in what *I* think?—I never thought they cared."

The general reaction, expressed or implied, was a feeling of hope that the present AMA administration was going to initiate some long-needed steps toward improving relations between the AMA and the advertisers.

In general, a number of the advertisers spontaneously stated that the present AMA operating organization, in its various departments, was the most cooperative and progressive that the AMA has had.

The typical advertiser reaction to AMA space-selling methods ran along the lines: "I never thought the AMA was at all interested in selling space. I thought they looked on advertising more or less as a favor to the advertisers and a source of some extra income which they don't especially need."

About three-quarters of the people we talked to said that they were perfectly satisfied, from their own viewpoint, with the low-pressure, non-promotional methods employed by the AMA.

When the question was put to them in terms of "How can the AMA get you to buy more space?", however, the answer was invariably, "They are going to have to *sell* me by showing me why I should buy more space in AMA publications, and to do this they are going to have to cultivate me considerably more and give me considerably more services than I have been getting."

The other quarter of the advertisers stated right off, "The AMA needs more promotion if it is going to be competitive to the throw-aways in selling space."

Only a handful of the largest and most important advertisers stated that they had frequent contact with JAMA space salesmen.

The large majority stated they seldom saw JAMA representatives, they received practically no promotional materials, and that in comparison to the materials with which they are bombarded by the throw-aways, the AMA matter was not very well done.

An eastern medical ad agency head stated:

"The salesman from JAMA comes in only about once a year. Though this is December, there has been no one here yet this year. JAMA puts out little promotional work, and that is poor compared to what we get from the others. They are mostly just circulated letters from Tom Gardiner. The pitch on the Student Journal isn't too bad, though.

"The JAMA salesmen should be better equipped."

A small ethical drug manufacturer made this comment:

"I have never had a salesman from the AMA call on me. As far as I can recall, I have never received any promotional literature. The AMA leaves you with the impression that it is always doing you a favor. Today, advertising of medical products doesn't have to be in JAMA and most of it is going elsewhere. A lot of this is done to the hidebound conservations of JAMA and the Councils which won't come up to date."

Along with these comments on lack of promotion is the frequent statement that the AMA has a really valuable piece of merchandise to sell, and that it is a shame it is not being promoted as it could be. Witness this ethical drug manufacturer's comments:

"The AMA doesn't seem to realize what a valuable piece of merchandise they have.

"There are constant personnel changes in medical advertisers. You have to keep selling the new people. I don't think the AMA has ever participated in specialty journal advertising promotion. They aren't promoting them at all. It isn't enough to send out a rate card.

"The AMA has never made any real effort to sell the advertisers. The Journal has been my bible. But you have to know your way around. They haven't sold either the advertiser nor the profession. I am sure everybody doesn't realize what you can get out of the Journal.

"While I find *Modern Medicine's* "Topics" on market research very valuable, I think that some of the non-AMA publications go too far and bother you too much.

"But the AMA has never gone far enough. This is especially true of the AMA special journals. They are good, but nobody is told about it.

"It is not enough to say, 'Only Council Accepted products are carried in our Journal'. There have been too many successes without Council Acceptance.

"The AMA attitude is that they are giving you a favor. This attitude is not conducive to selling. Henry, who was previously here in New York, just never came around—only about once a year."

An executive at one of the small drug firms pointed up the fact that personnel changes make continuous promotion necessary:

"I have been here only a year, and I have never seen an AMA representative nor any promotional literature of any kind. In my opinion, their salesmen should be out selling the book, and the AMA shouldn't behave as though it were doing us advertisers a favor letting us into the book. The throw-aways don't do this."

One of the larger ethical drug manufacturers stated:

"What do I think about the AMA space-selling and promotion techniques? There is damn little of the first, and none of the other.

"It doesn't really matter a damn bit to me, because I don't want to see them, since I already have more than enough to do, and it is more pleasant this way.

"For their own sake, however, they should get out and do some selling or one of these days they are going to find they haven't any new customers."

A midwestern medical supply firm put it this way:

"The AMA space salesman should definitely make more calls. Even though JAMA now gets the largest percentage of our media advertising, if their salesmen made more calls on me and had a decent story to tell, it is more than likely that we would increase our space in JAMA.

"The AMA doesn't make any effort to sell anything or help anyone with any problems. It's there if you want to use it, and it's perfectly okay with the AMA if you don't.

"Although this policy is okay with me, I suggest that a little more planning in a sales campaign would certainly be productive of excellent results for them."

A specialty food manufacturer made a similar statement:

"I don't think I have seen a space salesman from the AMA in the last ten years. I see Mr. Lyon at meetings, but can't remember when I had a call from one of their salesmen.

"*Modern Medicine* uses more aggressive sales methods. I have got to know their man, and I have confidence in him. And it does result in our buying more space in *Modern Medicine* than we would otherwise.

"Our company is growing, and so is our advertising budget. As of now, the increases in our budget for the most part go into *Modern Medicine*. We are also thinking of going into *Medical Economics*, although we have not done so as yet.

"I would really like to be sold on buying more space in JAMA, and I think I could be. A better sales presentation on the part of JAMA, if it did nothing else, would reinforce our own feelings. It would get us off the fence."

A number of the advertisers felt that merely seeing the AMA space salesmen more often would not be an answer to the problem. The space salesmen, they felt, were not sufficiently trained in the policies of the AMA nor the facts about the publications as media to be of any real help.

A medical ad agency head stated it as follows:

"It has turned out to be a waste of time to talk to the AMA men. Nothing is being done by them to help the advertisers. If you want to know what should be done, see anyone in the consumer field. Who buys, where do they buy, what do they buy? Consider *Mademoiselle* and *Charm* as two examples. They give a magnificent analysis of their markets. The JAMA salesman walks in and says, 'Why don't you buy?'. They should hire men to do a constructive job of salesmanship."

A large ethical drug manufacturer felt much the same way:

"As far as the space selling and promotional practices of the AMA are concerned, there just aren't any. But in view of the way the AMA doesn't use its salesmen for anything but errand boys, we don't want any. They make very few calls, and the AMA promotional material is scarce and lousy. From our point of view, this doesn't make any difference—in fact, we like it, because they don't bother us or take up any time.

"From their point of view, however, it's not very good. I don't know why the AMA doesn't let their men sell the book. It's a hell of a good product and the arch-conservatism of the AMA is ruining it."

Another medical ad agency man felt that the AMA salesmen's hands are tied by AMA policies:

"The AMA has very little promotional materials, and their salesmen make few calls and no presentations. I don't think this will improve until the AMA modifies its policies. It ties its salesmen's hands.

"Of all the medical books, the least promotional work is done by JAMA. The State journals do a little more. The throw-aways do the most.

"The AMA policy on trade names must be changed first, and in a hurry. Their salesmen should get out and sell. They should make calls—lots of them. The AMA should also help the advertisers with their general plans, and on specific problems involving the advertiser and the AMA.

"The last presentation we got was the AMA readership survey, which was presented in too complicated a fashion. The AMA salesmen use very poor sales techniques. However, help on specific problems has been good."

A third medical ad agency man, who was in general very favorable to the AMA, made the following comment:

"The AMA does practically no promotion. They should tell their story to medical agencies and to manufacturers. They can take cases and specific examples showing the effectiveness of the Journal.

"JAMA actually does a far better selling job than any other journal, but they don't tell that fact to the advertisers. The mass journals tell the advertisers they have to use them to sell. When they increase their budgets, they do so in the throw-aways, and not in the AMA publications. The manufacturers, being constantly reminded of *Modern Medicine* and *Medical Economics* by their direct mail promotion and sales calls, feel that the doctors are also being reminded just as often, though they aren't.

"The main thing I would like the Journal salesmen to do is to show me what JAMA can do for *my* clients."

A number of the advertisers expressed the sentiment that constructive selling by the AMA would unquestionably increase their use of AMA publications. A drug manufacturer, known as a good friend of the AMA, put it this way:

"If the AMA wants to sell more space, we are satisfied with our present allocations and it will take some doing, but they might be able to convince us,

through research and working with us, that we'd do better to spend *all* our money with the AMA by taking out two-page spreads or 12-page inserts. It would require a lot more cultivating of us than is now done, and it would require their giving us facts. If they could show us it was to our advantage, we would do it. I don't know whether they would be able to do this or not."

"If I were the AMA advertising manager, I would give the pharmaceutical industry the best evidence I could dig up that JAMA is the No. 1 spokesman for science and practice in this country, that it is editorially, and as an advertising medium, the most reliable for advertising.

"I would also sell the mantle of the AMA. I would sell it as the only journal with only *medical* advertising. I would also try to disabuse the advertisers of the belief that the AMA is serving any special interests.

"In promoting and selling JAMA, I would use direct selling and direct mail. JAMA can be sold only by keeping the respect and esteem of the physician and the advertiser."

An executive of one of the large ethical drug firms, known in the industry as a leader, had this to say:

"If I were promoting the AMA publications, I would try to find out what JAMA can offer and can do that other publications can't. I would then undertake an aggressive mail-promotion campaign.

"I would do this, not because JAMA is in need of advertisers, but to build up the special journals and to protect JAMA if things in the medical field retrench.

"I would also do a step-by-step redesigning of the publication. I don't think JAMA needs any more personal representation than they now have. It doesn't need the personal effort and pressure that the others do, because of its unique position in the field."

A consultant on medical marketing and advertising had some specific suggestions to make:

"I think that space sales in JAMA could be increased by a direct-mail campaign to firms whose products are acceptable. Other medical journals do this and get good results.

"Such a campaign might then be followed up by visits from space salesmen. The campaign should emphasize the *values* of advertising in JAMA. For example, the special importance of JAMA to GP's, who are the predominant type of physician and the importance of the Seal of Acceptance to physicians who are impressed by the fact that the ads are strictly limited and controlled. Use *snob appeal.* Convince the advertisers that you are really a high-class publication.

"I also think that JAMA should be more adequately represented at trade association affairs. Its representatives should get around more and *meet* people.

"It is not *competitive* enough at present. It has enormous prestige, but perhaps it is almost too dignified in its refusal to compete vigorously with its rivals.

"Space selling is a tough business for JAMA since it must compete not only with other journals but also with the other media, such as detailing and direct mail. The advertiser must be convinced that space purchases in JAMA are the best investment."

One of the previously quoted medical ad agency heads dwelt on the necessity for continuous promotion:

"The AMA needs a promotion manager to develop direct mail to medical ad agencies and manufacturers. Tell the true facts on AMA publications over and over again. Then advertisers will be more conscious of their value and budget increases will be more apt to go to AMA than the throw-aways.

"But don't go in for the high-pressure personal selling of the throw-aways. It isn't necessary and will cheapen the AMA's position."

A large ethical drug manufacturer suggested more service-type promotion pieces:

"*Medical Economics* and *Modern Medicine* both send us promotional stuff that is of real value to us. "Medical Marketing", "Economic Facts" and information on the preparation of advertising is of definite value to us.

"I think the AMA, as a long-term proposition, should provide to advertisers and prospective advertisers helpful information with the idea that by giving helpful service, it can build a warm spot for itself with the advertisers."

Another large ethical drug manufacturer put the same thing this way:

"We like to have facts to base our decisions on. At the present time, much of what we do is based merely on precedence. We would like to know, have the

conditions changed since the precedents were established? We would certainly like to know the answers to that."

Two advertising agency people and one manufacturer gave requests for readership surveys, which were typical of the expressed or implied wishes of the majority of the advertisers:

"I should like to be convinced that JAMA is actually read by doctors and not just filed."

"Continuing surveys by independent groups should be made of readership and other information about who the readers are. Certain other questions would be influential in getting advertisers to place ads, for example, regular media information. We would like to know such things as what is the value of regional inserts. The AMA should have some fulltime people in Chicago preparing information on the media value of JAMA and comparing it with other books. National, regional, and specialty influence should be measured, and these facts put in the hands of advertisers. Surveys on the order of *Medical Economics* should be studied. They are excellent. Because of the widespread distrust of AMA, however, readership and ad effectiveness surveys should be by independent agencies and certified as such."

"A good readership study would be very helpful. We would buy it if the AMA put it out. I believe the AMA is basically honest in that I have never had reason to believe otherwise."

Survey material should, however, be carefully worked out and carefully prepared, since a number of the advertisers expressed skepticism in regard to the typical magazine surveys. One of the large ethical drug manufacturers expressed this attitude:

"Watch out for this—everyone in the publishing field is running surveys to prove that they are the best deal. We question each and every survey that these fellows present. The AMA, however, is a high caliber outfit and we would probably believe that any survey they did and results they presented would be done in good faith."

There are also a number of miscellaneous suggestions for services which the advertisers would like from the AMA. The most frequently mentioned was a request for circulation breakdowns, information on JAMA readers by age, specialty, etc.

Other suggestions included information about what AMA services are available to advertisers, more hospital information, an abstract service which would furnish bibliographies on request, a library clipping service to furnish clippings of everything published in AMA journals on a particular subject, and a request that manufacturers should be notified about articles in which their drugs are recommended.

One person stated that he believed the AMA should do promotional work at pharmaceutical conventions. Another mentioned:

"AMA promotion should concentrate on firms with new products and prestige products, which are the natural market for JAMA. In its promotional literature, the AMA should continually emphasize the value of the Seal as a builder of prestige."

Nearly three-quarters of the advertisers interviewed requested information on topics which are already currently being covered in the survey on attitudes of physicians toward medical advertising, which is now in the field.

4. The AMA should increase the value of the Journal for its readers

As has been mentioned earlier, the large majority of the advertisers indicated that their attitude toward a publication was based primarily on what they thought was the attitude of the readers toward it. The more valuable a publication is to its readers, the more valuable it is as an advertising medium to advertisers.

The suggestions for improving the value of JAMA to its readers were basically of three kinds: suggestions for *technical or production* changes; suggestions for *editorial* changes, and suggestions for *advertising* changes.

The three main advertising changes suggested were: acceptance of only professional advertising; interspersing the ads with more editorial matter, if this can be done without offending the readers; and some kind of regulation of inserts.

(a) *Suggestions for technical or production changes.*—Roughly a third of the advertisers suggested that JAMA could be made more attractive as an advertising medium by improving the physical make-up or production methods used in preparing JAMA. Many of these involved comments on the quality of the printing and the paper stock used.

Typical of this type of comment is the one made by a medical advertising agency head:

"Do a better printing job. Reproductions are poor, stock is terrible. Format and layout are okay. I personally don't care whether or not the ads and the editorial matter are mixed."

An industrial chemical manufacturer commented:

"Look at such magazines as *GP* and *Post-Graduate Medicine*. They have good design, layout, paper, etc. JAMA can learn something from them."

A number of the comments on production changes were tied in with suggestions for overall modernization of the appearance and editorial presentation of JAMA. An example is the following, offered by a large ethical drug manufacturer who was fundamentally very favorable to the AMA:

"In my opinion, the whole make-up of the Journal is archaic. The British journals do a much better job—far superior—in spite of the limitations of good paper.

"We also carry a little space in *Today's Health*. Really, as a magazine, it is amateurish as hell.

"I don't think Austin Smith should feel that changes have to be made very slowly and gradually. Look at the *British Medical Journal*. That used to be terrible. Then they had Eric Gill redesign it and they changed it overnight.

"The AMA production equipment is definitely archaic. What they call a "bleed" is laughable."

A small drug manufacturer put more emphasis on the original articles:

"Typography and format should be cleaned up; articles should be shorter, summaries better. Long articles should be condensed; material should be updated. It is much too far behind.

"But most important, the articles are of little interest to the GP. There is considerably too much specialization.

"Reproduction should be better. There is too much show-through and offset. More care should be used in editing the magazine, and an advertising department section should be established that would work with the advertisers and help them with their problems."

A surgical instrument manufacturer was quite drastic in his suggestions:

"The format is lousy, they should redesign the book, they should intersperse editorial matter with ads, they should use better heads, and redesign the whole layout. They should run articles of more general interest, and they should not publish it as often as they do. The average doctor can't possibly read all of it regularly—it comes out too often and has too much in it. They should condense the technical reports like *Modern Medicine* and *Medical Economies* do. The articles should be no longer than one page. The summaries should be at the head, not at the end of the article. There should be more cuts and more color, and they should use a smaller format. They should sectionalize the book and let the advertisers go in the particular section which they want to hit. The editorial board should abstract each section and run a summary at the beginning of it. They should also cut the time okays for copy."

(b) *Editorial changes.*—The three main suggestions for editorial changes were concerned with presenting the material in the Journal in a more interesting manner; giving more attention and more space to material which is interesting to the average doctor, and giving less attention and space to unusual cases which are of interest only to a comparatively few specialists; and cutting down on the time-lag between the writing of an article and its appearance in the Journal.

These two comments, both from large ethical drug manufacturers, were typical of the comments regarding the "uninterestingness" of the editorial matter:

"My strongest objection is to the editorial matter, which is fundamentally uninteresting. JAMA would be very smart if it would model itself on the *Lancet* and the *British Medical Journal*. But this is probably impossible. It would involve the re-education of American doctors. They just can't write or express themselves in the way that British doctors can. I have no real quarrel with the subject matter. But as it is now written, JAMA is just hard to read."

"The atmosphere of JAMA is boringly pontifical. Medical writing needn't be dull continuously. I think there are make-up devices that could make JAMA more interesting to the physician. It, like the AMA, puts a high premium on orthodoxy—to hold out against change to the last ditch."

The fairly numerous suggestions that JAMA concentrate on serving the mass GP physician rather than the minority specialist are represented by the three

following comments, the first two of which were made by drug manufacturers, the last by a medical advertising agency head:

"Editorially, there should be more articles of interest to the GP. Most of the articles are over the heads of the GP's, and the specialists usually get their information from other journals. The abstracting could be improved. It is not complete enough in this respect."

"Material in JAMA is too technical for the MD of general work. JAMA is the best medical journal in the world, but it belongs in libraries, since it is only read for specific articles by MD's."

"Ultra-scientific articles should be cut down and more articles of interest to the GP should be run. There should be more review articles and better abstracts. The ad should come off the cover. *GP* and *Post-Graduate Medicine* are both much better looking books. *Modern Medicine* has much better abstracts. Either kill Tonics and Sedatives or get Fishbein back to do it."

The requests for making the articles in JAMA more timely were fairly widespread.

This first comment, by a medical marketing consultant, went further, stressing the part which JAMA plays as a medical news publication:

"I think it would be a great improvement if the editorial pages were made more newsworthy and included more about new products and developments. This, of course, is also the job of the advertiser. In fact, it should be a cooperative job between the advertiser and JAMA."

More along the usual line are these three comments made by various ethical drug manufacturers:

"Articles are too late. They are published in many cases a year or so after they are received. Most of the articles are too high-blown for the readers. As a result, the average doctor who receives JAMA reads neither the articles nor the ads."

"There is too much time-lag between the time a paper is submitted and when it is published in JAMA. This is especially true in the case of important papers. This is a frequent occurrence. I am under the impression that many times a paper doesn't appear in print until a year after it is submitted. Also, sometimes articles appear that are of no consequence, when there are important articles which are held up and kept waiting to be published. These things are important to the pharmaceutical advertiser, because many times these articles are favorable to a new product in which the advertiser is vitally interested."

"I have a specific suggestion for an improvement on the editorial side. Whenever JAMA carries articles on drugs where therapy changes frequently occur, for example in the field of antibiotics, there should be a note saying when the article was submitted and what changes have been made since then. Sometimes there is an eight or nine months delay between the submission and the publication of an article. Such articles should be brought up to date."

(c) *Changes in advertising policy.*—The comments on suggested changes in advertising policies centered around three main topics: acceptance of only professional products, or at least limitation of amount and higher standards for non-professional ones; requests for interspersing as much editorial matter with advertisements as would be agreeable to the readers; and regulation of inserts, with a definition of what is acceptable, so that all advertisers are treated impartially.

Nearly two-thirds of the advertisers definitely preferred to have JAMA accept only advertising of products of professional interest to the physician. A number of these centered their attack on cigarette advertisers who made pesudo-scientific claims.

The pattern of reasoning on the subject of accepting only professional advertising was very consistent. It was tied in directly with the requirement that only therapeutic products which have been accepted by a Council can be advertised in AMA publications. The advertisers consistently resented intensely the fact that they had products on which they had considerable difficulty getting Council Acceptance which appeared right alongside cigarette and soft-drink advertisements which had had practically no scrutiny by the AMA. This feeling was even more intensified in the case of ethical drug manufacturers who had compound products which they could not advertise in JAMA.

This comment from a large medical advertising agency man is typical:

"JAMA should have ethical ads only. It is certainly inconsistent to run such ads as the Philip Morris ads and at the same time impose such rigid restrictions on the ethical ads."

An ethical drug manufacturer expressed the same though a little differently:

"Only products of professional interest should appear in JAMA. Otherwise the value of it as an advertising medium is considerably lessened, particularly since most readers don't discriminate between ads subject to control and those that aren't."

Two drug manufacturers took a more positive approach in their views:

"The book is much too important to have valuable space being taken up by ads of no professional value."

"Only ethical products, or those of specific professional use, should be allowed in the book. There is no cookbook purpose behind JAMA. It is one of the best medical journals in the world and it shouldn't be all cluttered up with extraneous nonentities. There are too many ethical manufacturers who coud use the space to bring products of important professional use to the physician's eye."

Some of the advertisers took a more liberal view. For example, this medical advertising agency man:

"I don't blame JAMA personally for accepting non-professional ads as long as they don't insult the intelligence. It's good business. But it is strongly resented by my clients. In fact, they feel so strongly about the matter that although they are all increasing their ad budgets for 1953, they will all have fewer pages in JAMA than in 1952."

Cigarette advertising was heartily damned by nearly every advertiser with whom we talked. Even the non-professional advertisers in JAMA felt that way. The representative of one of the large manufacturers' trade associations stated it bluntly:

"Cigarette advertising in JAMA should definitely be eased out. 'More doctors smoke Camels than anything else' is just a bunch of crap. It adds nothing to the believability of other ads in the book, to put it mildly. I have no objection to the Buick ads. But the cigarette stuff is obnoxious to almost anyone, including members of the profession."

An ethical drug manufacturer stated:

"Food ads belong in the Journal. Cigarettes, especially Philip Morris ads, are completely out of place. Their exhibits—the rabbit's eye with a pseudo-scientific approach—is greatly resented by the manufacturer who has had the headaches of getting Council Acceptance."

A small drug manufacturer extended his restriction of non-medical advertising to the conventions:

"Non-professional products should be completely excluded from JAMA. This is extended to conventions, which have become like twice-a-year circuses. If the AMA expects its advertisers to be ethical, and enforces standards against them, it should at least do likewise to the non-medical advertisers. The non-ethical inclusions, and especially those of pseudo-scientific validity, have been making everyone sore. They should be tossed right out. The cigarette ads especially."

A large consumer advertiser who has very little advertising in JAMA stated:

"About JAMA advertising—when an advertiser advertises in JAMA, he should advertise to the reader as a human being, or he should talk to him in professional language. Mixing consumer talk with professional talk doesn't get very far. Such a practice degrades the publication. The car advertising is okay. But JAMA should definitely cut out cigarette advertising as it now appears. I object in general to any medical claims where there is no matter of medicine at all involved."

A publisher of medical books give this suggestion:

"Limit the proportionate amount of space allowed to nonprofessional ads in the book. Throw out all the phonies. This means especially cigarettes."

Most of the people who condemned non-professional advertising in JAMA condemned it also at the conventions. Here are two typical statements, the first by a large ethical drug manufacturer, the second by a manufacturer of X-ray equipment:

"The conventions have become a circus because of the type of people they let exhibit there. It takes an active imagination to associate them with the medical profession. They even display pots and pans. Make it more of a medical meeting and less of a circus—this is what they should do."

"The AMA has done itself discredit by securing a lot of diverse products which have no relationship to the medical field. This is very evident not only in JAMA but also at the conventions. The conventions are becoming a circus."

A medical advertising agency man stated:

"Conventions are a laughing-stock. Burlesque shows complete with life-and-death products and developments of legitimate advertisers."

Another ad agency man commented:

"Clean up conventions and take out of them the burlesque show routines."

This statement, offered by a large ethical drug manufacturer, introduces the idea of Council Acceptance at the conventions:

"Conventions first of all must be improved. They are like county fairs, and things are not only disorganized but ridiculous. Not only cannot samples of non-Council Accepted products be given out, but instead of trying to make a convention a dignified affair and keeping out the side-show experiences, the AMA spends its time sending spies around to find out if a manufacturer is giving away free headache powders. Even if a physician personally requests a product which is not advertised, we can't give it to him."

Three ethical drug manufacturers made these comments:

"Conventions are terrible. Our own queries show that physicians regard conventions as holidays, and as the least effective phase of the AMA operations."

"Conventions are terrible for advertisers. Besides too much midway activity, they are always out of the way. The point system, too, is very bad."

"The midyear clinical session is a poor thing. It could be good, but it is always in an out-of-the-way place. If you don't go, however, you get a bad spot in the main convention."

One ad agency man complained of discrimination at conventions:

"The AMA conventions are too much like county fairs. The point system is unfair and discriminatory. The ethical advertisers and exhibiters are unable to compete with the girly shows. The AMA is not consistent—it lets big advertisers do what small ones can't."

The last comment on conventions which we are quoting, made by a manufacturer of X-ray equipment, was concerned chiefly with samples:

"The objective at AMA conventions seems to be to collect free samples. In fact, some of the commercial firms even furnish shopping bags with their name on the side as another means of advertising.

"The conventions give the appearance of being tremendous affairs, crowded with people. As far as the exhibitors are concerned, however, the attendance is often not good, even in spite of the big crowds. At least half of the people who attend the conventions could not buy the products exhibited anyway.

"It might help if the AMA could tighten up a little better as to who is allowed to attend the convention. They are not so big that they cannot be handled except in certain cities. The clinical meetings are always handled in other parts of the country, and this adds greatly to our expense. We dropped the clinical meetings this year."

The question of inserts was mentioned spontaneously by the majority of the advertisers interviewed. About half of the advertisers expressed a definite dislike for the Pfizer Spectrum insert because they felt that it gave Pfizer an unfair advantage over the other advertisers and because they felt it made the AMA the publisher of the Pfizer house organ.

About a quarter of the advertisers expressed admiration and complete approval of the Pfizer insert, and regretted that they had not initiated the idea instead of Pfizer.

Roughly another quarter approved completely of the ad from Pfizer's point of view but felt that from the AMA's point of view, it was a mistake in policy to accept it, chiefly because if others followed the precedent, JAMA would end up as being a hodgepodge of house organs and editorial matter, with the reader confused as to which was which.

One medical ad agency man made the following favorable comment:

"Spectrum is a big help to the book. It dresses it up and makes it more interesting. The MD's will turn to it the way they do to *OP* and *PSM*. It helps the book in appearance and helps the advertisers because it brings on more interest and readership of the ads. The rest of the book ought to be as good."

Four different ethical drug manufacturers made these comments:

"I suppose the Pfizer insert is being criticized by a lot of people, but personally I consider it helpful rather than the opposite. I wish all advertisers would make their ads as interesting to the doctor as these Pfizer ads. I should like to see a campaign to encourage advertisers to produce *educational* copy of this kind."

"I think the Pfizer ad is an excellent idea as long as it remains as good as it is, and I think it will. Other advertisers can't complain. As a matter of fact, I think the greatest opposition comes from the competitors of JAMA, not from other advertisers."

"The Pfizer ad is a decided relief from the rest of the magazine. It is the only bright spot in the book. The rest of JAMA should come up to it, both editorially and productionwise. It is probably the only thing in JAMA that the physician really enjoys."

"It looks as though Pfizer now owns JAMA, but considering the high reputation of JAMA, this isn't too serious a consideration. JAMA must sell space, and this is one way to do it. I have no objections to the Pfizer insert or to the binding-in of an insert of this kind. As a matter of fact, it somewhat dresses up the book. The trouble is, too many people will probably read 'Spectrum' and not JAMA."

Two different medical ad agency people made unfavorable comments about Spectrum:

"This sort of thing can lead to trouble since the AMA is apparently publishing the house organ of Pfizer. Occasional inserts are okay, even as extensive as Spectrum, but should not be done regularly. It is a coup for Pfizer's ad boys, but it is bad for the AMA."

"As for the Pfizer ad, many agencies and manufacturers think that it nullifies the effectiveness of their own ads. It is no answer that they can do the same thing. I'm in favor of anything that will make the doctors more interested in JAMA, but I don't think Spectrum does this. It is also generally felt that there is AMA sponsorship of Pfizer in the sense that clearance was made easier for them."

Three ethical drug manufacturers also made critical comments:

"JAMA has sold out to Pfizer. It has cheapened itself. You get the impression that it will sell the whole magazine if anyone will pay for it."

"The Spectrum ad is deplorable. The whole principle of accepting large inserts from big companies is bad. Suppose other advertisers wanted to do the same thing? I feel sorry for the AMA. They are prostituting themselves. It doesn't affect us, however."

"The idea of binding a house organ into JAMA is a poor idea because it detracts from the value of the book. However, if inserts of this type are accepted, they should be limited to number of times and pages. Otherwise, JAMA is bound to accept other advertisers' inserts like this, and will become a journal of inserts. In fairness to other advertisers, Spectrum should be dropped or others accepted. The latter would be preposterous."

Other comments were offered regarding other advertising policies. The most frequenly offered one concerned the interspersal of advertising with editorial matter. About a third of the advertisers interviewed definitely stated that they would like to see ads interspersed, since they felt that this would improve the readership of the ads. Roughly another third stated that as advertisers, they would like to see the ads interspersed, but they knew that the physicians would not like this change, so they were willing to go along with the present arrangement. Another third stated that they were satisfied with the present arrangements, and did not want the ads interspersed.

About a quarter of the advertisers felt strongly that there should be an Index of Advertisers. Though a large number of the people we interviewed did not explicitly state their stand on this subject, we received the impression that the addition of an advertiser index would be universally appreciated by the advertisers.

An example of the comments made regarding mixing advertising and editorial matter is the following comment by an ethical drug manufacturer:

"It's difficult to say what to do about the position of the ads. From the advertisers' point of view, of course, they should be interspersed. But from the doctors' point of view, they are better as they are. You would probably spoil the high standard and professional integrity of JAMA if you interspersed the ads."

This suggestion, made by a medical equipment manufacturer, was also made by several others:

"The Table of Contents is good on the cover. It could be made a little more artistic. If the book goes only to the GP, it is satisfactory as it is. But if it also goes to the specialist, the book should be divided into sections: compare it to Time magazine—that's sectionalized—national affairs, foreign affairs, etc.

"JAMA could then be sectionalized by specialty. This applies both to the editorial matter and to the ads. It would then be possible to have the editorial matter more closely positioned to the ads."

A list of the individuals and firms whose opinions are represented in this report follows.

APPENDIX

Companies and individuals interviewed

Company	Individual	Title
Abbott Laboratories, North Chicago, Ill.	Charles S. Downs	Vice president in charge of advertising and public relations.
W. D. Allison Co., Indianapolis, Ind.	A. F. Hoop	Sales manager.
American Home Foods, Inc., New York, N.Y.	William Laurie	
American Meat Institute, Chicago, Ill.	Norman Draper	
American Pharmaceutical Co., New York, N.Y.	B. E. Wallach	Advertising manager.
Ames Co., Inc., New York, N.Y.	Paul De Haen	
Armour Laboratories, Chicago, Ill.	James Scheller	Do.
Ayerst McKenna & Harrison, Ltd., New York, N.Y.	Loren Simpson	
Batten, Barton, Durstine & Osborn, Inc., New York, N.Y.	Robert Anderson	
Bauer & Black, Chicago, Ill.	George Percy	Do.
Back Lee Corp., Chicago, Ill.	Charles Glasser	
Dr. S. H. Blackberg, Chicago, Ill.	Dr. S. H. Blackberg Miss Roberts	Assistant.
Borchardt Malt Extract Co., Chicago, Ill.	John J. McKeen	
Branstater & Associates, Inc., New York, N.Y.	Henry Branstater	
Burroughs-Wellcome Co., Tuckahoe, N.Y.	Cles Baker	Advertising manager.
Chilcotte, Morris Plains, N.J.	William Russell	Do.
Ciba Pharmaceutical Products, Summit, N.J.	Paul Roder	
Clay-Adams Co., Inc., New York, N.Y.	Emil Davidson	
Commercial Solvents, New York, N.Y.	John Croak	
Doherty Clifford & Shenfield, Inc., New York, N.Y.	Philip Reichert, M.D.	
Edison Chemical Co., Chicago, Ill.	Dr. S. M. Edison	
Cortez F. Enlee, Inc., New York, N.Y.	John Johnson	Vice president.
Ethicon Suture Laboratories, New Brunswick, N.J.	Mr. Sanford	Advertising manager.
Fellows Medical Manufacturing Co., New York, N.Y.	Miss Vahl	
B. Fougera & Co., New York, N.Y.	Robert Chase	
L. W. Frolich & Co., Inc., New York, N.Y.	Charles Lewis	
Geigy Co., Inc., New York, N.Y.	Perry Stocker	Do.
Gray & Rogers, Philadelphia, Pa.	Ed Thomas	
Grune & Stratton, Inc., New York, N.Y.	Henry Stratton	Vice president.
Harrower Laboratories, Jersey City, N.J.	Mr. H. Hettrick	
Arthur D. Herrick, consultant, New York, N.Y.	Arthur D. Herrick	
Hoffman Advertising, Inc., New York, N.Y.	Harry Hoffman	
Hoffman-LaRoche & Co., Nutley, N.J.	Mr. I. Content	Advertising manager (specialties).
Holland-Rantos Co., Inc., New York, N.Y.	Leo Cole	Sales manager.
Johnson & Johnson, New Brunswick, N.J.	Mr. P. Hoffman	
Jones Metabolism Equipment Co., Chicago, Ill.	Mr. Al Hart Dr. Jones	Advertising manager. President.
Jordan Advertising Agency, Chicago, Ill.	Charles Jordan	President.
Kelley-Koett Co., Covington, Ky.	Frank Teamons	Advertising manager.
Kiescutter, Associates, Inc., New York, N.Y.	H. M. Kiescutter	President.
Paul Klemtner & Co., Inc., Newark, N.J.	Paul Klemtner Paul Potter	President. Assistant to Paul Klemtner.
Lanteen Medical Laboratories, Evanston, Ill.	R. C. Kocher	President.
Leo & Febiger Co., Philadelphia, Pa.	Leo Hudson Mr. Wilcox Advertising personnel	Vice president.
Lederle Laboratories Division, New York, N.Y.	David A. Bryce, M.D.	Director of advertising and literature.
Lewis & Gilman, Inc., Philadelphia, Pa.	Ralston Lewis	
Liebel-Flarsheim Co., Cincinnati, Ohio	Vern Curran	Advertising manager.
Eli Lilly & Co., Indianapolis, Ind.	W. F. Krass	Do.
L. G. Maison & Co., Chicago, Ill.	Dr. L. G. Maison	President.

Companies and individuals interviewed—Continued

Company	Individual	Title
Mattern Mfg. Co., Chicago, Ill	Frank Madl	Sales manager.
Wm. Douglas McAdams, Inc., New York, N.Y.	DeForest Ely, M.D	
McNeil Laboratories, Inc., Philadelphia, Pa.	Henry McNeil	Vice president.
Merck & Co., Inc., New York, N.Y	Albert Carroll	Advertising manager.
	George Wolf	Assistant advertising manager.
William S. Morrell Co., Cincinnati, Ohio	Dr. Chuning	Adviser.
	Mr. Stensby	Advertising manager.
The National Drug Co., Philadelphia, Pa.	Harold Collins	
Noyes & Sproul, Inc., New York, N.Y	Miss Dorothy Noyes	Vice president.
Ortho Pharmaceutical Corp., Raritan, N.J.	B. J. Todd	Do.
Orthopedic Frame Co., Kalamazoo, Mich.	Harry Treace	
Parke Davis & Co., Detroit, Mich	Mr. Griffith	Director of professional relations.
	Mr. Braden Walker	Sales manager.
	Mr. Sichler	Director of advertising.
	Mr. Chase	Assistant director of advertising.
	Mr. Cotton	Assistant to Canadian manager.
	Mr. Ferren	Vice president of L. W. Frohlich Advertising Agency.
Pitman Moore Co	H. O. Ball	
Procter & Gamble Co., Cincinnati, Ohio	Mr. Werner	Public relations director.
Professional Equipment Co., Maywood, Ill.	T. H. Vets	President.
William H. Rorer, Inc., Philadelphia, Pa.	Gerald Rorer	Vice president.
Sandoz Chemical Co., New York, N.Y	Sam Fossle	
Schenley Laboratories, Inc., New York, N.Y.	Dr. Charles E. Dutchess	
Schering Corp., Bloomfield, N.J	John McDonald, M.D	
Julius Schmid, Inc., New York, N.Y	John Pringle	
G. D. Searle & Co., Skokie, Ill	John Scott	Advertising manager.
J. Sklar Manufacturing Co., Long Island City, N.Y.	Victor Filler	Do.
Smith, Kline & French Laboratories, Philadelphia, Pa.	Tobias Wagner	Advertising director.
E. R. Squibb & Sons, New York, N.Y	William Hoel	
Testagar Co., Inc., Detroit, Mich	Mr. M. S. Herman	Vice president in charge of sales.
	Mr. S. J. Heinreck	President.
J. Walter Thompson Co., New York, N.Y.	H. A. Wilt	
Upjohn Co., Kalamazoo, Mich	Jack Gauntlett	Advertising manager.
	Dr. E. G. Upjohn	Executive vice president.
U.S. Vitamin Corp., New York, N.Y	B. A. Fuchs	Assistant to president.
Henry K. Wampole & Co., Inc., Philadelphia, Pa.	Mr. Chiappini	
W. R. Warner & Co., New York, N.Y	Charles Silloway	Vice president.
Robert Wilson & Associates, New York, N.Y.	Robert Wilson	
Winthrop-Stearns, Inc., New York, N.Y.	Dr. Frank Stockman	Do.
Yearbook Publishers, Chicago, Ill	Mac Green	President.
	Mr. Williams	Advertising manager.

APPENDIX IX

A STUDY OF MEDICAL ADVERTISING AND THE AMERICAN PHYSICIAN PART II. THE PHYSICIANS' VIEWPOINT

An Opinion Survey Made for the American Medical Association *

RECOMMENDATIONS TO THE AMERICAN MEDICAL ASSOCIATION

The two main purposes of this study were to learn why JAMA advertising space sales have fallen behind those of MEDICAL ECONOMICS and MODERN MEDICINE and how to reverse this trend; and to gather information which will be useful in promoting JAMA.

The facts uncovered have pertinence in varying degrees to various departments within the AMA organization. This section of the report attempts to summarize the significance of the findings to the Councils, the Business Office, and the Editorial Department.

A. RECOMMENDATIONS TO THE COUNCILS

The findings indicate that the crux of the problem of selling advertising space in AMA publications lies in the fundamental relationship between medical manufacturers and the Councils.

The solution of this problem involves much more for the AMA than just advertising revenue: it involves as well the future strength of the leadership which the AMA can exert directly through the Councils on medical products, nomenclature, and medical advertising.

The medical manufacturer is torn two ways: he realizes that the AMA's restraining influence on medical marketing and medical advertising claims, through the Council Seals of Acceptance, is beneficial for the industry over the long term, and therefore tends to want to support it; but on the other hand, he rebels against the restraint in specific instances, knows from experience that he can sell the physician on the product without having the Seal, and can advertise it as he wishes through non-Council-supervised publications.

The question of whether or not to submit a particular product for Council Acceptance then becomes a problem of weighing the advantages of having the Seal against the disadvantages of requirements for Acceptance and the limitation of claims in advertising, in the specific instance.

The current trend seems to be for the medical manufacturer to circumvent the AMA by taking his product directly to the physician without submitting it to the Councils. Because of this fact, the AMA publications are to an increasingly large extent barred to him as advertising media, and therefore, he is necessarily relying more and more on ME and MM advertising pages to tell his product story.

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* by Ben Gaffin & Associates, Chicago, Illinois, August 31, 1953.

The main reason for this trend is that the manufacturer knows from experience that he can successfully advertise and market non-Council Accepted products as long as the product is not a controversial one, and his firm name is well-established. To get Council Acceptance in such a case is to bind himself to the limitation of claims allowed by the Council, submit to what he considers may be long-drawn-out and excessively formalistic negotiations, and get in return an approval which he believes has little or no practical value.

The solution to this problem facing the AMA seems to be four-fold:

1. Review the Council rules, make them as simple and clear-cut as possible, and eliminate all requirements which are not essential to the fundamental purposes of the Councils.

2. Streamline the administrative procedures involved in getting Council Acceptance so as to make it as easy and as quick as possible for the manufacturer, as long as he meets the essential requirements.

3. Undertake a broad educational program to inform the American physician why the Councils exist, how they operate, and why the physician should be prejudiced in favor of products which bear the Seal; and why the physician should use generic names in writing prescriptions.

4. Have Council or other top AMA staff members explain to the medical manufacturers why the Councils exist and how they operate, what is involved in getting Council Acceptance for a product, and why it is to the manufacturers' long-term advantage to getCouncil Acceptance whenever possible. This can be done through speeches at meetings of medical manufacturers and advertisers, through direct mail, through exhibits at medical conventions, and through presentations made to the manufacturers and advertising agencies by the AMA service representatives. In view of the fact that the personnel of the manufacturers and agencies are continually changing, it must be a continuous and never-ending process.

UNLESS THE AMA TAKES POSITIVE STEPS TO REVERSE THE PRESENT TREND, THE INFLUENCE OF THE COUNCILS WILL CONTINUE TO LESSEN AND THE MEDICAL PROFESSION WILL SUFFER THROUGH LOWER STANDARDS OF MEDICAL MARKETING AND ADVERTISING. ADDITIONALLY, THE AMA WILL FIND THAT ITS PUBLICATIONS WILL ATTRACT A CONTINUOUSLY DECREASING AMOUNT OF ADVERTISING.

B. RECOMMENDATIONS TO THE BUSINESS OFFICE

The survey of advertisers reveals an underlying belief on the part of the majority of advertisers that AMA space-selling and promotion methods have not kept up with the changing times and the changed competitive conditions introduced by the growth of ME and MM.

The advertisers generally feel that the underlying philosophy of selling of the AMA is outmoded: that advertisers no longer consider that the AMA is doing them a favor by allowing them to buy space in the pages of its publications. They feel, moreover, that the AMA, to get their business, must present evidence of the value of its publications as advertising media, that the advertising representatives should make a positive effort to convince them of the value of advertising in AMA publications, and that the representatives should also give a level of service comparable to that given by the representatives of the competitive publications.

Translating this into action, it means that the survey findings reveal the need for four areas of increased activity on the part of the business office:

1. Do considerably more, and better, direct mail promotion.

2. Train service representatives better on knowledge of the AMA, the Councils, and their basic policies and methods of operating.

3. Give service representatives more and better presentation materials, so they will have an opportunity to help the advertiser solve his problems, and can show him why Council Acceptance and the AMA publications will help him more than ME and MM, and other publications.

4. Exercise more sales-management control over the activities of the service representatives, to make certain that the right firms are called on at regular intervals, and that the men in the field are given more and better support by the main office.

Sections I through X of the physician survey findings will lend themselves for use by the business office both in the preparation of personal presentations by the advertising representatives, and for mailing as service pieces to advertisers. Moreover, there is considerable information which will furnish ammunition to the advertising representatives when competing against representatives of other publications for the advertiser's business.

C. RECOMMENDATIONS TO THE JAMA EDITORS

The JAMA readers strongly approve of the editorial changes made in JAMA in the last three or four years. This fact should encourage the present editors to continue their program of JAMA improvement.

One suggestion offered for the consideration of the readers was strongly approved: that of organizing the original articles in the Journal into sections -- for example, pediatrics, surgery, etc. This is an editorial policy decision involving considerations of which the average reader is unaware and therefor the editors may be quite justified in not following the suggestion. If, however, there are no reasons militating against it, the adoption of this change would be approved by two-thirds of the readers.

Most of the pressure to take the Saunders' ad off the cover and to expand the index revealsed in the 1950 survey, was relieved by cutting down the size of the ad. There is evidence, however, that the majority of readers would be pleased if the ad were entirely removed, and the space used for even further expansion of the Index.

One last suggestion involves basic advertising policy. It is obvious that there necessarily exists a basic conflict of interests between the business office, whose primary interest is increasing advertising revenue and the editorial office, whose primary interest is in turning out as professional a publication as possible. Often, what will increase advertising revenue will decrease professional standing.

It is probable that at present, the AMA cannot afford to remove the Saunders' ad from the cover, even though a more detailed index would be welcomed by the readers. Even less, at present, can the AMA probably afford to exclude non-professional advertising, even though nearly two-thirds of the readers would prefer it. Even excluding cigarette advertising, which is heartily damned by a third of the readers and substantially all of the professional advertisers, will involve giving up sizable revenue.

It is possible that raising professional advertising standards in the Journal may result in some compensating increase from the professional firms.

It seems to us that the change should be a gradual one, the timing of which will be determined largely by the rate of advertising revenue increase from the increased sales efforts of the business office. The steps to be followed, as we see them, are:

1. Concentrate sales and promotion efforts on professional medical advertisers. Accept non-professional advertising which is offered, but do not solicit it from new accounts.

2. As soon as financially possible, exclude cigarette advertising, and other non-professional products which tend to use pseudo-scientific or exaggerated advertising claims.

3. Remove the Saunders' ad entirely from the JAMA cover, and expand the Index to occupy the complete cover.

4. If and when the professional advertising revenues have been built up to the point where it can be afforded, establish the policy of carrying only professional medical advertising.

These steps, premised as they are on increased advertising revenue from professional firms, will probably require some years before complete adoption.

APPENDIX X

THE FOND DU LAC STUDY: An Intensive Study of the Marketing of Five New Ethical Pharmaceutical Products in a Single Market, Resulting in Some Theory of Scientific Marketing and Service Programs for Action

A Basic Marketing Study made for the AMERICAN MEDICAL ASSOCIATION*

1956

CHAPTER 1. OBJECTIVES

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The survey of pharmaceutical advertisers played a part in bringing about a number of policy changes: the institution of an index of advertisers, the exclusion of cigarette advertising, and the eventual dropping of the 58-year old Council Seal of Acceptance Program.

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This survey was designed to give information on: the U. S. physician market; how physicians learn about new products; comparable information

*by Ben Gaffin & Associates, Inc., Chicago, Illinois

on detailing, house organs, other direct mail and the medical journal as advertising media; attitudes of physicians toward Council Acceptance; JAMA as an advertising medium; the Pfizer Spectrum insert; physician ratings of the nine AMA special journals; and attitudes of physicians toward some JAMA editorial and advertising policies. Designed as it was, it was necessarily more broad than deep.

Deciding on Another Study

Throughout 1954, discussions were held on the advisability of designing another study to serve as the basis for a second series of mailing-pieces by the AMA to the pharmaceutical industry. The most promising topic for intensive and thorough exploration was the pay-off question of "How Physicians Learn About New Products."

This question is a vital one, since the pharmaceutical industry annually spends around $130,000,000 a year with almost no factual knowledge on which to base the allocation of this huge expenditure.

The Proposal on the Fond du Lac Study

In September 1954 we submitted a "Preliminary Proposal" for an Intensive Study of the Marketing of Some Pharmaceutical Products in a Single Marketing Area" to Mr. Gardiner and Mr. Lyon of the AMA Business Office.

The Objectives As We Started Out

The objectives of the study, as far as the pharmaceutical advertisers was concerned, were given as follows:

> "To uncover, in as much detail as possible, all relevant facts which have a bearing on the sale of a particular brand of the selected new and established products over competitive products, in this specific market. In other words, we will study the factors which have motivated the physicians to prescribe the specific drugs they prescribe; the factors which have motivated the pharmacist to stock the particular drug and competitive ones; the factors which have influenced the hospital in selections of specific drugs to use; and how much each of these three groups influence each other; and the relative weight of the influence of each upon each other.
>
> "Among the specific influences upon the doctor, the pharmacist, and the hospital, we will attempt to study the part played by the commercial communications channels; detailing, direct mail, and medical journal advertising; and the relative influence of the professional channels; journal articles, medical society papers, hospital news, word of mouth, etc.

pps. 1 and 2
by Ben Gaffin & Associates, Inc., Chicago, Illinois

"As in any sound research project, we will attempt to uncover general principles from the study of this particular local situation which may be applied in the future in such a way as to increase the desired results following from the application of this new knowledge."

The proposal then went into the reasons for the selection of this particular area of knowledge to study:

"To our knowledge, no previous study of this type and scope has ever been undertaken. The area covered is a most fundamental one on which all major marketing decisions are based. It is, moreover, our impression that less is known about this particular area than in any of the less important areas, though there are more divergent theories, 'seat of the pants' decisions, and pet hunches, followed in this area than in any other.

"If this study reveals a tenth of what we have reasonable hopes of learning, it will enable the American Medical Association to perform a service for the industry of such magnitude that the industry will be very mindful of AMA publications when setting up advertising media allocations."

p. 2
by Ben Gaffin & Associates, Inc., Chicago, Illinois

A STUDY OF MEDICAL ADVERTISING AND THE AMERICAN PHYSICIAN PART II. THE PHYSICIANS' VIEWPOINT -- An Opinion Survey Made for the American Medical Association

CHAPTER VII. ATTITUDES OF PHYSICIANS TOWARD COUNCIL ACCEPTANCE

From the survey of advertisers, we learned that the majority of medical advertisers believe that physicians attach little or no importance to the Council Seal of Acceptance in the case of a product which is not dangerous, especially if the manufacturer is well-known and of good reputation.

Medical advertisers generally believe that the Council's Seal has considerable value in the case of a new, potentially dangerous drug; or any drug put out by an unknown firm.

To learn the facts about the attitudes of physicians toward Council Acceptance, we asked them three questions:

> "When learning about a new product which is not particularly dangerous, do you usually have any special interest in whether or not it is 'Council Accepted,' or doesn't it make any difference?"
>
> "In the case of a drug which is not particularly dangerous, would you feel safer in prescribing it if it had the Council Seal of Acceptance, or wouldn't it make any difference?"
>
> "Which do you think is usually of greater importance to you in connection with a new drug -- the name of the manufacturer, or the fact that the drug has the Council Seal?"

On the first question (see Table 48), the answers of physicians as a whole broke down as follows:

71% have special interest,
27% makes no difference,
2% qualified or other.

There are some interesting variations on the part of special groups from this national average. The physicians who write over 100 prescriptions per week were considerably more inclined to be interested in Council Acceptance (85%) than those who write fewer prescriptions.

The full-time G.P. is more interested (77%) than the full-time specialist (68%).

The physicians of 40 and over were more interested (73%) than those under 40 (65%).

Geographically, physicians living in the East were the least interested (67%), while those in the South expressed a considerably higher interest (average, 79%). Physicians living in cities under 100,000 were considerably more interested (76%), than those living in cities of a million and over (62%).

p. 117, by Ben Gaffin & Associates, Chicago 4, Illinois, August 31, 1953

APPENDIX XI

A STUDY OF MEDICAL ADVERTISING AND THE AMERICAN PHYSICIAN PART II. THE PHYSICIANS' VIEWPOINT — An Opinion Survey Made For the American Medical Association

There seem to be no pronounced or consistent differences on the basis of variations in exposure to commercial advertising channels.

On the second question (see Table 49), the breakdown was as follows:

79% would feel safer,
20% makes no difference,
1% qualified or other.

The same relative differences between various groups holds true on the answers to this question as on the preceding.

The third question (see Table 50), produced the following overall breakdown:

55% Council Seal is more important than the name of manufacturer,
33% name of manufacturer is more important than Council Seal,
5% they are both equally important,
3% other factors are more important than either, and
4% undecided.

There are some differences between the national average and the averages for special groups which one would not expect from the answers to the two previous questions.

Twice as many physicians who wrote the largest number of prescriptions consider the Council's Seal as of greater importance than the manufacturer (60% vs. 30%); among those who wrote the fewest prescriptions, this difference dropped to 48% vs. 39%.

Full-time G.P.'s were highest by type of practice (57% for the Council Seal vs. 34% for the manufacturer), and Internists attached most importance to the Council Seal (66% vs. 28% manufacturer) of any of the specialities.

Most surprising, the physicians under 40 attached relatively more importance to the Council's Seal (56% vs. 35%), than did the physicians 60 and over (53% for Council Seal vs. 31% for manufacturer).

As in the preceding questions, the small town physician living in towns under 10,000 population was relatively more impressed by the Council's Seal (62%) than by the name of the manufacturer (31%).

pps. 117-118, by Ben Gaffin & Associates, Chicago 4, Illinois, August 31, 195

APPENDIX XII

THE FOND DU LAC STUDY: AN INTENSIVE STUDY OF THE MARKETING OF FIVE NEW ETHICAL PHARMACEUTICAL PRODUCTS IN A SINGLE MARKET, RESULTING IN SOME THEORY OF SCIENTIFIC MARKETING AND SERVICE PROGRAMS FOR ACTION

A BASIC MARKETING STUDY MADE FOR THE AMERICAN MEDICAL ASSOCIATION, 1956

By Ben Gaffin & Associates, Board of Trade Building, Chicago, Illinois

CONTENTS

(The Fond du Lac Study: An intensive study of the marketing of five new ethical pharmaceutical products in a single market, resulting in some theory of scientific marketing and service programs for action—A basic marketing study made for the American Medical Association by Ben Gaffin & Associates (full text).)

FOREWORD

The Fond du Lac Study has been sponsored and financed by the American Medical Association as the second in its series of basic studies in pharmaceutical marketing undertaken as a service to the pharmaceutical industry.

The first study, also undertaken as a service to the pharmaceutical industry, was titled "Advertising and the American Physician". Completed in 1953 by Ben Gaffin & Associates, it was made available as a series of twenty mailing pieces sent to pharmaceutical companies by the American Medical Association.

The earlier study emphasized, if it did not discover, the importance in physician education of pharmaceutical advertising and promotion to the medical profession. It revealed that physicians receive a large proportion of their postgraduate medical education from the advertising and detailing which are paid for by pharmaceutical companies.

The present study, through intensive investigation of the marketing of five new ethical pharmaceutical products in a single market, attempts further to help pharmaceutical companies develop more efficient methods of promoting their products.

Is Distribution Still Too Costly?

The 1939 Twentieth Century Fund study titled "Does Distribution Cost Too Much?" indicated that distribution cost paid by drug manufacturers was the highest of any class of products and that three-fourths or more of the retail price of a drug was going for costs and profits in the various stages of distribution.

If one asks today, "Does pharmaceutical advertising still cost too much?", the answer must be that any unnecessary cost, any waste of money spent for promotion and distribution of pharmaceutical products is "too much". What part of the $130,000,000 spent on medical advertising this year will be wasted is another question, but it must run into 8 figures.

The American Medical Association, as the most important single influence in the field of medicine, is recognizing its leadership responsibilities to the public, to the physician and to the pharmaceutical industry in sponsoring this series of basic marketing research studies. By helping the pharmaceutical industry do a more effective promotion job at decreasing costs, it helps make the promotional efforts more useful to the physician with less waste of his time and it helps the public obtain better drugs at lower cost.

Pharmaceutical Marketing Research

Marketing and opinion research is a new field, which the pharmaceutical industry is just beginning to discover. Yet, although this industry has been somewhat slower than some other industries to discover its value and uses, there is every indication that the pharmaceutical industry is now learning more at a faster rate about the real possibilities of marketing research than other industries which have been using it for twenty years or more.

Yet, the pharmaceutical industry is spending only tenths of mils for marketing research compared with thousands of dollars for laboratory and clinical research.

> The pharmaceutical industry has recognized the importance and need for product research as no other industry has. It annually plows back into the development of new products a greater percentage of its earnings than does any other industry.
>
> As the pharmaceutical industry learns more about the benefits of marketing research, this great discrepancy in allocation of research funds will be adjusted. Efficient marketing will be granted more importance than before in the industry's total contribution.

Sound Research Philosophy

The pharmaceutical industry is entering into market and opinion research at a sufficiently advanced stage that it can avoid some of the pseudo-scientific fads and escape some of the faulty generalizations of fledgling research efforts. The Fond du Lac Study can help the industry develop a sound philosophy of market and opinion research.

> The cornerstone of this philosophy is the appreciation of the individual and the recognition that all markets are people.
>
> The Fond du Lac Study shows that there is no such person as an "average doctor". The industry will see that its promotional efforts are not directed at "the American physician" but to all or part of the 160,000 individual human beings who are also physicians. Any categorization of these individuals is made solely for the convenience of people who have to deal with them. Although such categories may be useful, it must be remembered that they are basically arbitrary — the 160,000 individuals and not the categories are the reality.
>
> In studying man, it is either convenient or fashionable sometimes to view him through the eyes of the psychologist; sometimes through the eyes of the economist; sometimes through the eyes of the sociologist; the anthropologist; and the historian. We can and sometimes we have to use the tools of the various sciences, but we should not make the mistake of confusing what is only the man made categories of the specific social science with the actual persons.

Doctors Are Individual People

Each one of the 160,000 physicians in the U.S. is first and foremost an individual human being.

> He starts in life with a physical make-up including glandular structure, which gives him a certain temperament and predispositions which are the heritage of his ancestors. He grows up in an individual family environment where he is exposed to certain cultural, social, psychological, educational and other influences which mold his views and attitudes and behavior patterns, and to some extent modify the organic structure through which he acts. After receiving a basic education in his local environment, he is exposed for several years to the study of the basic sciences, and then for several more years to clinical studies. After a year or more of apprenticeship, he begins to have other human beings come to him for treatment for physical or emotional difficulties.
>
> After he finishes his medical school, he seldom or never gets any additional formal education. Most of the new ideas which he gets come from reading, from formal or informal discussions with other doctors, from printed advertising to which he is exposed, and to a large extent, from detail men from various pharmaceutical firms with whom he talks for a few minutes nearly every day.
>
> As a human being, he is comparatively quick or comparatively slow; he is comparatively hard-working or he is comparatively lazy; he is friendly or crabby; social or solitary; happy or unhappy. His morning contacts with his wife and children affect in a greater or lesser degree his attitude toward patients, toward co-workers, and toward detail men. His basic temperament, modified by his daily interpersonal relations, influence all his actions and attitudes to some extent.
>
> His human-beingness is modified by his being a physician. As a physician, both society and he himself set up some principles of belief and behavior which tend in certain respects to make him more like other physicians than like other groups who have different basic interests and approaches to life.

Safe Generalizations

We can safely make a number of generalizations about all human beings as human beings, including that they are social animals who are happiest when they have the respect and affection of the people around them.

We can safely make some generalizations about the 160,000 human beings who are the practicing physicians in the U. S.: that as physicians, they tend to be idealistic, and that taken as a group they tend more to be motivated by helping mankind than do other groups, such as, used car dealers.

We can make further, more specific generalizations about physicians on the basis of types of practice; For example, that the internist usually tends to be more of a student and to be somewhat more motivated by scientific proof than is the dispensing general practitioner.

We must always remember, however, that these are generalizations which we have made only for our own convenience, that the individual physician is the ultimate reality, and that we must make our generalizations fit the individual and not vice versa.

Appreciation

We wish to acknowledge the very generous cooperation which we received from nearly everyone we approached. We are especially grateful to the Ciba, Eaton, Geigy, Lederle and Upjohn managements and detail men, who furnished information requiring considerable of their time and efforts. We also thank the people in other pharmaceutical companies whose comments and counsel helped in the development of the study.

> Incidentally, we learned in the course of our research that there are no secrets in pharmaceutical marketing. Any firm or individual who is willing to go to the time and expense of collecting it can get nearly any information about any pharmaceutical company or the marketing of any existing pharmaceutical product. We, of course, included products only of companies that were willing to cooperate in the study.

We thank the officers and members of the Pharmaceutical Advertising Club of New York who gave counsel and took a continuing interest in the study. Most of all, we want to thank the physicians and pharmacists of Fond du Lac, Wisconsin, who were so hospitable in giving of their time and help in the interviews. We also thank the interviewers who worked with us on completing the background and depth interviews with the physicians and pharmacists, and the men from the University of Wisconsin School of Pharmacy who made the prescription audits.

Finally, we hope that this report will satisfactorily repay the American Medical Association for its financing of the Fond du Lac Study. We appreciate the patience of its executive staff in allowing us the time in which to develop a thorough report.

Ben H. Gaffin
Ben Gaffin & Associates, Inc.
Chicago, Illinois
May 15, 1956

SECTION I. INTRODUCTION TO THE FOND DU LAC STUDY

CHAPTER 1. OBJECTIVES

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> "If this study reveals a tenth of what we have reasonable hopes of learning, it will enable the American Medical Association to perform a service for the industry of such magnitude that the industry will be very mindful of AMA publications when setting up advertising media allocations."

Eight Approaches

The proposal then recommended developing a series of separate drug case studies, with the marketing of each product studied from eight separate approaches:

(1) the marketer and the program which he developed for the drug

(2) the detail man and what he did in the specific market

(3) the sales audit to enable us to trace prescriptions to specific individual physicians

(4) the pharmacist, and his comments, criticisms and suggestions on the product marketing

(5) the influence of the hospital on the marketing of the products

(6) the influence of the local medical society on the marketing of the product

(7) the influence of the clinics on the marketing of the product

(8) the influences acting on the physician: "Intensive interviews with the physician — possibly a series of interviews will be required — will uncover in as much depth as possible the various factors which have influenced the physician in his personal use and prescribing of the products. Among these influences will be the formal ones — the detail man, direct mail advertising and journal advertising. There will also be the informal influences — word of mouth comments of other physicians, hospital staff meetings, etc."

The Objectives As We See Them Now

In retrospect, now that the Fond du Lac Study is completed, we feel that we have more than accomplished the original study objectives. It has been the most complex study we have undertaken, both because of the ambitiousness of our goals and because of the tremendous amount of data of all kinds which we accumulated, which have required months of study.

> We would now add the following objectives to the list of those we contemplated originally. To describe the marketing of new pharmaceutical products from two points of view — from the viewpoint of the new product and from the viewpoint of the market. To determine as far as possible why and how the reception given different types of pharmaceutical products differs so widely. To analyze why a certain few doctors account for the bulk of the prescriptions for one drug and another group for the bulk of prescriptions for another drug.

> To bring the findings together for a final objective we would seek the general principles that might be applied to the marketing of other new drugs — even to the development of a formula to be used as an advance check list for scientific marketing.

In the following sections of the report it will be seen that the Fond du Lac Study furnishes a basis for advancing knowledge along the lines of all the objectives we have mentioned. We would be the last to say that this one study contains all the answers, or even a single final answer for any one objective, but it does give better understanding of all of them and underscores what, once stated, may appear to be some self-evident truths.

CHAPTER 2. METHODS AND PROCEDURES

The Fond du Lac Study was authorized the end of September 1954. Between the authorization of the study and our talk on the study to the Pharmaceutical Advertising Club of New York in April 1955 the following study steps were completed:

Selection of the Marketing Area

It was decided that the marketing area would have to be located in the Middle West, since each of the other geographical areas seem to possess stronger regional characteristics. Several dozen potential markets were considered and discarded because of various factors which would have made the completion of the field work more difficult or impossible.

Wisconsin was recommended by Dr. Frank Dickinson of the AMA on the basis that it has one of the best state medical statistical reporting offices in the country. Mr. Earl Thayer, the Public Information Director of the Wisconsin State Medical Society, discussed possibilities for selection and finally concluded that the Fond du Lac area was the best one for our purposes, since it is reasonably close to the U. S. average in terms of population per active physician (U. S. 958, Oshkosh, Appleton, Fond du Lac, Primary Center, 1180) hospital beds per thousand population, proportions of various specialties of physicians, mixture of agricultural and industrial employment, and lack of predominating nationality extractions. The fact that this community is insulated from strong university influence, though not isolated; the fact that nearly all of the doctors in the area are on the staff of the same hospital, belong to the same county medical society, and in general are exposed to the same influences to a much more equal degree than in other markets that were considered — all of these factors led to choice of Fond du Lac.

Preliminary Investigation of the Fond du Lac Market

A preliminary investigation of the marketing area was made, statistics were gathered on the composition of the market and interviews were made with each of the 14 pharmacies in the area, all but one of which agreed to cooperate on the study. We learned from other sources that this one exception accounted for probably fewer than ten prescriptions per month.

> The fact that the study director had lived in this test market was of considerable help both in understanding some of the influences which might not have otherwise been understood and in obtaining the cooperation of the large number of people without whose help the study would have been impossible.

Personal Discussions with Manufacturers

On the basis of our talks with the Fond du Lac pharmacists, we made a preliminary list of fourteen drugs in various fields of therapy which seemed suitable on a tentative basis. We then discussed the concept of the study, Fond du Lac as the tentative market in the study, the list of tentative drugs, and the willingness of the manufacturer to cooperate with fourteen advertising managers of pharmaceutical manufacturing firms. Mr. Richard L. Hull of Smith, Kline & French was very helpful on reviewing the tentative drug selections. As the result of these talks, final selection of the drugs to be studied was made.

Developing Study Plan and Procedures

Many people with whom we discussed the study during the following weeks made helpful suggestions regarding the study plan and procedures. Among these were Mr. Gerald L. Long and Mr. Spencer M. Fossell of the New York Pharmaceutical Advertising Club.

During March and April of 1955 we finalized the study plan and procedures. We decided first to interview each of the 55 physicians using a formal questionnaire which basically covered the same information as that in the 1953 national study on advertising and the American physician. This questionnaire was modified to include questions regarding the specific drugs to be studied.

We planned also to audit prescriptions in all Fond du Lac pharmacies to end up with a separate IBM card for each prescription on the five drugs we were studying and the principle competitive drugs in each of these groups. By this method we could analyze not only the total sales figures for each drug but also by individual physicians and we could study practices of individual physicians regarding the drugs separately and in relation to each other.

Armed with the background information on each physician, and with a table showing what prescriptions the physician wrote during the audit period, we would then go back to the physician for an informal discussion interview during which we would probe into the factors which led him to do what he did.

> In April 1955 we outlined the final study plans in a talk to the New York Pharmaceutical Advertising Club.

Physician Background Interviews

The physician background interviews were completed during May 1955.

> The questions asked in the background interviews are reproduced below. The booklet referred to in the questions was merely a convenient method of placing the lists of advertising media, drugs, medical journals, and pharmaceutical company house organs, in front of the physician for his consideration.

Physician Background Interview

1. There are so many new drugs being developed today that it is hard for a physician to keep current. Which one of the methods listed on the front page of this booklet do you find most important to you personally in learning about new drugs?

ADVERTISING IN MEDICAL JOURNALS	NATIONAL MEDICAL CONVENTIONS
COUNTY MEDICAL MEETINGS	PAPERS OR ARTICLES IN JOURNALS
DETAIL MEN	STAFF MEETINGS AT HOSPITAL
DIRECT MAIL FROM DRUG FIRMS	OTHER

2. If you will turn to the second page of that booklet, you will find a list of drugs. Which ones of them have you prescribed?

FURADANTIN ACHROMYCIN PAMINE SERPASIL BUTAZOLADIN

3. Since they are all fairly new drugs, can you tell me what month you first prescribed them?

4. Where did you happen to get the information about _____ which led you to prescribe it? Anywhere else?

5. As you remember it, which of the five drugs have never been discussed with you by detail men?

6. Which of the six drugs have you ever received as samples?

7. Other than the samples you receive, do you ever dispense drugs yourself instead of writing a druggist's prescription?

8. (IF "YES"): Which, if any, of those five drugs have you dispensed yourself?

9. In writing a prescription, how do you usually designate it — by trade-name, name of manufacturer, or how?

10. About how many prescriptions did you happen to write in the last 7 days?

Besides the medical profession's efforts, medical manufacturers spend about 160 million dollars every year to inform physicians about new developments. By answering the following questions as accurately as possible, you can help have this money spent in ways that will do physicians the most good.

11. Of the four sources of information from manufacturers, which one do you find most worthwhile for learning about new products — medical journal advertising, company periodicals, detailing or direct mail?

12. Which do you consider least worthwhile to you personally?

Now I'm going to ask some questions about your reading of medical journals and publications. We realize you have little or no time for reading, and that it is probably interrupted. But even if it is hard for you to do, please try to answer these questions as accurately and as completely as possible, because we are going to project these figures.

13. On the third page of the booklet there is a list of 15 medical publications. Which of these do you happen to receive?

AMERICAN JOURNAL OF MEDICAL SCIENCE
AMERICAN JOURNAL OF SURGERY
AMERICAN JOURNAL OF OBSTETRICS & GYNECOLOGY
ANNALS OF INTERNAL MEDICINE
ANNALS OF SURGERY

ARCHIVES OF INTERNAL MEDICINE
CURRENT MEDICAL DIGEST
G. P.
JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION
MEDICAL ECONOMICS

MODERN MEDICINE
MEDICAL TIMES
PEDIATRICS
SURGERY, GYNECOLOGY & OBSTETRICS
SURGICAL CLINICS OF NORTH AMERICA

14. Which of these publications on the list have you happened to read or look through during the last 30 days?

15. From the point of view of usefulness in your everyday practice, which one of these publications on the list do you consider most valuable to you personally?

16. Which publication do you feel most duty-bound to read?

17. Which publication do you enjoy reading the most?

18. You no doubt know that the AMA has discontinued its Council Seal of Acceptance. Do you think they should have dropped the Council Seal, or not?

19. Why do you say that?

20. Do you happen to read the Journal of the American Medical Association regularly -- that is, at least half the issues?

21. Have you noticed any changes in the AMA JOURNAL in the last three or four years?

22, 23. (IF "YES"): Were there any changes you especially liked? Which ones?

24, 25. Were there any changes you didn't like? Which ones?

Another method many drug firms use to inform physicians about their products are company periodicals, also called "house organs".

26. On the fourth page of the booklet is a list of eleven company periodicals put out by leading drug firms. Which of these do you happen to receive?

Abbott Laboratories — WHAT'S NEW
Hoffman LaRoche — THERAPIA
Lederle — BULLETIN
Eli Lilly — PHYSICIANS BULLETIN

Merck — MERCK REPORT
Parke Davis — THERAPEUTIC NOTES
Pfizer — SPECTRUM
Sharpe & Dohme — SEMINAR

Schering — MEDICINE IN THE NEWS
Upjohn — SCOPE
Ciba — SYMPOSIA

27. Which of these do you usually read or look through?

28. What company do you think usually does the best job on its periodical?

Now for a few questions on direct mail medical advertising.

29. About how many pieces of medical direct mail advertising (other than periodicals) have you received during the last 7 days — as close an estimate as possible?

30. Of these, about how many pieces have you read or looked at during the last 7 days?

31. Who usually decides which pieces you will read — do you look them over yourself, or does your girl weed them out first?

32. On what basis are they weeded out — by company, type of product, sample, appearance, or how?

33. What company do you think usually does the best job on its direct mail?

The last method, though the most expensive, which medical manufacturers use to maintain contact with physicians is the detail man.

34. Do you usually see all detail men that call on you, or do you make it a practice to see only some, or none of them?

35. On what basis do you select those you see?

36. About how many detail men have you seen during the last seven days?

37. What company do you think usually does the best job of detailing?

Now a few questions on professional meetings.

38. Did you attend the AMA meeting in San Francisco last June?

39. Did you attend the AMA meeting in Miami last December?

40. Do you plan to attend the AMA meeting in Atlantic City in June?

41. How many state medical conventions have you attended in the last twelve months?

42. How many local or county medical society meetings would you say that you attended in the last twelve months?

43. Have you attended any special meetings with other doctors in the last twelve months? What organizations were they?

44. Please turn to the back page of the booklet and tell me which one of these categories best describes your present practice.

FULL-TIME GENERAL PRACTITIONER
FULL-TIME SPECIALIST
GENERAL PRACTITIONER WITH SPECIAL INTEREST
FULL-TIME EMPLOYEE OF COMMERCIAL FIRM
OTHER

45. What is your speciality?

EYE, EAR, NOSE & THROAT	PEDIATRICS
INTERNAL MEDICINE	SURGERY
OBSTETRICS & GYNECOLOGY	OTHER

46. Do you hold a certificate from the American Board in your speciality?

47. Are you affiliated with any hospital or clinic? Which ones?

48. Are you a member of the American Medical Association

49. How many years have you been practicing medicine?

50. And how many years have you been practicing in the Fond du Lac area?

51. What medical school did you attend?

52. Do you expect to be in Fond du Lac most of next month — June, that is, or are you planning your vacation then? When will you be away?

The Prescription Audits

We retained William S. Apple, Ph.D., Assistant professor of Pharmacy Administration, at the University of Wisconsin School of Pharmacy, to undertake the audits. He arranged to have two graduate pharmacists, Mr. David Sanders and Mr. Robert Hammel who were working on their doctorates in pharmacy administration to make the audits in the 13 pharmacies which were cooperating in the study. They made a selection of competitive drugs in each of the five fields of therapy and completed the audit as their contribution to the study.

The budget did not allow for doing an audit of the entire year's prescriptions; so that four single weeks equally spaced were covered: beginning May 9, 1954; September 12, 1954; January 9, 1955; and May 8, 1955.

The competitive drugs which were selected for inclusion in the audit are shown here under each of the five which we were studying:

Achromycin
- Aureomycin
- Chloromycetin
- Ilotycin
- Terramycin
- Tetracyn

Butazolidin
- Pabalate
- Pabirin
- Sodium Salicylate
- Sodium Free Pabalate

Furadantin
- Mandalomine
- Pyridium
- Serenium
- Sulamyd
- Thiosulfil

Pamine
- Pamine with Phenobarbital
- Antrenyl
- Banthine
- Banthine with Phenobarbital
- Co-Elorine
- Prantal
- Pro-Banthine
- Pro-Banthine with Phenobarbital

Serpasil
- Raudixin
- Raused
- Rauniloid
- Reserpoid
- Serpasil with Apresoline
- Thorazine

We have since learned that some of the above drugs are not comparable and that some others should probably have been included.

For the purpose of the audit, IBM marking sensing cards were used for later punching and tabulating. The audit was made during June 1955.

Informal Interviews with Physicians and Pharmacists

The informal interviews with physicians and pharmacists were completed the last of June and the first two weeks of July 1955 by Mr. William Chappell, research director of Abbott Laboratories, who was interested in observing our methods, and three Ben Gaffin & Associates staff members, Messrs. John Flaherty, Hal Mitchell and Ben Gaffin.

Prior to each interview, the interviewer reviewed the background questionnaire and the prescription audit tabulation report for the physician whom he was going to interview.

To insure comparability of these interviews, a 13-point topic list was developed which each interviewer carried and referred to during the course of the interview. As an experiment, most of the interviews were tape recorded, with the permission and prior knowledge of the physician. These interviews, some of which wandered far afield, were later thoroughly edited in our office and transcribed according to an interview analysis outline. The topic list follows:

TOPIC LIST FOR INFORMAL INTERVIEW

1. Attitudes toward the company.
2. Attitudes toward the product.
3. Does he prescribe it? Exclusively or with competitive product.
4. What does he prescribe it for?
5. When does he first remember hearing about it? Where?
6. What was the direct occasion for his starting to prescribe it?
7. What other impressions were made?
   1. Detail men (Who?)
   2. Direct mail (What kind?)
   3. Ads in Medical Journal (Which?)
   4. Sampling
8. Professional impressions
   1. Papers in journals (Which?)
   2. Medical meetings (Which?)
   3. Hospital staff meetings (What?)
   4. Other Doctors (Who, when, where, what?)
   5. His clinic influence
   6. The druggist influence
   7. The hospital influence
   8. The local medical society
9. Where did he learn dosage, uses, etc?
10. What experiences has he had with the drug?
11. Does he still use the drug?
12. Does he expect to continue? What is his present attitude?

SUMMARY

13. Is there any particular way he prefers to learn about new products? (Why?)

Pharmaceutical Manufacturer Interviews

While the physician interviews were being completed, we developed and sent out a questionnaire to each of the manufacturers who had agreed to cooperate with us on the product study: Ciba, Eaton, Geigy, Lederle, Upjohn. The questions, which covered the manufacturer's marketing program for the drug, follow:

Manufacturer's Questionnaire

The American Medical Association, as a contribution to pharmaceutical marketing, is financing this study of the marketing of five non-competitive ethical drug products. Essentially, it is a study of how physicians learn about new products, and what leads them to start prescribing them.

The information you furnish here will be held in strict confidence. You will have an opportunity to approve or disapprove the publication of any of this information before it will be released.

If we can get complete information on cost figures, it will make the study more worthwhile, both for you people and for the industry. Where the management chooses not to release this information to us, we shall have to use estimates of what the figures are.

We sincerely believe that you will be helping your own company, as well as the industry as a whole, by cooperating fully. We, on the other hand, will cooperate with you by not revealing anything which might injure your company or its interests.

1. (a) Was this a product of your company's own research, or was it obtained by licensing, purchase, or how?

   (b) How long a time lapsed from the time you first began working on the idea of this product until you started full-scale marketing?

   (c) Did you do any marketing research on it -- test markets, sample surveys, etc.? (Please describe)

   (d) When did you first market the product?

   (e) When did you begin national distribution?

2. Approximately how much do you figure it cost your company to bring the product to the point of marketing it?

3. (a) What did you consider as the main use (s) for the product at the time you first introduced it to the market?

   (b) Was this original concept of its uses modified later? (if "Yes") In what way? How did this happen?

4. What was the overall marketing and promotion program you followed in introducing the product to the market?

   (a) Preliminary sampling or testing -- what, when and estimated cost.

   (b) Exhibits at medical meetings -- what, when and estimated cost.

   (c) Detailing -- what, when and estimated cost.

   (d) Direct mail -- what, when and estimated cost. (Please furnish copies of representative ads)

   (e) Medical journal ads -- what, when and estimated cost. (Please furnish copies of representative ads)

   (f) Other -- what, when and estimated cost.

5. What information, favorable or unfavorable, about the product went to physicians through the national professional channels, to your knowledge:

   (a) Papers or articles in journals -- how many? (Please furnish examples or bibliography, if possible)

   (b) Papers or articles at medical meetings -- how many? (Please furnish examples or bibliography, if possible)

   (c) Other -- what, when? (Furnish any materials possible)

6. (a) In the Fond du Lac, Wisconsin marketing area (Fond du Lac and Chilton), what detail man or men have detailed this product? (names, addresses and phone numbers).

(b) Would you have any objection to our interviewing this man (these men) on exactly what he (they) did, and when?

7. Our study plan calls for studying the local professional influences, and then informal interviews with each of the 40-some physicians in the Fond du Lac-Chilton area and with the 12 pharmacists there. We will do our best to learn which of the influences directed at the physician and pharmacist concerning your product registered, and which were the major and contributory influences in getting him to prescribe your product (if he does prescribe it). We have started an audit on the sale of your product in the 12 pharmacies in this area, by physician, to learn the relative value of the results of the various influences.

Do you have any suggestions or criticisms which may help to make this study of greater value to you and the industry? If so, what?

Detail Men Interviews

Each of the cooperating pharmaceutical manufacturers furnished us names of the detail man or men who detailed its product under study in the Fond du Lac area from the time the product was first introduced to May of 1955.

We wrote each detail man enclosing an interview outline as well as a list of physicians and pharmacies in the Fond du Lac area to refresh his memory.

At our request, these men telephoned us instead of mailing their replies. These interviews, which lasted from 30 minutes to 2½ hours, were recorded and were later analyzed and typed in convenient form.

These telephone interviews were made the last of July and the first of August 1955.

The questions which we sent to the detail men for discussion over the telephone were as follows:

Detail Man Interview Outline

We are interested in gathering as much factual data as possible about your activities regarding the marketing of the drug _____ in the Fond du Lac area. Your answers, as accurately as you can estimate them, will prove of value to the AMA, the physicians, your company and ultimately to you. All questions refer only to efforts made in the Fond du Lac area.

1. How did your company introduce the product to the Fond du Lac physicians and druggists?

2. When did you begin to detail this drug? Year _____ Month _____?

3. Was much direct mailing done by your company regarding this drug before you began detailing it? After you began detailing it?

4. Approximately how many hours did you spend familiarizing yourself with the drug before you began detailing it in Fond du Lac?

5. Which of the physicians and pharmacies on the attached list did you call on and detail about this drug?

6. On the average, how much time did you spend detailing this drug with the physicians? The druggists?

7. While you were promoting this drug, what proportion of your total working time in the Fond du Lac area do you estimate you used doing so?

8. Did the physicians appear to be familiar with the product prior to your detailing them? Was this also true of the druggists?

9. Was there advertising in the J. of the AMA or the Current Medical Digest that you felt was particularly effective in informing the physicians of this new drug?

10. When did you call on first, the doctors or the druggists, when you began detailing this drug?

11. Did you leave samples with the doctors; the druggists? If so, approximately how much?

12. Do you usually detail more than one drug during your visits with physicians; with druggists?

13. In the promotion of this new drug, how would you rank the effectiveness of:

_____ Direct mail advertising
_____ Journal advertising
_____ Reprints of professional articles regarding the drug
_____ Samples

Basically, the above information is the sort that we are seeking but other questions will, of course, arise as we talk to you. We will be most appreciative of any information that you can pass on to us that will supplement the above and improve our knowledge of how you promoted this new drug.

Tabulating the Audit Materials and Background Interviews

This concluded the field work on the Fond du Lac Study. We now had on a national scale the reports on how the manufacturer set up the marketing program and carried it out for each of the five drugs.

From the detail man, we had the story of the localized product promotion.

For each of the 55 physicians we had the background interview, the prescription audit tabulation sheet which showed the number of prescriptions and the total cost for each prescription he wrote on each of 33 drugs during each of the 4-week periods. Additionally, for all but a few physicians, we had the extensive informal interview containing greater details on how he happened to start prescribing those of the drugs under study which he prescribed; his attitudes and mental images of the drug firms; as well as his personal evaluations of the various channels of marketing communication and other comments.

Finally, we had the early, informal interviews with most of the pharmacists, covering nearly the same material as that covered in the informal interview with the physicians.

Analysis of Data and Final Report

In the months between September 1955 and May 1956 we have worked over the data, resisting the increasing pressures to get the study completed in favor of developing a report of maximum value to the AMA, the cooperating manufacturers, and the pharmaceutical industry.

In January of this year, Robert Lyon of the AMA gave a speech to the Pharmaceutical Advertising Club of New York on the basis of our then uncompleted analysis. Dr. Merle Crawford of Mead, Johnson & Company, spoke to the Midwest Pharmaceutical Manufacturers' Association in February 1956 from the same incomplete materials. We assume the responsibility for any incorrect interpretation of the meaning of the study conveyed by those preliminary talks.

We believe that this, the official report, will correct any former misconceptions of the Fond du Lac Study.

CHAPTER 3. WHAT THE STUDY MEANS

We believe that the Fond du Lac Study is a pioneering study in several ways: in subject matter, in methodology, in intensity, and in conclusions.

> It is one of the first studies attempting to get at how to improve marketing communication with physicians.
>
> It combines a number of innovations in method, starting with the promotion program of the manufacturer and following the prescription audit with interpretive personal interviews of the prescribers.
>
> It investigates the Fond du Lac medical community most thoroughly, using every technique that would conceivably add to understanding.
>
> It contains conclusions of far reaching importance, and the five principles which it offers as an approach to a science of pharmaceutical marketing can have marked influence upon pharmaceutical advertising and promotion.

Not A Sample Survey

The Fond du Lac Study is not a sample survey. It is a complete study of a single marketing area — including every physician, the only hospital, the detail men for the products studied, every pharmacy (but one), and every prescription of certain ethical drugs filled there during four full-week periods.

> We have taken a microcosm and placed it under the microscope, as it were, to see how it works. From looking at it first one way and then another we have learned a great deal that we could not have hoped to learn through the typical, large-scale, national study.

Not Necessarily Projectible

The findings on the five drug in the Fond du Lac area are not necessarily projectible to the national market. They are the facts in Fond du Lac; they may prove to be true nationally; but we would neither operate on that assumption nor advise others to do so. As far as the national market is concerned the Fond du Lac Study provides hypotheses for further testing.

> For example, we would urge the executives at Ciba not to assume that three-quarter of their Serpasil sales come from internists nationally, just because that was the case in Fond du Lac. We suspect that Serpasil is predominantly an internists' drug but, until verified, our suspicion is only a theory. The same reservation must be held for the other specific findings in the Fond du Lac market.
>
> We hope in future studies to be able to test whether the hypotheses hold true on a national basis and to what extent they need to be modified to fit the larger market.

But The Principles Are True

We should emphasize that, while the specific facts reported for Fond du Lac are not necessarily true elsewhere, the principles derived from the Fond du Lac Study are universally true and universally applicable.

> The five principles of scientific pharmaceutical marketing which we define are true. They may not be complete and they may some day be restated to have more meaning, but as general principles they are true.
>
> Any manufacturer who approaches the marketing of a new product according to the steps outlined in Section VI — if he carries out these steps intelligently and thoroughly — is certain to develop a more efficient, more effective and more scientific marketing program.

Not The Last Word

We by no means believe that the Fond du Lac Study is the last word. It is a pioneering study that makes a beginning and points the way for future work.

> We recognize the ambitiousness of a program of learning how to predict and control human behavior. We offer these findings with humility and ask that the shortcomings be weighed against the possible contribution to the development of further research and to the future of scientific pharmaceutical marketing.

SECTION II. DESCRIPTION OF THE FOND DU LAC MARKET

CHAPTER 1. FOND DU LAC AS A CONSUMER MARKET AND MEDICAL SERVICE AREA

The area included in this study comprises Fond du Lac, Wisconsin, the five satellite towns of Chilton, Mount Calvary, Brownsville, Rosendale and Theresa, and the open country intervening. The area is roughly an oval, with the city of Fond du Lac at the center, measuring about 40 miles from Chilton to Theresa and about 28 miles from Rosendale to the eastern boundary. It includes the greater part of Fond du Lac County and touches upon Calumet, Dodge and Sheboygan counties.

The nearest city of any size is Oshkosh, 16 miles away. Milwaukee is 60 miles southeast, Green Bay 60 miles northeast, and Madison 70 miles southwest.

Population Characteristics

The population of the area is approximately 60,000 inhabitants, of whom about half live in the city of Fond du Lac.

Population per square mile is about 80 persons, compared with the United States average of 51 and the Wisconsin average of 61.

Probably somewhat more than half of the people are of German extraction, although there also are strong Irish, French and other nationality backgrounds — all of which are in process of commingling through intermarriage.

The two major religious denominations in the area are Catholic and Lutheran, with sizeable representations of Episcopalian and Evangelical groups.

Employment in the area is about one-half in business and trade, a quarter in manufacturing and a quarter in farming.

Fond du Lac is in the heart of the Wisconsin dairy country and is a major dairy center. Its largest single manufacturer is Giddings and Lewis, which employs 2,500 people in the manufacture of machine tools.

Other General Features

The Fond du Lac (Foot of the Lake) area encloses the southern half of Lake Winnebago, the largest inland body of fresh water lying within one state.

Lake Winnebago and other smaller lakes nearby provide facilities for boating and fishing. Summer cottages abound. The several golf clubs are popular places for meals and drinks. Both duck and deer hunting are popular with the residents.

The city has excellent public and parochial (Catholic and Lutheran) school systems. It has several private schools and a junior college, which is Catholic operated.

The area is served by an evening newspaper, the Fond du Lac Commonwealth Reporter. The Milwaukee Journal and the Chicago Tribune are the chief Sunday newspapers and compete as dailies with the local paper. The local radio station is KFIZ.

Railroads serving the area are the North Western, the Milwaukee and the Soo lines.

St. Agnes Hospital

All but four of the physicians within the Fond du Lac area are on the staff of St. Agnes Hospital in Fond du Lac.

St. Agnes Hospital originally was an Episcopalian hospital but is now operated by the Sisters of St. Agnes, a small order of Catholic nuns whose mother house in in Fond du Lac.

The hospital has 400 beds, of which 100 have been added in the last two or three years. It has its own pharmacy administered by a nun who is a registered pharmacist.

Also in the area are the Fond du Lac County Hospital, a mental institution, and the Wisconsin Home for Women, a State prison, neither of which has a resident physician.

Clinics

The area has seven clinics, with which about two-thirds of the doctors are affiliated.

The Fond du Lac Clinic, with 12 affiliated physicians, is the largest. The next largest clinic has 7 members, while at the other extreme two clinics have but two members each.

55 Physicians

When the field work was in process, a total of 55 physicians were practicing in the Fond du Lac area. Eleven doctors, all of them general practitioners, lived in the five satellite towns while the other 44, including all of the specialists and general practitioners with special interest, had their practices in the city of Fond du Lac.

An essential part of the study is the individualness of the physician but, since it was understood that doctors would not be identified by name, descriptive code letters have been assigned to them by type of practice:

21 general practitioners	G.P.A. — G.P.U.
11 general practitioners with special interest (part-time specialists)	
4 with special interest in obstetrics and gynecology	P.T.A. — P.T.D.
5 with special interest in surgery	P.T.E. — P.T.I.
2 with special interest in: anesthesiology, gynecology and urology	P.T.J. — P.T.K.
21 specialists	
3 internists	Int. A. — Int. C.
6 ophthalmologists and eye, ear, nose and throat specialists	Eye A. — Eye F.
6 surgeons and orthopedic surgeons	Surg. A. — Surg. F.
6 other specialists: anesthesiology, obstetrics and gynecology, pathology, pediatrics, radiology, and urology	Spec. A. — Spec. F.
2 former surgeons now in general office practice	G.O.P. A. — G. O.P. B.

As is true nationally, about half of the specialists and general practitioners with special interest here have certificates from the American Boards.

Eight retired doctors also reside in the area but are not included in the study.

13 Pharmacies

The Fond du Lac area has a total of 13 pharmacies currently licensed. Nine of these are public pharmacies in the city of Fond du Lac, one is an exclusive pharmaceutical outlet run in conjunction with a clinic, two are pharmacy-general merchandise stores in Chilton, and the other is the St. Agnes Hospital Pharmacy, which fills prescriptions only for bed patients in the hospital.

Two other pharmacies in smaller towns let their licenses lapse several years ago because the nearby physicians dispensed all their own prescriptions. At the time of the study, 10 doctors reported that they dispensed drugs regularly, 6 admitted occasional dispensing, and the rest stated that other than samples they did no dispensing.

Three Fond du Lac pharmacies fill two-thirds of all the prescriptions filled in the area.

Following are our estimates of average weekly numbers of original prescriptions filled, based on the four weeks of our audits:

Pharmacy code	Original prescriptions per week
Total, all pharmacies	1745
1	720
2	235
3	210
4	140
5	110
6	100
7	60
8	50
9	40
10	30
11	25
12	15
13	10

Retail Sales

The approximately 20,000 households in the Fond du Lac area account for almost $75,000,000 in retail sales a year — about $3600 a household, or $1100 per capita.

Thus, Fond du Lac people spend somewhat more at retail than the average for the country as a whole and a little more than the average for Wisconsin. Compared with $3600 a household in the Fond du Lac area, the national average is about $3100 and the State average is about $3300. Compared with the local $1100 per capita the national average is about $960 and the State average is about $1000.

Drug Store Sales

Drug stores in the fond du Lac area do an annual business totaling about $2,250,000. This amounts to about $110 a household or about $35 a person.

National drug store sales average out to about $97 a household and $30 a person, while the corresponding figures for Wisconsin are about $87 and $27.

(The above figures are rough estimates for 1950 based upon information obtained from "Consumer Markets", a Standard Rate and Data Service publication)

Prescription Sales

Since Drug Topics estimates that a little over 21 per cent of all drug store sales are prescriptions, it would appear that prescription sales in the Fond du Lac area amount to something like $475,000 a year.

This amounts to approximately $24 a household and $7 a person.

If the average prescription price in Fond du Lac is the same as the national average of $2.33, as reported in Drug Trade News, then approximately 200,000 prescriptions are newly written — refills accounting for a large share of the total sales.

CHAPTER 2. HOW FOND DU LAC PHYSICIANS KEEP CURRENT ON NEW DRUGS

Physicians in the Fond du Lac area appear to have as wide a variety of information sources about new pharmaceutical products as doctors elsewhere across the country have.

Furthermore, they show as much individuality in choosing among the available sources as other doctors do.

In the background interviews we asked broad questions about which one source of new product information each physician considered to be most important to him, which one of the commercial sources he found to be most worthwhile and which one he considered to be least worthwhile to him personally.

In later chapters of this report we will report also what sources the doctors remember as having first acquainted them with each of the five drugs under study.

Most Important Information Source

Detail men and articles in medical journals are selected by the most physicians in the Fond du Lac area as their most important sources of information about new drugs.

These two sources are named by 20 and 19 doctors each; and no other source is credited as being most important by more than four doctors:

"Which do you find most important to you personally in learning about new drugs?"

Total doctors	55
Detail men	20
Papers or articles in journals	19
Advertising in medical journals	4
Direct mail from drug firms	4
National medical conventions	2
County medical meetings	2
Staff meetings	2
Reference books	1
Post graduate courses	1

The above list is as varied as that found in our national survey in 1953, but by no means exhausts all the possible ways in which doctors learn of new products. The sources which doctors think of as being generally most important are not necessarily the ones through which they learn of every new drug. For example, recommendations of other doctors are often recalled when a doctor reconstructs the history of his use of a particular drug, and one physician credits a pharmacist for telling him of Serpasil.

Most Worthwhile Commercial Source

Because many of the sources by which physicians learn of new pharmaceutical products are not under control of the pharmaceutical company, it is desirable to ask the physician to evaluate the commercial sources of information separately.

When the discussion is confined to the commercial sources, detailing is reported to be most worthwhile by about twice as many doctors as name all other methods combined. Every one of the media has the support of at least five physicians, however.

"Of the four sources of information from manufacturers, which one do you find most worthwhile for learning about new products?"

Total doctors	55
Detailing	31
Company periodicals	7
Medical journal advertising	5
Direct mail	5
No choice	7

Conversely, direct mail is reported to be least worthwhile by more than half of the physicians in the area.

"Which do you consider least worthwhile to you personally?"

Total doctors	55
Direct mail	30
Medical journal advertising	16
Detailing	5
Company periodicals	1
No choice	3

Detailing as an Advertising Medium

The large majority of physicians in the Fond du Lac area, 39 of the 55 (or 71%) see all detail men who call on them.

Only two of the doctors say that they refuse to see any detail men and the other 14 are more or less selective about which ones they grant an audience — most often deciding on the basis of the company represented. The 1953 survey found almost the same situation among physicians nationally, with 74% seeing all detail men.

Some doctors say that they are visited by as many as ten detail men a week, while others willing to see them have none call on them. The most typical number seen in one week is about three detail men.

"About how many detail men have you seen during the last seven days?"

Total doctors	55
None	6
One	3
Two	8
Three	16
Four	6
Five	9
Six or more	7

Five companies are each named by more than one Fond du Lac physician as usually doing "the best job of detailing": Eli Lilly, named by 9 doctors; Parke Davis, by 8; Abbott, by 5; Hoffman LaRoche, by 3; and Upjohn, by 3.

Comments about Detailing

In the informal interviews many of the doctors elaborated on their opinions about detailing and their attitudes toward detail men, making suggestions as well as criticisms.

Some of the most favorable comments are made by doctors G.P.C., G.P.S., P.T.B., P.T.F., P.T.G., and Eye E.

Dr. G.P.C.: "Detailing is of prime importance. I don't understand the attitude of doctors who push the detail man aside and refuse to listen to him. The detail man is an excellent source on indications and contra-indications, dosages and comparisons between products."

Dr. G.P.S.: "Good, fast detailing is the best means of communicating with us. It's the personal contact that counts. We don't have time to go through the professional literature, and the detail man can provide us everything we need. Of course, his word is likely to be biased and we resent his spending 25 or 30 minutes trying to detail on their entire line. Good detailing should take about 5 minutes and should be a fast summary."

Dr. P.T.B.: "I prefer to learn about new drugs that way. (detailing). The other media are too uncertain and leave it up to the doctor to sort it out. The detail man, on the other hand, is quite careful about what he tells the doctor because of possible repercussions later. Generally, they are quite considerate of my time and will sit outside until I can listen to them."

Dr. P.T.F.: "To me, detailing provides the quickest information with the least effort on my part. I rely on it wholeheartedly."

Dr. P.T.G.: "The detail man is the first contact, the really effective contact. Then, the direct mail and other sources add their little bit to keep me reminded that the product is available."

Dr. Eye E.: "The only means of contacting me is the detail man. I see a lot of them and try to listen to them all.

Most doctors seem to want fast detailing but an occasional one, like Dr. G.P.R., looks at it differently. —

Dr. G.P.R.: "I like to take plenty of time with the detail man so that we can cover the drug as thoroughly as possible. If two companies have comparable drugs out, I prescribe the one whose detail man I like best. This applies to large groups of drug products and it has developed a kind of mutual aid society between the detail man and me. I resent any pushing to get me to try a particular product."

Some doctors look to detailing to fill them in on products they have heard about elsewhere —

Internist B.: "When I hear about a new product, I question the detail man on his next trip."

Surgeon F.: "Once a doctor has become aware of the existence of a new drug, it is often the detail man who provides the final motivation which convinces the doctor he should give it a trial."

Dr. G.P.N., a dispenser: "Doctors should keep notes on questions and to show when their supply is low. Then when a detail man comes in, his time can be used more efficiently."

Some suggestions for detailing as given by a few physicians —

Internist C.: "The detail man should be careful of the authorities he quotes, and the technical literature he leaves should be scrupulously accurate."

Dr. P.T.E.: "If the detail men could lead me directly to outside sources in journals or articles, I might feel more kindly toward their efforts."

Dr. Eye A.: "I would like to see the literature and the detailing linked together. That is, it would be a good idea to have the literature on new products a week in advance of the detail man. That way I might have a chance to glance at it and then ask him specific questions."

Surgeon C.: "I can't always talk to the detail man but just ask him to leave literature on the product in question. Reprints of journal articles and definitely technical material would be a big help."

Fond du Lac area physicians differ among themselves as to the technical competency of the detail man. --

Dr. P.T.A.: "I think of the detail man not as a salesman but more as a friend and educator who can give out technical details."

Dr. G.P.H.: "I regard them as salesmen and not as technical experts. Only one of them around here has a pharmacy background and only one has had pre-med training."

Dr. P.T.H.: "They are primarily salesmen who are trying to push their products, and the stuff they present is primarily advertising and is biased."

Dr. P.T.J.: "If you want my reaction to that, it's this. I may not be scientific enough to go into a lot of details but I like a detail man who comes in and assumes that I know something about his product and that I haven't got a lot of time to waste with him. He will give me the high spots and literature, then get up and go. I don't like to listen to a lecture about drugs."

Dr. Eye A.: "Detail men are salesmen and they are just as good as their sales manager. They apparently do what he tells them to do. They aren't particularly technical and always just study the same literature which they give the doctor and give him a quick summary of it. That helps, because it gives the doctor an idea of generally what the product is. Then, if he wishes he can read up on it."

A most common feeling is that the detail man should not try to high pressure the doctor, as summed up here in this one quotation --

Dr. G.P.I.: "The doctor should not allow the detail man to practice medicine."

Sampling

Every one of the doctors in the Fond du Lac area had received samples of one or more of the five drugs in the study, and all are familiar of course, with the sample method of introducing new products.

No general questions were asked about sampling on the background questionnaire but the subject was discussed in the informal interviews with the doctors.

Attitudes toward sampling range from strong approval to strong disapproval, with certain pet peeves very evident —

Dr. Eye C.: "Samples are of great value in giving the product a real clinical test, provided the sample package is large enough for a trial. Two tablets of a product strike me as being particularly absurd."

Dr. G.P.D.: "Samples help in becoming familiar with a new product since they enable us to try them on our own to get a direct clinical impression. I do object to being deluged with samples of a wide variety in which I have no interest whatsoever — such as, vitamins."

Dr. G.P.B.: "Samples from the big houses we use, from the small ones we don't use."

Dr. P.T.G.: "They are a means of trying a new drug product so that if a patient develops an allergy or if the drug is not immediately effective, the patient is not paying for high cost products which are not going to work."

Dr. P.T.C.: "I set the samples on my desk and look at them for a few days until I am familiar with the trade name and the appearance of the bottle or package and know how to spell the name. The literature piles up and gets thrown out, but the sample is likely to stay a little longer."

Dr. P.T.A.: "Samples are a sort of handy thing to have. I give them out often where I know the patient will find it hard to pay for the prescription."

Surgeon C.: "My primary use of samples is for my own family."

Surgeon E.: "I refuse most samples. I prescribe on the basis of laboratory tests or because I believe the drug is the most effective one in the particular case. I would not utilize the samples if I had them."

Dr. G.P.J.: "I don't go much for samples, because I dispense some and it will get patients started on it and I will have to order it. Then I would have to have a regular drug store. I don't hand out any samples for that reason."

Medical Journal Reading

Most Fond du Lac physicians subscribe to more medical journals than they are able to read but each of them manages to look through at least one.

When shown a basic list of 15 of the more popular medical journals, the physicians reported that they receive an average of about 5 journals apiece and that they read or look through an average of three each.

"Which of these 15 medical publications do you happen to receive? Which have you happened to read or look through during the last thirty days?"

Total doctors	Received 55	Read or looked through 55
One journal	4	11
Two journals	1	11
Three journals	11	13
Four journals	8	8
Five journals	14	7
Six journals	6	3
Seven journals	7	1
Eight or more	4	1

The problem which the busy physician is confronted with in reading his journals is well stated by Dr. P.T.B., who receives 10 of the 15 journals and gets to read only three or four —

"I lay aside those with particular articles I want to read. Then they pile up in a stack until one day I close my eyes, pick up the stack of books and dump it out."

The most commonly received as well as the most often read medical publications in the Fond du Lac area are the Journal of the American Medical Association and Medical Economist.

Here are the top eight journals in number of mentions on both scores —

Total doctors	Received 55	Read or looked through 55
Journal of the A.M.A.	47	35
Medical Economics	47	35
Modern Medicine	39	22
Medical Times	24	10
Current Medical Digest	21	13
G. P.	19	17
Surgery, Gynecology and Obstetrics	14	10
Annals of Surgery	11	7

A somewhat larger number of doctors claim regular readership than report reading a journal within the last 30 days. For comparison with the 35 shown above for JAMA, a total of 41 say that they read at least half of the JAMA issues.

The top three journals in number of mentions as the most valuable are JAMA with 13 mentions, G.P. with 7 and Modern Medicine with 6. The top two for enjoyment in reading are Medical Economics with 17 mentions and JAMA with 10. JAMA is the only publication which as many as five doctors say they feel "duty bound" to read.

Comments about Journal Articles

Speaking broadly, it appears that to many physicians of Fond du Lac professional articles seem to be the most reliable source of new product information — or that such articles would be the most reliable source if they could be published sooner.

Some doctors will wait for journal publication before using a new drug —

Internist C.: "The most desirable source by far is direct articles in the literature. Ordinarily I will use a new drug only after reading an evaluation by a known authority."

Surgeon C.: "I am interested only in reports on clinical tests as a basis for my decision to use a drug or not."

Dr. G.P. R.: "One good article on a new drug product will do more to convince me that I should try it than unlimited detailing and advertising will do."

Dr. G.O.P. A.: "I will wait for a considerable length of time before trying a product until technical data appears in the journals."

But others feel that they either cannot wait or cannot take the time for professional articles —

Surgeon F.: "Characteristically, I go to the table of contents first and then directly to the article that interests me. Sometimes I search through the literature for technical material, but I know that many physicians do not have the time for that sort of searching. I will trust a reprint of an article more than the literature put out by the pharmaceutical house."

Dr. Eye A.: "Journal articles are the best source of data in the long run. It is a very long time before they are out, however, so the only practical thing is to rely on detailing and whatever other data is immediately available."

Dr. G.P. E.: "I have a conflict here. I trust professional evaluation above any other source, but at the same time I do not have sufficient reading time to dig through the journals."

Journal articles also come in for their share of criticism —

> Surgeon E.: "The value of professional articles hinges directly upon the name of the author and his professional reputation. I have a suspicion of statistics since they can prove almost anything depending upon the way they are applied. This places most professional writings on a par with pharmaceutical house literature and advertising. I would not trust one above the other."
>
> Dr. G.P. H.: "I have one complaint about medical journals and their use of chemical and generic names. The individual physician has to somehow make the tie-up with the particular brand or trade name. This is confusing since a doctor not only has to know that a product is available but where to get it and what to call it. If you prescribe by generic name, the druggist may even call you back to ask for the trade name."

Comments on Journal Advertising

Just as in the case of other media, some Fond du Lac area doctors appear to rely heavily upon advertising in medical journals while others say that they ignore it.

First, some of the favorable comments —

> Dr. P.T. A.: "I am truly a cover-to-cover reader of the journals and so I have to read all of the ads."
>
> Dr. P. T. D.: "To me there is no real distinction between the ads in the journals and the scientific articles. I read the journals a lot, so I pick up a good deal of scientific information on products."
>
> Dr. G.P. C.: "I like journal ads — particularly those with pictures, charts and graphs. An attractive ad helps a good deal to stimulate my interest in a product."
>
> Dr. Eye C.: "The advertising in the professional publications is a more reliable source once a detail man has made me aware of the existence of a product."

Next, some comments about the auxiliary effect of journal advertisements —

> Internist B.: "I do not often notice them except for very new products which I have not heard about before. Seeing the ad lets me ask questions of the detail man his next time around."
>
> Dr. G.P. K.: "I read them if they deal with a product I am interested in and which I have heard about somewhere else."
>
> Dr. P.T. G.: "Such ads are a reminder to me, because they raise a certain amount of skepticism about whether a drug will do what it claims to do."

And some comments of those who accept journal advertising with reservations —

> Surgeon E.: "They are a valuable source, but I resent advertising which is non-professional. What the average doctor is looking for is a drug to do a specific job, so if the advertising gives technical detail without ballyhoo he is satisfied."
>
> Dr. Eye D.: "It is often too long before definite data are out on a drug so sometimes I try a product from specifications in the ads, but I don't like to do this unless it is not going to be at all risky."

Finally, the inevitable disclaimers about advertising —

> Dr. G.P. M.: "I never look at the ads too much."
>
> Surgeon F.: "I rarely look at the journal ads."
>
> Dr. G.P. H.: "I never read journal advertising."

Reading of House Organs

Fond du Lac area physicians receive company periodicals from pharmaceutical firms in even greater abundance than medical journals, and they look through or read these house organs in fairly high proportions.

> The doctors were shown a list of eleven company periodicals. On the average each doctor said that he received nine of these publications and that he usually read or looked through six or seven of them. While seven doctors say that they never look at company periodicals, 15 indicate that they look through all eleven.

"Which of these company periodicals do you happen to receive? Which of these do you usually read or look through?"

	House organs received	Read or look through
Total doctors	55	55
No house organs	-	7
One or two	2	4
Three or four	3	6
Five or six	5	8
Seven or eight	5	6
Nine or ten	12	9
All eleven	28	15

Three company periodicals are each singled out by five or more doctors as doing the best job. They are:

> Symposia of Ciba, named by 11 doctors
> Therapeutic Notes of Parke, Davis, named by 10 doctors
> What's New of Abbott, named by 5 doctors

Reading of Direct Mail

Fond du Lac physicians, like doctors everywhere, are deluged with direct mail advertising. Only two of the 55 say that they read or look at all of the direct mail they receive.

Most doctors in the area say that they receive more than 50 direct mail pieces a week and most doctors indicate that they read fewer than 9 of them.

"About how many pieces of medical direct mail advertising (other than periodicals) have you received during the last seven days — as close an estimate as possible? Of these, about how many pieces have you read or looked at during the last seven days?"

	Pieces received	Read or looked at
Total doctors	55	55
None	-	14
1-9 pieces	1	25
10-24 pieces	3	9
25-49 pieces	13	2
50-99 pieces	15	2
100 or more	22	1
Don't know	1	2

Five of the doctors say that they never read direct mail, two report reading all of it, and of the remaining 48, all but four say that they do the sorting themselves. Whether they or their girls do the sorting, here is the basis for the choices made, some using more than one method:

Total sorting	48
Sort by specialty, type of product, subject matter	23
Sort by company name	9
Read about new products, discard duplications	9
Sort by appearance of piece	5
Sort by information on envelope	5
Read if I have time	3
Other methods	2
No special way, don't know	2

Only three companies are singled out by as many as three doctors for doing the best job on direct mail —

Smith, Kline & French,	4 mentions
Abbott Laboratories,	4 mentions
Pfizer Laboratories,	3 mentions

Comments about Direct Mail

Direct mail has relatively few strong supporters among physicians of the area, but a few do depend upon it —

> Dr. G.P. H.: "Direct mail is my first choice. I especially like the small file cards that I can file away for reference. Direct mail is the fastest form of communicating and, I think, the most efficient."
>
> Dr. G.P. E.: "Direct mail is of help as a stimulus to start looking for more complete data. Advertising in general helps me to familiarize myself with new product names and applications. I usually let the mail pile up and then read it all at one time."
>
> Dr. Eye A.: "It keeps me posted but I see only the better stuff — I mean technical pamphlets containing scientific material. The rest goes in the round file (waste basket)."

Suggestions for improving the impact of direct mail are made by a few physicians —

> Dr. G.P. L.: "Repetition of the same material every few days is a source of irritation, not a source of information. It is very wasteful. Direct mail should be attractive, short and concise descriptions of the drug, uses, abuses, cautions, and so forth. Be informative. This probably won't please the ultra-scientific men, but it would certainly help the ordinary practitioners."
>
> Internist B.: "I dislike the flood of mail across my desk. I would rather receive one letter three to five pages long from the director of research for a particular house when a new product comes out."
>
> Dr. P.T. C.: "I will not open or read any mail unless it has a licked stamp on it."

A number of doctors apparently associate direct mail with their waste baskets, as exemplified in this one quotation —

> Dr. P.T. H.: "This morning, as an example, I picked up the direct mail at the desk and dumped all of it immediately. It is purely advertising."

Meetings and Conventions

Not counting hospital and clinic staff meetings, physicians of the Fond du Lac area report attending more than 10 professional meetings a year on the average.

About half of them (26) say that they attend practically every county medical society meeting and a fourth (13) think that they miss only one or two local meetings a year.

The record for attendance at state and national conventions during the preceding year was held by one of the older doctors, Dr. G.O.P. A.; and all but six doctors had attended at least one convention. The average number of state and national conventions attended was 1.8 per physician. Only one doctor in the area does not belong to the American Medical Association.

In addition, 38 of the doctors had been present at one or more meetings of other professional organizations. Each of the 38 mentioned two organizations on the average, and some attended several meetings.

Comments about Other Doctors as Information Sources

Despite their frequent meetings and contacts with other physicians and their own sometimes contradictory testimony when speaking later about learning of specific drugs, most doctors do not give much general credit to other members of the profession for telling them of new pharmaceutical products.

Here are some of the exceptions who state that they often learn of new drugs from other doctors —

Dr. G.P. R.: "Now that I think about it, I place my professional contacts in first importance."

Dr. G.P. J.: "You talk these things over with fellows specializing in certain fields and use what they recommend in referred cases."

Dr. P.T. F.: "Other doctors help considerably in passing along information on new products. Furadantin is a case in point. I first heard of it from Specialist A."

Dr. P.T. D.: "Undoubtedly the best is a direct recommendation from another physician whose professional standing is unquestioned. When I really want to know about a drug in a hurry, I call my friends at the hospital."

Dr. G.P. M.: "I think you feel better about a new drug if you hear about it at a medical meeting — somebody else's experience with side effects and so on."

More typical of the statements made by other physicians are these:

Dr. P. T. J.: "Once in a while the doctors will get together and talk about it after meetings."

Dr. G.P. H.: "Specific discussions between doctors on new products are the exception rather than the rule, except in cases of consultation."

Dr. Eye C.: "I mentioned these two doctors at the clinic for a couple of new drugs, but I don't think of them as really reliable sources as far as learning about all products."

Prescriptions Written

The extent of prescription writing done by Fond du Lac area physicians is subject to the highest individual variation.

For the week preceding the background interviews nine doctors indicated that they wrote no prescriptions, while seven doctors estimated that they wrote more than 100 apiece.

"About how many prescriptions did you happen to write in the last seven days?"

Total doctors	55
Over 200 prescriptions	1
151-200 prescriptions	2
101-150 prescriptions	4
51-100 prescriptions	8
31-50 prescriptions	12
11-30 prescriptions	9
1-10 prescriptions	10
No prescriptions	9

The above distribution is very important because it means that 7 of the 55 doctors wrote almost half of the prescriptions.

Or looked at the other way, half of the doctors, 28 of the 55, accounted for only 10% of all the prescriptions.

Of course, some of the low prescribing doctors do their own dispensing, so that prescription writing does not give full measure of their importance to the pharmaceutical manufacturer. It seems probable, however, that dispensers as a group tend not to use new drugs so readily as prescribers do.

Individual Use of Sources

The following chart lists the 55 physicians in order of the amount of prescribing done and shows usage of the different sources of information by each one.

Doctor	Most important source	Controlled source		Journals read	House organs read	Direct mail read in week	Detail men seen in week	Meetings a year		
		Most worthwhile	Least worthwhile					Local medical societies	State-National AMA	Other professional organizations
Int. A	Ref book		Detlng	2	7	1-9	4	9	2	4
G.P. A	Detlng	Detlng	Jnl ads	6	11	1-9	10	6	2	2
G.P. B	Detlng	Detlng	Jnl ads	7	11	1-9	10	6	2	0
HEAVY PRESCRIBERS (101-150 PRESCRIPTIONS WEEKLY)										
P.T. A	Detlng	Detlng		5	4	10-24	3	8	2	1
P.T. E	Jnl arts	Co. mags	Jnl ads	3	0	0	2	9	2	0
P.T. B	Detlng	Detlng	Jnl ads	3	5	0	6	All	1	2
P.T. C	Detlng	Detlng	Dir mail	2	0	0	5	8	2	2
ABOVE AVERAGE PRESCRIBERS (51-100 PRESCRIPTIONS WEEKLY)										
G.P. C	Detlng	Detlng	Dir mail	5	11	10-24	3	9	1	1
P.T. F	Detlng	Detlng	Dir mail	3	9	1-9	3	All	2	1
Spec. A	Convtns	Detlng	Dir mail	1	1	0	5	6	1	4
P.T. J*	Detlng	Detlng	Jnl ads	3	9	1-9	9	All	1	1
G.P. D	Detlng	Detlng	Dir mail	1	11	10-24	3	All	2	3
G.P. E	Jnl ads		Dir mail	4	9	10-24	3	All	2	0
Eye A	Dir mail	Dir mail	Jnl ads	4	11	25-49	5	6	3	2
G.O.P. A	Jnl arts		Detlng	4	3	1-9	2	All	5	3
AVERAGE PRESCRIBERS (31-50 PRESCRIPTIONS WEEKLY)										
G.P. F	Jnl arts	Dir mail	Detlng	1	5	1-9	3	8	3	3
P.T. G	Detlng	Detlng	Dir mail	2	11	0	8	4	0	2
Spec. B	Jnl ads	Co. mags	Dir mail	3	11	1-9	1	8	2	1
G.P. G	Meetings	Detlng	Jnl ads	2	3	1-9	3	All	2	3
Eye B	Jnl arts	Detlng	Dir mail	1	3	0	5	8	1	2
P.T. H	Detlng	Detlng	Dir mail	2	0	0	5	All	2	3
Int. B	Dir mail	Jnl ads	Detlng	8	0	?	4	All	2	1
G.P. H	Dir mail	Detlng	Jnl ads	3	10	50-99	5	5	1	0
G.P. I	Stf mtg	Detlng	Dir mail	2	4	?	0	6	1	0
G.O.P. B	Detlng	Detlng		4	5	1-9	5	8	4	0
Eye C	Jnl arts	Co. mags	Dir mail	1	10	1-9	0	All	2	0
P.T. I	Post grad	Jnl ads	Dir mail	2	0	0	2	All	1	0

LIGHT PRESCRIBERS (11–30 PRESCRIPTIONS WEEKLY)

Doctor	Most important source	Controlled source		Journals read	House organs read	Direct mail read in week	Detail men seen in week	Meetings a year		
		Most worthwhile	Least worthwhile					Local medical societies	State National AMA	Other professional organizations
Int. C*	Jnl arts		Dir mail	2	0	0	3	9	3	2
Eye D	Jnl arts	Co. mags	Jnl ads	3	7	25–49	2	All	3	4
Eye E	Detlng	Detlng	Dir mail	1	6	10–24	3	All	0	0
G.P. J*	Jnl ads	Detlng	Dir mail	1	2	1–9	4	4	1	1
G.P.K *	Jnl arts	Detlng	Dir mail	6	7	0	5	All	2	1
Surg. A	Jnl arts	Detlng	Jnl ads	4	2	1–9	1	All	3	1
P.T. K*	Jnl arts	Detlng	Jnl ads	5	10	50–99	2	All	2	3
G.P. L*	Detlng	Dir mail	Jnl ads	2	8	10–24	8	4	1	1
Spec. C*	Jnl arts	Detlng	Jnl ads	5	9	1–9	3	9	1	1

VERY LIGHT PRESCRIBERS (1–10 PRESCRIPTIONS WEEKLY)

Surg. B*	Jnl arts	Detlng	Dir mail	3	2	0	4	9	0	1
Surg. C	Jnl arts	Co. mags	Dir mail	4	9	1–9	2	8	2	4
G.P. M*	Detlng	Detlng	Dir mail	3	11	1–9	3	All	2	1
G.P. N*	Detlng	Dir mail	Jnl ads	5	11	1–9	3	2	1	0
Surg. D	Detlng	Jnl ads	Dir mail	3	6	1–9	2	7	0	0
Surg. E	Stf mtg		Dir mail	3	11	10–24	3	5	2	0
G.P. O*	Jnl arts	Detlng	Dir mail	6	11	1–9	7	All	1	0
G.P. P*	Jnl arts			2	3	1–9	0	6	0	0
G.P. Q*	Dir mail	Dir mail	Co. mags	3	7	1–9	3	All	1	1
Spec. D	Meetings	Detlng	Dir mail	2	10	0	1	All	4	3

NON-PRESCRIBERS (0 PRESCRIPTIONS WEEKLY)

G.P. R	Jnl arts		Dir mail	4	11	100+	4	All	2	3
G.P. S*	Detlng	Detlng	Jnl ads	5	0	0	5	All	4	0
Surg. F	Jnl arts	Detlng	Dir mail	4	6	10–24	3	All	2	2
G.P. T*	Detlng	Detlng	Dir mail	3	5	1–9	2	5	1	0
G.P. U*	Jnl ads	Jnl ads	Dir mail	1	11	1–9	3	5	2	1
P.T. D	Convtns	Jnl ads	Dir mail	1	11	1–9	4	All	3	1
Eye F	Jnl arts	Detlng	Jnl ads	1	5	0	0	0	0	0
Spec. E	Jnl arts	Co. mags	Detlng	5	8	1–9	0	All	2	1
Spec. F	Detlng	Co. mags	Dir mail	1	11	10–24	0	All	2	1

*Dispenses drugs.

Some very illuminating comparisons are available in this chart, largely confirming for the Fond du Lac area some of the national findings of our 1953 study:

Contrasts between the seven heavier subscribers and the nine non-subscribers are most marked —

The heavier prescribers place more reliance on detail men — five of the seven say that detailing is the most important source of information about new products; and they see an average of six detail men apiece in a week. The heaviest prescriber of all, however, rates detailing as the least worthwhile commercial source of information, although he saw four detail men in the week.

Non-prescribers saw an average of only 2½ detail men in 7 days, but this is not entirely due to disinclination on the doctor's part — both specialists, for example, say that they would welcome any detail man who wished to call on them.

The fact that more detail men called on G.P.'s A. and B. than on any other doctors indicates that they probably recognize the importance of these two heavy prescribers.

Another difference between the heaviest prescribers and non-prescribers is in their readership of medical journals.

Two of the heavier prescribers read an unusual number of journals, bringing the average up to four journals a doctor as compared with only about three journals for the non-prescribers.

Heavier prescribers as a group read an average of only six company periodicals while the non prescribers read an average of seven or eight.

Heavier prescribers show somewhat less interest in direct mail and do not so often report perfect attendance at county medical society meetings as the non-prescribers do.

Finally, the heavier prescribers comprise one internist, two general practitioners and four general practitioners with special interest.

The non-prescribers include four specialists, four general practitioners of whom three are dispensers, and one general practitioner with special interest.

SECTION III THROUGH VIII

FOND DU LAC STUDY

1956

SECTION III:

The Marketing of Five New Ethical Pharmaceuticals and What Happened to Them in Fond Du Lac From the Product Point of View.

SECTION III - Chapter 1. The Story of CIBA's Serpasil

DEVELOPMENT OF THE TRANQUILIZERS

Serpasil and the drugs included for study with it are considered here as tranquilizers for mental and emotional disturbances, since this seems to have become their main common usage. Most of them were originally developed as hypotensive agents to lower blood pressure, but the tranquilizing side effect has assumed greater importance.

The drugs in this group, except Thorazine, were developed from Rauwolfia serpentina, a snake-like root from India long used in that country as a cure-all. In 1931 two Indian chemists isolated five crystalline substances from the dry powdered snake root; and in 1949 success was reported in the use of some of these substances in reducing high blood pressure.

Experiments with these snake root substances attracted the interest of a number of pharmaceutical manufacturers at about the same time.

Raudixin, the powdered whole root, was brought to the market first, in May 1953, by Squibb.

Rauwiloid, which Riker introduced very shortly thereafter, is an alkaloidal extract obtained from the snake root.

Serpasil was the outcome of attempts to isolate the active ingredients from Rauwolfia serpentina which had been started at Ciba in 1947. A research team there succeeded in 1952 in isolating reserpine, the most active snake root component. It was marketed in powdered form in November 1953 as Serpasil.

Thorazine, a derivative of phenothiazine, was originally introduced by Smith, Kline & French for control of nausea, vomiting and hiccups, but is now used extensively as a tranquilizer.

Rau-sed, which is the alkaloid reserpine, was the second snake root drug introduced by Squibb.

Reserpoid, also alkaloid reserpine, is an Upjohn product.

Serpasil-Apresoline is a combination which has more effective hypotensive action than Serpasil, its fellow Ciba product.

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NATIONAL PROMOTION OF SERPASIL

Ciba already had a large investment—approaching $1,500,000—in its forthcoming product when Raudixin and Rauwiloid came on the market. The impressive rating of Raudixin in the Nielsen drug report speeded up the entry of Serpasil into the field.

The first year's national advertising and promotion effort for Serpasil cost in rough figures about $1,900,000.

The largest incurred expense was for detailing, Serpasil having been the company's featured detailing item since its introduction. An estimate of the 1954 cost of detailing comes to about $900,000

Direct mail for the first year—self-mailers, letters, enclosures, etc.—required roughly $400,000

Journal advertising represented a cost of ..... $250,000 (two-thirds in the first six months and one-third in the second six months, when an equal size journal campaign was being run for Serpasil-Apresoline).

Sampling was very heavy also—a small pre-introductory supply was sent to each drug store, and physicians were sampled liberally through detail men and direct mail $200,000

Exhibits, in commercial and scientific sections at medical meetings where permission was granted to feature the item, and at selected hospitals $150,000

It may be noted here for future remark that Ciba did no test marketing or marketing research on the product other than referring to the Nielsen figures. The ratios of one-and-a-half million dollars for technical research and development and almost two million dollars for advertising and promotion to practically nothing for marketing research are not uncommon in the pharmaceutical industry. This is a constant source of amazement to many practitioners of scientific marketing in other fields.

PROFESSIONAL EVALUATION OF SERPASIL (RESERPINE)

Reserpine has been the subject of considerable professional attention since its isolation from the other snake root substances; and a large amount of clinical experimentation has been reported in the literature and at meetings.

At the time of the study, over 200 articles on reserpine had appeared in journals and about 150 papers had been devoted exclusively to it at medical meetings. The product had received mention along with other items in numerous other papers also.

Two meetings of the New York Academy of Science had been devoted entirely to reserpine. Ciba helped finance these meetings, and paid for very widespread distribution of abstracts and a book on the full proceedings.

GENERAL PUBLIC INFLUENCE

The tranquilizing drugs have caught the popular imagination to an unusual degree; and there have been a number of articles in the lay press on "New Hope for the Insane," "Miracle Pills for the Mind," and similar titles.

While such articles have no official status, they unquestionably create interest both in physicians and patients, or relatives of patients. Although physicians frequently complain about the patient who asks to be treated with a drug he has read about, there probably is no stronger incentive to send them seeking professional information about it.

This public influence is difficult to determine, since physicians would no doubt underrate its importance. We believe, however, that it is a most important influence in the case of many drug products.

SERPASIL DETAILING IN THE FOND DU LAC AREA

It can reasonably be assumed that the 55 practicing physicians in Fond du Lac and its satellite towns received their fair share of direct mail, journal advertising, journal articles, exposure to convention exhibits and papers at meetings. The same is probably true for detailing, but through our interviews with the detail men it is possible to elaborate somewhat on their approaches locally.

Two men detailed for Ciba in this area during the year of study—one who covered the territory at the time Serpasil was introduced until August 1954 and a replacement who then took over. The original detail man was briefed on Serpasil at a three-day regional meeting in Chicago in November 1953. Later that month he made his first detail on Serpasil in the Fond du Lac area.

His schedule called for three days in Fond du Lac and he was able to see about six doctors a day. Every six weeks he returned for another three days, always calling upon the 15 doctors he considered most important and, by rotation, upon three or four others each of whom he visited only once or twice a year. It is interesting to note that 10 of the 12 physicians who wrote Serpasil prescriptions during our audit period were among the 25 or so that he detailed during its first year. Whether they prescribed because of his detailing or he selected them as the most likely prescribers cannot be determined, but probably it worked both ways.

Not only did he leave samples of Serpasil with each physician, but also simultaneously with his first visit to Fond du Lac the company mailed samples to them.

He spent about 9 hours on each visit detailing the pharmacies in Fond du Lac, and he left with each an initial supply of 25 Serpasil tablets. He also called on the hospital, setting up an exhibit there and visiting both the hospital pharmacy and laboratories.

During Serpasil's first year he also detailed other drugs, but devoted 80 to 90 per cent of his effort to this one drug. He estimated that he spent 40 to 50 minutes of each working hour waiting and only 10 or 20 minutes in actually talking with physicians and pharmacists.

The second detail man carried along in much the same pattern, but visited Fond du Lac only six times a year for two days each time. He devoted only about half of his efforts to Serpasil. Neither one of the two men detailed physicians outside of Fond du Lac proper; and only 36 of the 55 doctors remembered ever having been detailed on this drug.

TRANQUILIZER SALES

Hypotensives and tranquilizers have developed a market of respectable size in the Fond du Lac area but are not a type of drug that is prescribed every day by every physician.

For example, 35 of the 55 doctors indicated during the interviews that they had prescribed Serpasil and 39 said they had prescribed Thorazine. During the four weeks when the prescription audits were made, only 26 doctors prescribed any of the seven drugs in this group. They wrote a total of 110 prescriptions selling at $455. On an annual basis this would amount roughly to 1450 original prescriptions, or a $6000 market exclusive of refills and direct dispensing.

However, the demand for these products increased substantially during the early part of the audit period.

The number of prescriptions for the seven tranquilizers almost tripled between the May and September 1954 audits and leveled off thereafter.

	Original Prescriptions 7 drugs	
Week of audit	*Number*	*Price*
May 1954	13	$ 48
September 1954	36	150
January 1955	30	144
May 1955	33	113

SERPASIL SALES

During the prescription audit periods, a total of 28 prescriptions for Serpasil were filled for 12 physicians. This was about a third of those who reported ever prescribing it.

The price of these prescriptions was $102. This means that Serpasil accounted for a fourth (25%) of all tranquilizer prescriptions and for 22 per cent of the dollar volume of original prescriptions. In terms of annual sales this translates into about 365 prescriptions and $1325 at retail, exclusive of refills and direct dispensing.

Looked at another way, the 55 Fond du Lac area physicians may be considered as representing 1/3000th of all practicing physicians in the country. This market's share of the Serpasil development cost then comes to about $500 and about $635 of the first year's promotion. This may be compared with the $1325 retail sale figure for original prescriptions filled.

CONCENTRATION OF SERPASIL PRESCRIPTIONS

A most remarkable revelation of the prescription audits is the fact that over half of the Serpasil prescriptions during the audit periods were written by three physicians. Furthermore, all 3 of these doctors are full-time internists.

	Four-week Serpasil prescriptions	
	Number	*Price*
Total	28	$102
Internist B	8	$30
Internist C	5	20
Internist A	3	14
Nine other prescribers	12	38

The three internists in Fond du Lac thus accounted for 57 per cent of the prescriptions of Serpasil and for 63 per cent of their dollar value.

This finding that Serpasil was predominantly (although not exclusively) an internists' drug in Fond du Lac has important implications for marketing strategy.

SOURCES OF INFORMATION ABOUT SERPASIL

Important differences are observable between the prescribers and non-prescribers of Serpasil in their exposure to information about the product.

In the first place, the great majority of Serpasil prescribers remembered having been detailed on Serpasil, and all but two said that they had received samples of the product. In contrast, fewer than half of the non-prescribers were detailed or received samples.

	Internists	*Other Serpasil prescribers*	*Non-prescribers*
Total	3	32	20
Serpasil discussed by detail men	3	25	8
Serpasil received as samples	3	30	9

Although "other prescribers" of Serpasil most often report that detail men led them to make their initial prescriptions, the internists credit professional sources for theirs.

"Where did you happen to get the information about Serpasil which led you to prescribe it?"

	*Internists**	*Other prescribers*
Total	3	32
Detail men	—	15
Papers, articles in journals	1	10
National conventions	2	3
County meetings	—	3
Direct mail	—	2
Journal advertising	—	1
Staff meetings	—	1
Other sources	—	4

(some physicians named more than one source of information)

Two of the internists were among the early prescribers of Serpasil.

*Accounted for 57 per cent of prescriptions written—and 63 per cent of dollar volume for Serpasil during the prescription audit periods.

"Can you tell me what month you first prescribed Serpasil?"

	Internists	*Other prescribers*
Total	3	32
1953	—	4
January-April 1954	2	4
May-August 1954	1	9
September-December 1954	—	7
January-April 1955	—	8

GENERAL SOURCES OF INFORMATION

Local Serpasil prescribers place more emphasis on detailing as a source of information about new drugs generally than do nonprescribers.

But none of the internists mentions detail men as his most important source, even though two of them see all detail men who call and the other sees those from the leading pharmaceutical houses.

"Which of these methods do you find most important to you personally in learning about a new drug?"

	Internists	*Other Serpasil prescribers*	*Non-prescribers*
Total	3	32	20
Detail men	—	15	5
Papers, articles in journals	1	11	7
Journal advertising	—	2	2
Direct mail	1	2	1
National conventions	—	—	2
County meetings	—	1	1
Staff meetings	—	—	2
Reference books	1	—	—
Post-graduate courses	—	1	—

In fact, two of the internists go against the trend by saying that to them detailing is the least worthwhile commercial medium.

"Which of the four sources of information from manufacturers do you find most worthwhile for learning about new products?"

	Internists	*Other Serpasil prescribers*	*Non-prescribers*
Total	3	32	20
Detailing	—	22	9
Company periodicals	—	2	5
Journal advertising	1	2	2
Direct mail	—	4	1
No choice	2	2	3

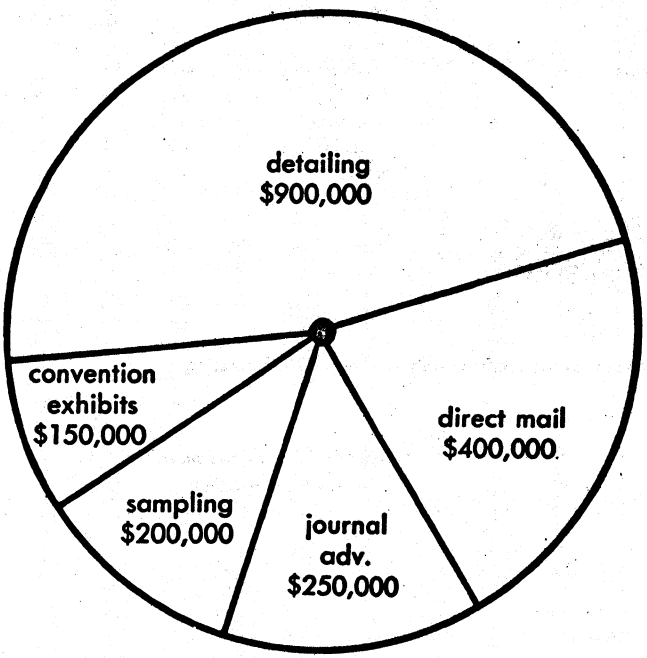
"Which do you consider least worthwhile to you personally?"

	Internists	*Other Serpasil prescribers*	*Non-prescribers*
Total	3	32	20
Direct mail	1	15	14
Journal advertising	—	13	3
Detailing	2	2	1
Company periodicals	—	1	—
No choice	—	1	2

THE SERPASIL MARKETING MIX

Ciba already had a large investment—approaching $1,500,000—in its forthcoming product when Raudixin and Rauwiloid came on the market. The early impressive rating of Raudixin (Squibb) in the Nielsen drug report speeded up the entry of Serpasil into the field.

The first year's national advertising and promotion effort for Serpasil cost, in rough figures, about $1,900,000.



SUPPORT FOR SERPASIL IN MEDICAL JOURNALS

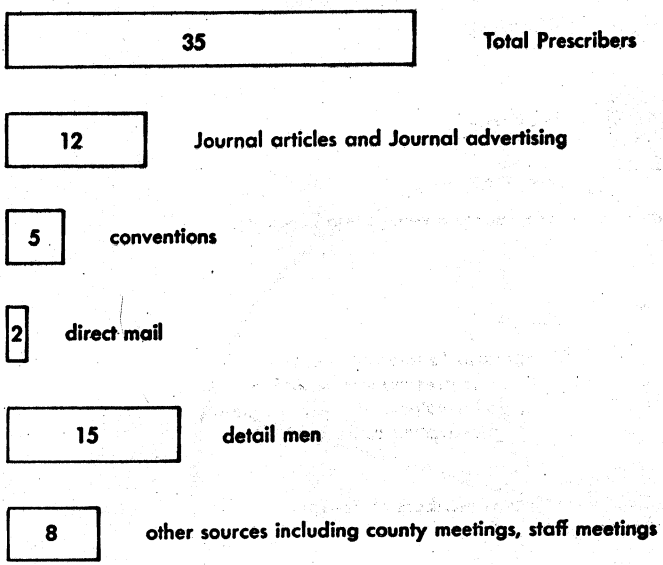
Reserpine has been the subject of considerable professional attention since its isolation from the other snake root substances; and a large amount of clinical experimentation has been reported in the literature and at meetings.

At the time of the study, over 200 articles on reserpine had appeared in journals and about 150 papers had been devoted to it at medical meetings. The product had also received mention along with other drugs in numerous other papers.

Two meetings of the New York Academy of Science had been devoted entirely to reserpine. Ciba helped finance these meetings, and paid for very widespread distribution of abstracts and for a book on the full proceedings.

CORRELATION WITH SOURCES OF INFORMATION ON SERPASIL

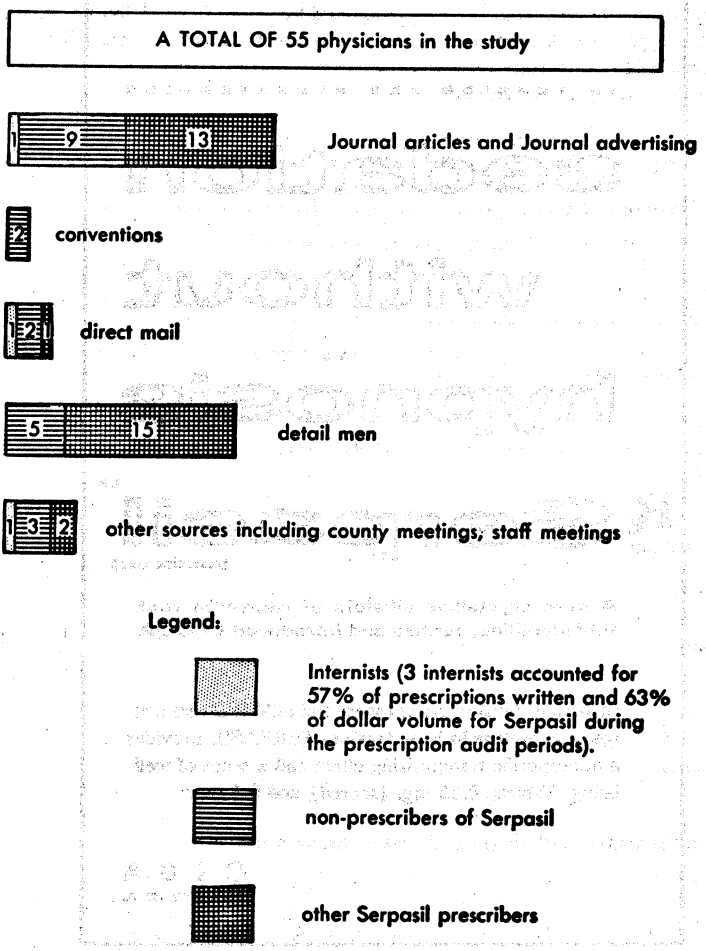
"Where did you happen to get the information about Serpasil which led you to prescribe it?"*



*some physicians named more than one source of information

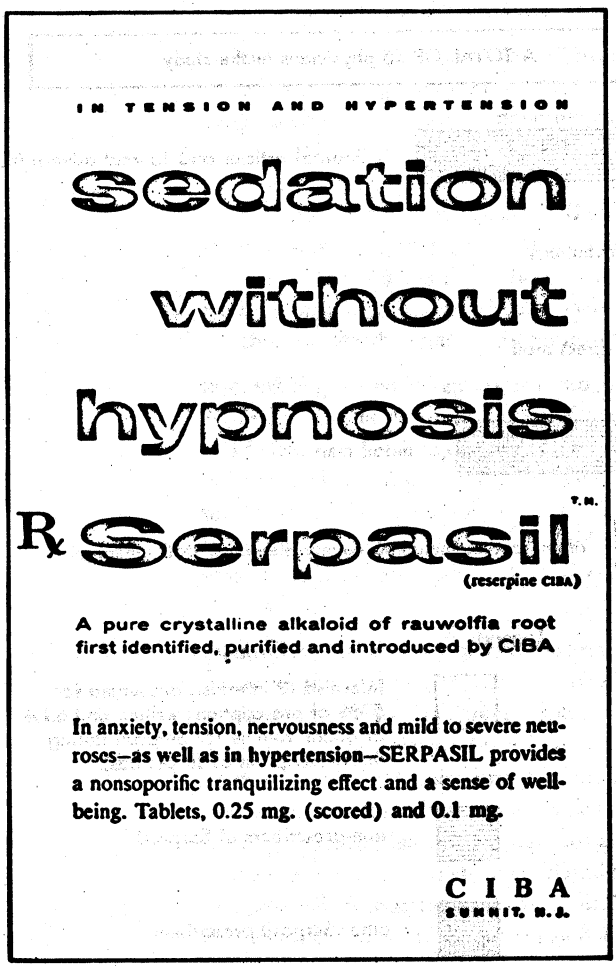
GENERAL SOURCES OF INFORMATION

"Which of these methods do you find most important to you personally in learning about new drugs?"



CHARACTER OF SERPASIL JOURNAL ADVERTISING

Ciba ran multiple half pages and full page ads in each issue of a selected journal list. Copy and art emphasis was on drug action and product name.



INTERVIEW PROFILE G.P. "E"

G.P. "E" is one of the younger doctors, only recently admitted to practice. He is on the staffs of the hospital and a small clinic. So far, he has attended all local medical society meetings and most conventions at the state level.

He learned about some of the drugs on our list while a resident in training. In fact, he did some experimental work there on one of them. A more-frequent-than-average prescriber, he admits that he is more susceptible to most advertising than many other doctors are. He sees all detail men, uses samples on a trial basis, reads or looks through every house organ that he receives and the direct mail that is more comprehensive than single sheets or cards.

To him, medical journal advertising is the most worthwhile source of information and direct mail the least. His original use of both Butazolidin and Serpasil was impelled by advertisements he read in journals. He receives four of the leading journals, reads all four, and considers J.A.M.A. the most useful to him personally.

As he reconstructs it, he gets his preliminary information on new products from detailing and from direct mail, both of which stimulate him to look for information in the journals. He regards the professional articles as a more certain and accurate check on the products, and he leafs through the journal advertising to remind himself about them. Then comes the first trial during which he prescribes the drug. If the reactions are favorable, he continues to use it.

Because of his relatively recent experiences in training, he also tends to keep close to the recommendations of others on the hospital staff about products they are utilizing on an experimental basis.

MEDICAL JOURNAL READING

Most Fond du Lac physicians subscribe to more medical journals than they are able to read, but each of them manages to look through at least one.

When shown a basic list of 15 of the more popular medical journals, the physicians reported that they receive an average of about 5 journals apiece, and that they read or look through an average of three each.

"Which of these 15 medical publications do you happen to receive? Which have you happened to read or look through during the last thirty days?"

The response indicates the following number of journals were received and read:

Total doctors	*Received* 55	*Read or looked through* 55
	%	%
One journal	4— 7.2	11—20.0
Two journals	1— 1.8	11—20.0
Three journals	11—20.0	13—23.6
Four journals	8—14.5	8—14.5
Five journals	14—25.4	7—12.7
Six journals	6—10.9	3— 5.4
Seven journals	7—12.7	1— 1.8
Eight or more	4— 7.2	1— 1.8

The problem which the busy physician is confronted with in reading his journals is well stated by Part-Time Specialist B, who receives 10 of the 15 journals and gets to read only three or four—

"I lay aside those with particular articles I want to read. Then they pile up in a stack until one day I close my eyes, pick up the stack of books and dump it out."

SECTION III - Chapter 2 - The Story of Eaton's Furadantin

DRUGS FOR URINARY TRACT INFECTIONS

Four other drugs were included for study in the group which may be considered as competitive with Furadantin. Strictly speaking, however, two of them are analgesics rather than antibacterial agents.

Pyridium and Serenium, Sharp & Dohme and Squibb products, respectively, are azo dyes and established urinary tract analgesics.

Mandelamine, made by Nepera, is a combination of two older drugs, methenamine and mandelic acid. Mandelamine's action is bacteriostatic and it appears to be competitive with Furadantin.

Thiosulfil (an Ayerst product) is a modern sulfonamide used for urinary tract infections. It is competitive with Furadantin both in indications and in timing since it appeared on the market at about the same time.

Furadantin, or nitrofurantoin, was first synthesized in 1948 after Norwich and Eaton had been working on the nitrofurans since 1939. It was brought to market in February 1953 and announced to urologists. In 1954, it was made available to the entire profession.

NATIONAL PROMOTION OF FURADANTIN

Dollar estimates of the amount of Furadantin advertising and promotion are not readily at hand, but some idea of the cost may be obtained through indicated use of various media.

At the time of the study about 150 different pieces of direct mail had been sent out—

12 mailings were made in 1953 to urologists only

110 mailings were made in 1954 to urologists, pediatricians, and general practitioners

25 mailings were made in the first quarter of 1956 to the above groups plus obstetricians and gynecologists.

Some mailings were also sent to druggists, technicians, and hospitals.

Furadantin was detailed nationally, although not until October 1954 in the Fond du Lac area.

A sizable part of the advertising budget was devoted to journal advertising. The 1954 journal schedule serves as an example—

American Journal of Medicine	12 insertions
Annals of Internal Medicine	12 insertions
California Medicine	12 insertions
GP	12 insertions
J.A.M.A.	60 insertions
Journal of Urology	12 insertions
Medical Examiner	17 insertions
Medical Times	12 insertions
Modern Medicine	12 insertions
World Medical Journal	1 insertion
New York State Journal of Medicine	12 insertions
Journal of Pediatrics	7 insertions
American Druggist	10 insertions

Samples of Furadantin had been sent to or left with selected physicians and about half (28) of those in the Fond du Lac area recalled receiving samples.

Eaton had helped defray the expense of scientific exhibits at four national conventions of urologists and the profession and at one meeting of the New York Academy of Medicine. In addition, from the introduction of Furadantin up to the time of this study, Eaton had shown commercial exhibits at 66 medical conventions.

The only market research done for this product consisted of prescription panel surveys to check the size of the market, the competition, etc. No test markets were used.

FURADANTIN DETAILING IN THE FOND DU LAC AREA

No detail man was assigned by Eaton to the Fond du Lac area until October 1954.

After that, the Eaton representative visited Fond du Lac eight to ten times a year for two days each time. On his first visit he stopped at the largest pharmacy to make an inventory of similar or competitive drugs and left samples.

In order to work efficiently he went through the entire list of physicians in Fond du Lac (he did not visit the surrounding towns) and eliminated unlikely users of Furadantin—such as surgeons, pathologists, radiologists, anesthetists, etc. He further refined his list by including only those whom he expected to be the heaviest users of the drug. These physicians he called upon three or four times to discuss Furadantin. All those on whom he called knew something of the drug already. In his first year in Fond du Lac he spent about 80% of his time pushing Furadantin. This amounted to some 40 hours, only a fraction of his office waiting time.

On each visit he stopped at the pharmacies and at St. Agnes Hospital as well.