REPORT TO THE INTERGOVERNMENTAL RELATIONS SUBCOMMITTEE COMMITTEE ON GOVERNMENT OPERATIONS HOUSE OF REPRESENTATIVES

RELEASED

Contracts Between The Food And Drug Administration And Georgetown University For Support Of A Laboratory Of Clinical Pharmacology B-164031(2)

Department of Health, Education, and Welfare

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

FEB. 24, 1970

COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON, D.C. 20548

B-164031(2)

Dear Mr. Chairman:

This is our report on the review of the contracts between the Food and Drug Administration and Georgetown University for the support of a laboratory of clinical pharmacology. The review was made pursuant to your request of April 21, 1969.

During our review, we discussed the matters included in this report with responsible officials of the contracting parties, but we did not obtain written comments from the Department of Health, Education, and Welfare nor from Georgetown University.

We plan to make no further distribution of this report unless copies are specifically requested, and then we shall make distribution only after your agreement has been obtained or public announcement has been made by you concerning the contents of the report.

Sincerely yours,

Elmer B. Staats

Comptroller General
of the United States

Addressee

The Honorable L. H. Fountain
Chairman, Intergovernmental
Relations Subcommittee
Committee on Government Operations
House of Representatives

Contents

ABBREVIATIONS

CPEHS	Consumer Protection and Environmental Health Service
HEW	Department of Health, Education, and Welfare
FDA	Food and Drug Administration
GAO	General Accounting Office
PHS	Public Health Service
VA	Veterans Administration

COMPTROLLER GENERAL'S REPORT TO
CHAIRMAN, INTERGOVERNMENTAL
RELATIONS SUBCOMMITTEE
COMMITTEE ON GOVERNMENT OPERATIONS
HOUSE OF REPRESENTATIVES

CONTRACTS BETWEEN THE FOOD AND DRUG ADMINISTRATION AND GEORGETOWN UNIVERSITY FOR SUPPORT OF A LABORATORY OF CLINICAL PHARMACOLOGY

Department of Health, Education, and Welfare B-164031(2)

D I G E S T

WHY THE REVIEW WAS MADE

The Food and Drug Administration (FDA) contracted with Georgetown University for the establishment and operation of a laboratory of clinical pharmacology in Washington, D.C. The Chairman, Intergovernmental Relations Subcommittee of the Committee on Government Operations, House of Representatives, questioned the limited benefits being obtained under the contracts and expressed his concern to FDA. In March 1969 the agency terminated the contract arrangement, effective June 30, 1969.

The General Accounting Office (GAO) was asked to obtain information on areas of interest to the Subcommittee staff, such as

--FDA's selection of the contractor,

--FDA's authority to award the contracts,

--the relationship of research conducted under the contracts to FDA's mission as a regulatory agency, and

--the extent of multiple financial support of research projects by FDA and others; primarily pharmaceutical manufacturers.

GAO also inquired into the accomplishment of contract objectives.

Georgetown University and the Department of Health, Education, and Welfare have not been given an opportunity to formally examine and comment on the contents of this report.

FINDINGS AND CONCLUSIONS

A key factor in FDA's selection of Georgetown as the contractor was its proposal to provide a decentralized laboratory which would make available the specialized research resources of the various departments of the medical school under the coordination of a laboratory director. According to the FDA Project Officer, however, this decentralized approach had certain disadvantages in that researchers did not work

as a cohesive operating organization and were sometimes preoccupied with their own research. (See pp. 5 to 7.)

The contracts' broad scope permitted Georgetown to perform studies not directly related to FDA's mission as a regulatory agency. However, GAO believes that there is no basis for questioning FDA's authority to enter into the contracts because annual appropriation acts for FDA contain general contracting authority and because its appropriations have included funds which were requested from the Congress for a proposed contract supporting a laboratory facility. (See pp. 8 to 10.)

GAO believes that FDA did not make it clear in the appropriation hearings that the contractor would be permitted to conduct studies not related directly to FDA's mission in addition to investigations requested by FDA. GAO believes also that FDA's initial budget justification to the Congress indicated that the contractor's services would be in response to specific FDA needs in carrying out its regulatory functions. (See p. 9.)

FDA contributed to the support of 30 research projects initiated by Georgetown in addition to special studies requested by FDA. Some of the projects received financial support from both FDA and pharmaceutical manufacturers. FDA officials expressed concern that, under this arrangement, researchers might be put in the position of working for FDA, a regulatory agency, and for a member of the industry subject to FDA's regulatory authority. The contracts with Georgetown did not provide for disclosure of and safeguards against possible conflicts of interest on the part of contractor personnel conducting studies both for FDA and pharmaceutical manufacturers. (See pp. 11 to 13.)

The primary reasons for FDA's entering into the contracts with Georgetown were (1) to provide prompt scientific evaluations of drugs or other products and (2) to enhance the professional development of the FDA staff by enabling their participation in research and training. These two objectives were not achieved during the 3-year term of the contracts to the satisfaction of either FDA or Georgetown. Special studies requested by FDA were not completed as promptly as FDA had anticipated, and participation by FDA personnel in research and training was less than both contracting parties had expected. (See pp. 14 to 22.)

GAO believes that FDA should have taken certain administrative actions to better achieve contract objectives. These actions should be considered in the event that future contracts of this nature are awarded by FDA. (See pp. 21 and 22.)

CHAPTER 1

INTRODUCTION

The General Accounting Office has reviewed the contracts between the Food and Drug Administration and Georgetown University for the support of a laboratory of clinical pharmacology. The scope of our review is described on page 23.

FDA operated under the direction of the Commissioner of Food and Drugs, who was responsible to the Consumer Protection and Environmental Health Service (CPEHS) of the Department of Health, Education, and Welfare (HEW) at the time of our review. A major part of FDA's mission is to protect the consumer by ensuring that foods, drugs, cosmetics, and therapeutic devices are safe and properly labeled.

FDA awarded cost-reimbursement-type contract number 66-3 dated February 24, 1966, and follow-on contract number 68-42 dated June 21, 1968, to Georgetown for establishing and operating a laboratory of clinical pharmacology. The objectives specified by FDA in the contracts were:

1. To conduct studies increasing the knowledge of drugs and the mechanisms of drug actions.

2. To develop techniques for correlating adverse effects of drugs in animals with similar effects in the human, and vice versa.

3. To develop improved methodology for controlled drug trials.

4. To enhance professional development of the FDA staff through participation in research and training.

5. To perform prompt investigations of drugs as requested by FDA.

The contracts authorized a maximum of $916,677 for reimbursement through June 1969. Georgetown records showed that costs incurred under the contracts at June 30, 1969, totaled $762,520, of which $685,347 had been reimbursed by FDA. The $762,520 covered salaries ($438,633), fringe benefits and overhead ($151,373), supplies ($112,196), equipment ($48,555), and travel ($11,763). Contract terms provided that the title to equipment purchased under the contracts pass to the Government.

CHAPTER 2

SELECTION OF CONTRACTOR

In February 1965 an FDA official informed the Subcommittee[1] of the Committee on Appropriations, House of Representatives, that one of FDA's problems was being unable to promptly obtain information on scientific evaluations of drugs or other products. He stated that FDA needed a regularly available laboratory of clinical pharmacology in the Washington, D.C., area to supply this information.

In June 1965 FDA discussed the possibility of establishing such a laboratory with representatives of three medical schools in the District of Columbia--Georgetown University, The George Washington University, and Howard University. During this discussion a representative of Georgetown asked FDA whether it was interested primarily in a self-contained laboratory that would have the capabilities for conducting all research studies or in a decentralized approach which would use and coordinate the specialized services of the various departments of the medical school. An FDA official informed the applicants that each should submit a proposal which would be best suited to its organization and system of conducting research and that FDA had no preference in this respect. He also stated that the proposal should express the applicant's concept of what type of laboratory it could offer to best meet FDA's needs. FDA's formal request for contract proposals, dated August 18, 1965, expressed no preference for a decentralized or a centralized organization.

An evaluating committee appointed by FDA's Medical Advisory Board along with FDA staff members visited each of the three medical schools and evaluated their proposals for establishing and operating a laboratory. In December 1965 the committee reported the following observations.

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[1] Subcommittee on Department of Labor and Health, Education, and Welfare and Related Agencies.

Georgetown University

Georgetown University proposed a decentralized laboratory designed to cross departmental lines and bring together the total research resources of the Georgetown Medical School and affiliated hospitals. The research was to be carried out by subspecialists in the various departments, with overall consultative assistance from the central unit. In the committee's opinion the Georgetown University facilities and staff would be able to undertake the vast majority of specific FDA requests for studies. The committee believed also that the director of the proposed laboratory would have sufficient backing from the administration of the medical school, as well as sufficient cooperation from the department heads, to see that such studies were carried out.

George Washington University

George Washington University's proposal for a laboratory was based upon a strong central unit in the College of Medicine, which would perform most of the research. The general opinion of the committee was that participation of other departments within the College of Medicine would not be especially enthusiastic. The committee believed that the proposed laboratory would be able to perform specific studies for FDA in a few areas but that it might be unable to cooperate or provide services in a great many other areas.

Howard University

Howard University's proposed plan was restricted to limited areas of endeavor. It basically involved the Department of Medicine and Pharmacology with only peripheral participation on the part of other departments.

In their report the committee members stated that, after careful evaluation of the three proposals and objective consideration of the approaches of the three schools, it was their opinion that Georgetown would be best able to

perform the required work. They concluded that the broad, decentralized approach and the enthusiastic attitude of key faculty leaders of Georgetown would best meet the needs of FDA. The Medical Advisory Board accepted the committee's conclusions and unanimously recommended that FDA award the contract to Georgetown University for establishing and operating the laboratory. Therefore, FDA awarded the contract to Georgetown in February 1966.

Although FDA had considered Georgetown's proposal to provide a decentralized laboratory that would draw on the specialized resources of the various departments of the medical school to be a key factor in the selection of a contractor, FDA's Project Officer informed us of certain disadvantages resulting from the decentralized approach. FDA's Project Officer told us that the researchers operated independent of the laboratory director rather than as a cohesive organization and were sometimes preoccupied with their own research. Also, he stated that, in his opinion, there was a tendency to use FDA funds for ongoing studies initiated by researchers in their own areas of interest. We were unable to determine the extent to which the decentralized approach may have affected the accomplishment of contract objectives. (See ch. 4.)

CHAPTER 3

AUTHORITY TO CONTRACT AND SCOPE OF CONTRACT SERVICES

We inquired into FDA's authority to enter into the contracts with Georgetown and the extent to which the research performed related to FDA's regulatory mission. HEW's Assistant General Counsel for Administrative Affairs informed us that FDA's general contracting authority had appeared for a number of years in the annual appropriation acts for that agency. The provision referred to in the appropriation acts is, as follows:

> "*** payment in advance for special tests and analyses and adverse reaction reporting by contract, ***."

For the specific authority to enter into the contracts with Georgetown, FDA's Deputy Director, Division of General Services referred us to the hearings before the House of Representatives on FDA's fiscal year 1966 appropriation bill where the Director of FDA's Bureau of Medicine described the purpose of providing funds for the laboratory. The functions of the laboratory as proposed by an FDA official were, as follows:

> "*** the laboratory would take as a basic scientific effort an important project on either adverse reactions to drugs or methods of action of drugs, but to then be available upon request to accept a problem in which we wanted a 30 or 45 or 60 day answer."

Also, in connection with the House appropriation hearings for fiscal year 1966 FDA submitted a budget justification in which the purpose of the proposed contract was described as follows:

> "*** Support of a clinical pharmacological laboratory facility in the Washington, D.C., area to resolve matters of conflict which may develop during the processing of investigational drugs,

new drug applications, possible litigation or seizure, or upon the report of adverse drug reactions and to substantiate testimony in administrative hearings and court cases ($320,000): ***"

Under the contracts, Georgetown was permitted to initiate basic and applied research in the area of drugs and clinical pharmacology in addition to making special studies for FDA. The first contract, awarded in February 1966, did not require prior FDA approval of Georgetown-initiated studies. However, the second contract, awarded in June 1968, required FDA approval.

During the term of the contracts, FDA paid support, in whole or in part, for 30 projects initiated by Georgetown in addition to the special studies requested by FDA. FDA's Project Officer informed us that none of the 30 projects related directly to FDA's mission as a regulatory agency. In a January 1969 memorandum to the Commissioner evaluating the accomplishments under the contract, however, he stated that the research projects initiated by Georgetown contributed "somewhat to the general field of clinical pharmacology."

We have included as appendix II a complete list of the projects initiated by Georgetown and receiving FDA support during the contract period.

CONCLUSION

We believe that, in view of FDA's general contracting authority referred to above and the fact that the Congress appropriated the funds requested by FDA for the purpose described in the fiscal year 1966 appropriation hearings, there is no basis for questioning FDA's authority to enter into the contracts.

We believe, however, that the oral presentation to the House Appropriations Committee regarding the nature of laboratory services needed by FDA did not make it clear that Georgetown would undertake research work not related directly to FDA's regulatory function in addition to investigations requested by FDA. Moreover, in our opinion, the agency's

budget justification presented to the Committee for the initial $320,000 of contract funds needed to support a laboratory of clinical pharmacology indicated that the contractor's services would be in response to specific FDA needs in connection with its regulatory function regarding the safety of drugs.

CHAPTER 4

MULTIPLE SOURCES OF FUNDING FOR RESEARCH PROJECTS

Under the contracts with Georgetown, FDA provided partial monetary support to several specialty sections of the laboratory which also received funds from other sources including pharmaceutical manufacturers. Under this arrangement Georgetown researchers were put in the position of receiving support from FDA--a regulatory agency--and from a member of the pharmaceutical industry which was subject to FDA's regulatory authority. FDA was aware, prior to the award of the contract, that the laboratory would receive some support from pharmaceutical manufacturers; however, FDA did not provide in its contracts for disclosure of and safeguards against possible conflicts of interest on the part of contractor personnel conducting studies both for FDA and pharmaceutical manufacturers.

The possibility of conflicts of interest was discussed during conferences between FDA and Georgetown officials in October and November 1968. During these conferences, it was pointed out that FDA might be paying the salaries of individuals at Georgetown who were conducting studies in support of an industry project. During the October conference, the Commissioner of Food and Drugs recommended that a document reviewing the possibility of conflicts of interest be distributed to researchers in the laboratory.

In accordance with the Commissioner's recommendation, the Georgetown project director issued in November 1968 a memorandum emphasizing the need for the researchers to be alert to situations in which conflicts of interest were possible. This memorandum included a statement previously made by the associate dean for research, requiring researchers to inform him of all negotiations for support of research by industry. The memorandum further stated that, because FDA-requested studies often involved problems related to a specific pharmaceutical company's drug, any contact or correspondence with such a company by a laboratory researcher should be fully and openly documented.

In December 1968 FDA officials discussed with the General Counsel of HEW the need for a statement to clarify relationships between the Government, academic researchers, and commercial sponsors. Following these discussions, the Commissioner stated, in a January 1969 memorandum submitted to the Administrator of CPEHS, that a variety of commercial and governmental organizations might be concurrently supporting projects in the same section of the Georgetown laboratory and that such concurrent support could result in the following situations:

1. An investigator performing a study requested by FDA might be conducting a similar or related study on the same drug for its manufacturer.

2. An investigator performing a study requested by FDA might be conducting a similar or related study while acting as a consultant for a manufacturer competing with the manufacturer of the drug under study.

3. An investigator with FDA support might be conducting a study of an investigational drug of interest to him, thus indirectly causing FDA to contribute to the development of the product.

4. An investigator might be acting as a consultant for a manufacturer and be asked by FDA to perform a study on one of the manufacturer's products. A similar situation might occur if the investigator were acting as a consultant to a competing manufacturer.

The Assistant Administrator for Administration, CPEHS, stated in a February 1969 memorandum to the Commissioner that, because of the questions regarding possible conflicts of interest and other problems with the contract, a new contract should be developed containing safeguards in these areas. This was not done because FDA decided in March 1969 to terminate the contract with Georgetown, effective June 30, 1969.

As shown in appendix II, FDA supported a number of Georgetown-initiated studies which also received support from drug manufacturing companies. We discussed these projects with Georgetown officials who acknowledged that

research conducted by the laboratory was supported by FDA, other Government agencies, and drug manufacturers. They told us that researchers in charge of laboratory sections operated semi-independently and that support for their research was channeled through the University from numerous sources. (See app. III.) They told us further that funds provided by FDA were not sufficient to support all the laboratory sections and were made available to those sections which were in greatest need of equipment and salary support.

In May 1969 we discussed with FDA's Deputy Director of General Services the need for contractual safeguards covering situations where, as in the case of the Georgetown contract, contractor personnel may be providing services to FDA and to members of an industry which is subject to FDA's regulatory authority. He informed us that, as a result of the experience with the Georgetown contract, he had been conferring with the General Counsel of HEW on developing an appropriate statement for future contracts which would avoid potential conflicts of interest.

CHAPTER 5

ACCOMPLISHMENT OF CONTRACT OBJECTIVES

FDA's primary reasons for entering into the contracts with Georgetown were (1) to have a readily available facility that would perform, upon request, prompt studies of drugs and other products and (2) to enhance the professional development of the FDA staff by enabling their participation in research and training. Our review showed that these two objectives were not reached, during the 3-year term of the contracts, to the satisfaction of either FDA or Georgetown. Special studies requested by FDA were not completed as promptly as anticipated and FDA personnel participated less than expected in research and training activities of the contractor.

SPECIAL STUDIES REQUESTED BY FDA

In pointing out the need for a readily available laboratory facility during the 1966 appropriation hearings, FDA explained that from time to time problems emerged which involved the testing of drugs and other products and which needed rapid solution. Furthermore, in its request of August 18, 1965, for a contract proposal, FDA stated that speed of compliance was essential and that the special FDA-requested studies should be given priority over other projects. The contract specified prompt performance of drug investigations requested by FDA but did not specifically state that such investigations be given priority over other work of the contractor.

Our review showed that a number of problems were experienced by both parties which delayed the completion of special studies requested by FDA. These problems are discussed in the following paragraphs.

Delay in approval of protocols

For some requested studies FDA delayed approving the protocols[1] submitted by Georgetown, which prevented prompt completion of the studies. In a meeting between FDA and Georgetown officials in August 1968, the Georgetown project director complained of FDA delays in approving protocols for studies. He specifically mentioned two protocols on isoniazid and para-aminosalicylic acid which were submitted on April 11, 1968. According to information furnished to us by the Georgetown project director, these protocols were not approved by FDA until October 15, 1968.

In an October 1968 meeting between FDA and Georgetown officials, FDA's Project Officer stated that one of the difficulties within FDA had been the delay in processing Georgetown protocols on drug equivalency studies requested by FDA. He stated, however, that many of the organizational difficulties causing delays within FDA had been overcome.

Delay in approval of equipment requests

Another problem experienced by FDA and Georgetown was the delay in approving requests for equipment. For example, on February 12, 1968, Georgetown submitted a purchase request for a recorder and scanner, at a total estimated cost of $3,140, for use on an FDA-requested study of comparative therapeutic equivalency of "brand" versus "generic" prednisones. FDA granted approval to purchase this equipment on April 25, 1968--over 2 months after the request was received--even though the original information submitted by Georgetown was used as the basis for approval.

These delays are inconsistent with FDA's statement in the fiscal year 1966 appropriation hearings in the House of

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[1]Protocol is a plan for conducting a research study. It contains background information, justification for the study, proposed research methods, and steps for meeting the project specifications.

Representatives that such studies should be accomplished within 30 to 60 days.

In some instances, Georgetown's equipment requests did not meet FDA standards. FDA's Project Officer stated in an April 12, 1968, memorandum evaluating Georgetown's request for equipment that, in some cases, Georgetown had not provided proper justification of equipment needs. Specifically, he pointed out that the research projects for which the equipment was required were not identified and that the relationship of equipment need to project objectives was not adequately described. In June 1968 he submitted guidelines to Georgetown for preparing requests for equipment.

Uncertain funding status

FDA's commitments for funding the contracts with Georgetown were made for relatively short periods of time, which, according to Georgetown officials, adversely affected its ability to perform services under the contract. The first contract dated February 24, 1966, originally ran from March 1, 1966, to February 28, 1967, but was extended successively to cover four additional periods ending September 30, 1967, November 30, 1967, December 31, 1967, and May 31, 1968. The second contract dated June 21, 1968, originally covered the period June 1, 1968, to January 31, 1969. This contract was extended to March 31, 1969, and then to June 30, 1969.

According to a May 1968 memorandum of contract negotiations between FDA and Georgetown, the contractor was experiencing difficulties in hiring new staff members because of the uncertain status of the contract. FDA's Medical Advisory Board agreed in October 1968 that uncertainties of FDA financial support led to an insecure position at Georgetown. This was also a principal complaint voiced by Georgetown officials to representatives of the Board who visited the laboratory in November 1968.

Not all studies received
contractor's priority attention

According to FDA's Project Officer, Georgetown did not give priority to FDA-requested studies. He stated in a

May 1968 memorandum to the Director of FDA's Bureau of Medicine that, except perhaps for the Georgetown project director, the interest of investigators at Georgetown in collaborating with FDA was minimal. He explained that the project director prepared the protocols and planned the FDA-requested studies and that the technical work was fitted in with other Georgetown programs. Subsequently, in evaluating the contract, FDA's Project Officer stated in a January 1969 memorandum to the Commissioner that Georgetown's progress on the studies had been slow and that he believed Georgetown tended toward giving the FDA projects low priorities by fitting them in with Georgetown's ongoing laboratory research.

Georgetown officials informed us that, in their opinion, prompt attention was generally given to FDA-requested studies; but they conceded that work on the FDA-requested study of the cathartic properities of Decholin was not started because the principal investigator was fully occupied with ongoing laboratory research. We were unable to determine when this study was requested and canceled or the reason why the study was canceled.

Inadequate communications

We found that there was also an apparent problem of inadequate communication between the two contracting parties. A consultant to FDA's Bureau of Medicine stated in a February 1968 memorandum to the Director, Division of Research and Liaison, Bureau of Medicine, that coordination and communication between the Georgetown investigators and the FDA staff could be improved. He noted that FDA seemed to have submitted informally some of its requests for studies and that inadequate communications apparently had led to results that were less than satisfying.

FDA's Project Officer stated in a May 1968 memorandum to the Director, Bureau of Medicine, that closer collaboration was needed; and he recommended a high-level conference between FDA and Georgetown. Such a meeting was held in August 1968, at which time the Georgetown project director stated that communications between his group and FDA had practically ceased to exist. At that time, it was

agreed that periodic sessions would be held to exchange information. We noted that, beginning in October 1968, several of these sessions were held.

One factor which may have added to the difficulties in communication between FDA and Georgetown was the frequent replacement of the FDA Project Officer assigned to administer the first contract. During the first contract period, March 1966 through May 1968, four project officers were successively appointed. A December 1968 report by representatives of FDA's Medical Advisory Board who visited Georgetown in November stated that the Georgetown staff had complained that changes in personnel at FDA made communications difficult.

Unforeseen difficulties

In our discussions regarding reasons for delays in performing FDA-requested studies, Georgetown officials told us that some of the studies took longer to complete than anticipated because of unforeseen difficulties experienced during their performance. They cited in particular the following example:

Study No. 17: Meprobamates

February 15, 1968	Georgetown submitted protocol for study to FDA.
February 21, 1968	FDA approved protocol.
March 1, 1968	FDA notified Georgetown to discontinue the study but shortly thereafter approved its continuation. Subsequently, problems were encountered in performing drug measurements because established scientific procedures being used did not give sufficient accuracy.
November 27, 1968	Georgetown submitted a purchase request for a sandbath which was needed to obtain accurate measurements of Meprobamates.

January 2, 1969 — FDA approved acquisition of this equipment. According to the Georgetown project director, the American supplier did not have this particular piece of equipment in stock; therefore, the sandbath was ordered from the German manufacturer. The Georgetown project director told us that the equipment was shipped in about a month but that delivery was further delayed because of a dock strike. The equipment was not received until May 1969. (See app. I for status of this project.)

Other examples of unforeseen difficulties which delayed completion of FDA-requested studies were cited by the Georgetown project director. For example, established scientific procedures used for conducting drug measurements and studies proved to be unsatisfactory on two studies. Also, some of the work on another study was subcontracted and the subcontractor failed to perform the work promptly. In May 1969 the overall status of the 28 studies requested by FDA was as follows:

Completed	9
Still in progress	11
Terminated after work began	1
Not started	3
Cancelled before work began	4
Total	28

PROFESSIONAL DEVELOPMENT OF FDA STAFF

A specific objective of the Georgetown contracts was to enhance the professional development of the FDA staff by their participation in research projects, lectures, conferences, clinics, and other activities.

Our review showed that several problems were encountered which adversely affected the participation of FDA personnel in research projects. A consultant to the Bureau of Medicine pointed out as early as December 1967 that only two members of the FDA staff had participated in research projects at Georgetown; however, at that time he believed that it was too early to draw any definite conclusions as to the success of the professional development program.

Representatives of FDA's Medical Advisory Board participated in the consultant's evaluation of the contract. One of the representatives stated at the December 1967 Board meeting that there was not as much participation in research and education activities by the FDA staff as had been expected. He also noted that most of the research projects suggested by FDA personnel for professional development purposes were not well conceived and were not undertaken. The representatives recommended that FDA officials suggest to their staff the importance of research possibilities at Georgetown. They also recommended that FDA scientists spend some of their own time on research because time available during working hours is limited.

Our discussions with FDA officials confirmed that FDA personnel had limited time available for research, which contributed to the lack of participation in University activities. According to FDA officials, only six FDA employees had participated as of May 1969 in research at Georgetown over the 3-year duration of the contracts.

In a January 1969 memorandum to the FDA Project Officer, representatives of FDA's Medical Advisory Board pointed out problems with regard to adequate participation by FDA staff members in research projects at Georgetown. The representatives stated that a number of the Georgetown faculty were

resistant to the concept of joint planning of investigations by FDA and medical school personnel.

It appeared that part of the problem was also attributable to FDA's delay in appointing a professional development officer. In a memorandum to the Commissioner dated January 31, 1969, FDA's Project Officer stated that the collaboration with Georgetown and the organization of the training program had been hindered by the failure of FDA to appoint such an official. In February 1969 FDA appointed a professional development officer to provide guidance and assistance to personnel interested in research and training activities, including the training contemplated under the Georgetown contracts.

Some problems were also encountered regarding participation in the lecture portion of the training program. In December 1967 the special consultant to the Bureau of Medicine pointed out that most of the Georgetown lectures had been given at D.C. General Hospital, which made it difficult for FDA staff members to attend because of the loss of time involved in traveling to and from the hospital. He recommended that more lectures be held at FDA offices. The location of the lectures was discussed by FDA and Georgetown officials in May 1968, at which time Georgetown officials agreed to consider holding future lectures at FDA rather than at D.C. General Hospital.

After the award of the second contract in June 1968, more lectures were held at FDA and FDA officials informed us that this change in location substantially increased participation. They estimated that 6 to 12 persons had attended each session when the lectures were held at D.C. General Hospital, whereas from 25 to 60 persons had attended the sessions held at FDA offices.

CONCLUSIONS

In general, we believe that communication and understanding between FDA and Georgetown concerning the principal contract objectives and the methods by which these objectives could best be accomplished were inadequate. As a result, these objectives were not met to the full satisfaction of either contracting party.

We believe that FDA should have taken certain administrative actions to minimize the problems discussed in this report. The contracts should have contained specific requirements for justifying the purchase of equipment. Also, if the time factor was as important as indicated by FDA in the House appropriation hearings for fiscal year 1966 and in FDA's request for contract proposals issued in 1965, the contract should have provided that FDA-requested studies be given priority over studies initiated by the contractor.

Furthermore, inasmuch as FDA considered the professional development of its personnel to be an important objective of the contract, a more formal training program should have been established.

We believe that these actions should be considered in the event that future contracts of this nature are awarded by FDA.

CHAPTER 6

SCOPE OF REVIEW

Our review was directed toward specific areas of concern, in the administration of the contracts with Georgetown University, as expressed to us by the Subcommittee staff--such as selection of the contractor, FDA's authority for awarding the contracts, relationship of research supported by FDA to its mission, and the extent of multiple support of research projects by FDA and other sources, including pharmaceutical manufacturers. Our review was also concerned with other aspects of administration of the contracts and the accomplishment of contract objectives.

We examined pertinent contract files available at FDA and applicable contract data and accounting records at Georgetown. We also held discussions with FDA and Georgetown officials.

APPENDIXES

GEORGETOWN UNIVERSITY

LABORATORY OF CLINICAL PHARMACOLOGY

STATUS OF FDA-REQUESTED STUDIES

AS OF MAY 15, 1969 (note a)

Requested study and purpose	Date requested	Date started	Date completed or status
No. 1. Measurin--To determine whether there was any difference between the effect of Measurin and Bufferin on fecal blood loss in human subjects	7-66	8-66	11-66
No. 2. Effects of gelatin on fingernail growth and strength	Canceled by FDA		
No. 3. Mellaril (Thioridazine)--To investigate the cardiotoxic properties of Mellaril (a tranquilizing drug) to determine if it produces arrhythmais (irregularity of heartbeat)	9-66	Approximately 9-66	8-67
No. 4. Diapulse--Trial of the efficacy of Diapulse shortwave therapy in the treatment of otitis media and arthritis	10-66	1-67	2-67
No. 5. Carmine Red--Sterilization of Carmine Red--a substance derived from ground-up beetles	After 8-66	12-66	2-67
No. 6. Behavioral dependence on central nervous system tropic drugs--To determine the neurophysiological aspects of drug dependence and withdrawal	Prior to 10-66	1-67	Nearing completion
No. 7. Cross-dependence and cross-tolerance produced by central nervous system depressant drugs--To determine if certain of the widely used minor tranquilizing drugs will substitute for other central nervous system depressant agents to which tolerance and withdrawal symptoms have been produced in rats	Prior to 10-66	1-67	Nearing completion
No. 8. Effects of various chemical agents on learning--To attempt to determine the effect of various chemical compounds on the learning process in rats	Prior to 10-66	1-67	Nearing completion
No. 9. Behavioral teratology		Never started	
No. 10. Cardiovascular effects of drug tolerance and dependence		Never started	
No. 11. Detection of aflatoxin and other mycotoxins--To study the immunological aspects of aflatoxin as it possesses high lethality even in small doses	Approximately 12-66	3-67	Terminated during 2-68
No. 12. Toxic effects of Sominex--To investigate the mydriatic effects of Sominex to determine if products containing the same chemical produce dilation of the pupils	12-66	5-67	5-68
No. 20. Decholin--To study the cathartic properties of this drug as industry made claims of its efficacy and the literature made claims of denial of its efficacy		Canceled by FDA	

GEORGETOWN UNIVERSITY

LABORATORY OF CLINICAL PHARMACOLOGY

STATUS OF FDA-REQUESTED STUDIES

AS OF MAY 15, 1969 (note a) (continued)

Requested study and purpose	Date requested	Date started	Date completed or status
No. 21. Collyria--To investigate the toxic effects of pupillary dilator drugs in Collyria	12-67	5-68	Completion expected 6-69
No. 25. Comparability of various erythromycins		Canceled by FDA	
No. 26. Tolbutamide studies in animals		Never started	
Task Order A: Evaluation of external cardiac defibrillators--To establish (1) the relative safety and efficacy (in dogs) of this alternating current defibrillator and of a commercially available direct current defibrillator and (2) a model experimental system for testing of defibrillators	8-68	9-68	11-68
Task Order B: Biostatistical analysis of drug comparability data--To analyze the results of FDA-conducted biologic availability comparisons of different products of various antibiotics		Never officially formulated as a Task	
Comparative studies of therapeutic equivalency of "brand" versus "generic" drugs--To compare the pharmacologic availability of various theoretically equivalent drug products in man			
No. 13. Diphenylhydantoin	7-67	10-67	Spring of 1968
No. 14. Prednisone	Spring of 1967	Fall of 1967	Completion expected 6-69
No. 15 Chloramphenicol	Prior to 9-67	9-67	10-67
No. 16. Sulfisoxazoles	-	1-68	2-68
No. 17. Meprobamates	-	2-68	(b)
No. 18. Tripelennamine	Fall of 1967	1-68	(b)
No. 19. Diphenhydramine	Fall of 1967	1-68	(b)
No. 22. Ferrous sulfate	-	2-68	Completion expected 6-69
No. 23. Isoniazid		Canceled by FDA	
No. 24. Para-aminosalicyclic acid	3-68	11-68	Completion expected 6-69

[a]The information in this appendix is based on FDA records, progress reports submitted by Georgetown, and our discussions with FDA and Georgetown officials.

[b]Studies are to be completed by FDA subsequent to June 30, 1969.

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GEORGETOWN-INITIATED PROJECTS

RECEIVING FDA SUPPORT (note a)

Georgetown project	Sources of support
CARDIOVASCULAR PHARMACOLOGY SECTION:	
Chemotherapy of hypertension	Veterans Administration (VA) prime support FDA partial support
Cooperative study on antihypertensive agents and morbidity	VA prime support FDA partial support Drug industry partial support
Comparison of potassium-losing and potassium-sparing diuretics and diuretic combinations	FDA partial support VA prime support
Trial comparing Catapres and Methyldopa in treatment of hypertension	Drug industry prime support FDA partial support
INFECTIOUS DISEASES SECTION:	
Controlled, double-blind trial--Efficacy of high doses of adrenal cortico-steroids versus placebo in acute, severe, life-threatening bacterial infections	FDA total support
Renal clearance of nephro toxic antibiotics in patients with degrees of renal disease	FDA total support
Comparative bactericidal action Kinetics of Kanamycin, Gentamicin, and the Polymyxins	FDA total support
Controlled trial--Comparative efficacy of Cephaloridine, Lincomycin, and Nafcillin in the management of acute gram-positive coccal infections	FDA partial support Drug industry prime support
Controlled trial--Initial presumptive therapy for serious acute gram-negative rod infections	FDA partial support Drug industry prime support
ONOCOLOGY SECTION:	
Nonsurgical treatment of pulmonary neoplasm	Public Health Service (PHS) prime support FDA partial support

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GEORGETOWN-INITIATED PROJECTS

RECEIVING FDA SUPPORT (note a) (continued)

Georgetown project	Sources of support
ONOCOLOGY SECTION (continued):	
Clinical trial of Hadacidin (NSC-521778) at three fractionated dose levels	National Cancer Institute--PHS prime support FDA partial support
A clinical pharmacologic study of chemotherapy and X-ray therapy in lung cancer	National Cancer Institute--PHS prime support FDA partial support
Phase 1 studies of porfiromycin (NSC-56410)	National Cancer Institute--PHS prime support FDA partial support
PSYCHOPHARMACOLOGY SECTION:	
Studies of the local anesthetic receptor	PHS prime support FDA partial support
Studies of the actions of Droperidol in cats	General Research Support prime support FDA partial support
Studies of the role of sympathomimetic drugs in the superior cervical ganglion of cats	General Research Support prime support FDA partial support
Development of a method for localized perfusion of the fourth ventricle in unanesthetized decerebrate cats	FDA full support
RENAL PHARMACOLOGY AND TOXICOLOGY SECTION:	
Study of the application of dialytic techniques for the treatment of chronic renal failure	FDA partial support Primary sources--John A. Hartford Foundation, Georgetown University Kidney Research Fund; Pharmaceutical Manufacturers Association Foundation
Clinical and toxicological investigation of dialyzable poisons	Same as above
Investigation of certain aspects of applied renal physiology	Same as above

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GEORGETOWN-INITIATED PROJECTS

RECEIVING FDA SUPPORT (note a) (continued)

Georgetown projects	Sources of support
NEUROPHARMACOLOGY SECTION:	
Metabolism of L-DOPA in patients with Parkinson's disease	Drug industry prime support FDA partial support
Metabolism of diphenylhydantoin in patients with diphenylhydantoin-resistant epilepsy	FDA total support
Relationship of blood and cerebrospinal fluid levels of diphenylhydantoin	FDA total support
Alteration of diphenylhydantoin in blood levels as a result of simultaneous therapy with barbiturates	FDA total support
The value of creatine phosphokinase levels in cerebrospinal fluid as an aid in the diagnosis of brain tumors	FDA total support
Oral absorption studies in zarontin	Drug industry prime support FDA partial support
Gas chromatography analysis of Dilantin metabolites in urine and blood	Drug industry prime support FDA partial support
Disc electrophoresis on spinal fluid in the normal as compared to the patient with multiple sclerosis and other neurologic diseases	FDA total support
Fluorometric measurement of spinal fluid protein	FDA total support
Chromatographic separation and fluorometric measurement of spinal fluid gamma globulin	FDA total support

[a]The information in this appendix is based on progress reports submitted by Georgetown and our discussion with the project director at Georgetown.

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SOURCES OF SALARY SUPPORT FOR GEORGETOWN

RESEARCHERS WORKING ON FDA-REQUESTED PROJECTS (note a)

Researcher	FDA requested studies being worked on	Sources of researchers' salary support as of February 1969	Percentage of support
A	Nos. 1, 4, 13, 15, and 24	FDA contracts	80
		Georgetown University	20
B	Nos. 1, 2, 13, 14, 16, 18, 19, 20, and Task Order "B"	FDA contracts	72.5
		Georgetown University Computer Center	27.5
C	No. 13	FDA contracts	100
D	Nos. 1, 14, 16, 17, 18, 19, and 24	Department of Biochemistry, Georgetown University	27
		Georgetown Clinical Laboratory	66
		General research support grant--medical, National Institutes of Health	4
		General research support grant--dental, National Institutes of Health	3
E	No. 1	Professional education improvement grant, National Institutes of Health	16
		Follow-up study in area of preventive medicine (National Institutes of Health and Ford Foundation)	52
		General research support grant, National Institutes of Health	24
		Ford Foundation Research Center	8
F	No. 1	General research support grant, National Institutes of Health	39
		National Institutes of Health	22
		Grant support with co-researcher, National Institutes of Health	13
		Professional education improvement grant, National Institutes of Health	22
		Grant support with co-researcher, National Institutes of Health	4
G	No. 3	Veterans Administration	100
H	No. 4	Training grant, National Institutes of Health	100

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LABORATORY OF CLINICAL PHARMACOLOGY

SOURCES OF SALARY SUPPORT FOR GEORGETOWN

RESEARCHERS WORKING ON FDA-REQUESTED PROJECTS (note a) (continued)

Researcher	FDA requested studies being worked on	Sources of researchers' salary support as of February 1969	Percentage of support
I	Nos. 5 and 16	Department of Microbiology, Georgetown University	18
		Georgetown Clinical Laboratory	66
		Department of Medicine, Georgetown University	7
		General research support grant, National Institutes of Health	9
J	Nos. 12 and 21	D.C. General Hospital	100
K	Nos. 6, 7, and 8	FDA contracts	100
L	Nos. 14, 17, and 19	FDA contract ($2,400)	Unknown
		D.C. General Hospital	"
M	Nos. 18 and 20	Professional education improvement grant, National Institutes of Health	43
		Department of Medicine, Georgetown University	57
N	No. 22	General research support grant, National Institutes of Health	37
		Department of Medicine, Georgetown University	63
O	No. 24	Department of Medicine, Georgetown University	100
P	Task order "A"	Heart Institute training grant, National Institutes of Health	71
		Heart Institute teaching grant, National Institutes of Health	29

[a]This information was obtained from Georgetown officials.