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SUPPLEMENT

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* OFFICIAL LEUKEMIA SOCIETY LIST OF GRANTS reprinted from recent report...(Page S-5)

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* OFFICIAL REPORT OF SENATE APPROPRIATIONS CMTE. ACTION on H-E-W health appropriations for the fiscal year which began July 1, but not covering appropriations for NIH, which were detailed in portion of cmte. report reprinted in "The Blue Sheet" Supplement Aug. 7, is photographically reproduced in this issue. The entire report will be debated by the Senate upon its return Sept. 4 from the Natl. Party Conventions recess; is expected to be adopted with little or no change, then go to a conference cmte. for adjustment of the differences between House and Senate before returning to each house and then the President for approval. Final appropriations could be made as early as October, as late as December:

KEY PORTIONS OF GENERAL ACCOUNTING OFFICE'S REPORT TO CONGRESS ON PROBLEMS HAMPERING THE USE OF GOVT.-SPONSORED DRUG RESEARCH

(A report sent by the Comptroller General of the U.S. Elmer Staats to the President of the Senate and Speaker of the House on August 12)

INTRODUCTION

The General Accounting Office has examined into the administration of grants for research in medicinal chemistry awarded to public and private institutions by the Department of Health, Education, and Welfare (HEW). These grants were administered by the National Institutes of Health (NIH) as a constituent bureau of the Public Health Service (PHS) until April 1, 1968, when NIH was established as a separate operating agency within HEW. Our review was made pursuant to the authority of the Budget and Accounting Act, 1921 (31 U.S.C. 53), and the Accounting and Auditing Act of 1950 (31 U.S.C. 67).

Our review was directed primarily toward departmental policies and procedures and practices of NIH and other cognizant organizational units of HEW for facilitating the achievement of research objectives in the potential development of drugs and obtaining optimum benefits toward the treatment of diseases and disabilities of man. This particular aspect of the administration of grants for research in medicinal chemistry was reviewed by us because we noted indications that certain university research investigators were having difficulty in obtaining suitable means for screening and testing compounds prepared by them for further development into useful medicinal drugs. ****

BACKGROUND

Under the Public Health Service Act (42 U.S.C. 241), HEW has broad responsibilities to promote and coordinate research in the field of health and to make information concerning such research and its practical application available to the public. Under this authority, the Surgeon General, through NIH, has made grants-in-aid to support research in universities, colleges, hospitals, laboratories, and other public and private institutions. Medicinal chemistry is one of the important research areas supported by Federal grants.

General Information On Medicinal Chemistry Grants

NIH has two Medicinal Chemistry Study Sections responsible for the scientific review of grant applications and for recommending those areas in which research in medicinal chemistry should be performed. According to NIH statistics, during fiscal year 1967 about 560 grants, totaling about $13 million, were awarded to grantee institutions for support of research in medicinal chemistry. During fiscal years 1962-67, PHS awarded about 3,000 grants, totaling about $53 million, for this type of research. These grants are intended to encourage research and to stimulate new investigations in fields needing exploration, including the discovery of potential drugs that may be developed for use in the prevention and treatment of diseases and disabilities of man.

Seven of the eight institutes of NIH, together with the National Institute of Mental Health (NIMH),[1] support medicinal chemistry investigations in the areas of their own research interest. For example, the National Cancer Institute supports investigations in the preparation of compounds for use in the chemotherapy treatment of leukemia and other forms of cancer while support for preparation of compounds for use in the treatment of hypertension is provided by the National Heart Institute.

Grants for research in medicinal chemistry are awarded to institutions in behalf of investigators to support programs which usually involve the preparation of chemical compounds. Depending upon the investigators' particular approach, new compounds may result from either isolation of potentially active substances from natural materials or preparation of potentially active compounds from various chemical materials.

Development of a compound into a medicinal drug involves numerous steps which can be broadly classified as screening and testing. Screening involves a determination of biological activity and potential usefulness of a compound. Screening may be provided in two general categories, broad screening and specific screening. Broad screening is generally designed to evaluate many compounds quickly and to reveal

[1] The NIMH grants included in our review were awarded when NIMH was a part of NIH. On January 1, 1967, NIMH was constituted as a separate bureau.

biological activity in areas that may need more specific screening. Specific screening is designed to provide preliminary data on the utility of compounds which is used to support an investigational new drug application to the Food and Drug Administration (FDA)

Compounds which indicate activity in an area of particular interest are subjected to testing to obtain further information. Testing is generally conducted in two phases -- first on animals and then on humans -- and is designed to provide the data necessary to support a new drug application to the FDA.

Facilities for screening or testing compounds such as those prepared under NIH-supported research comprise four general sources: Government test services, commercial and nonprofit testing laboratories, academic institutions, and the pharmaceutical industry. The principal Government test services used by NIH are the Cancer Chemotherapy National Service Center for cancer chemotherapeutic agents and the Walter Reed Army Institute of Research for antimalarial agents. The findings discussed in this report contain specific comments concerning the availability and adequacy of the several sources of screening and testing services.[1]

Patent Aspects Of Medicinal Chemistry Grants

The scientific and technological advances resulting from NIH-supported research activities frequently include patentable inventions such as potential new drugs. These inventions are subject, in general, to the provisions set forth in the President's 1963 overall Statement of Government Patent Policy and are governed, in particular, by HEW's patent regulations.

In October 1963, the President issued a Statement of Government Patent Policy which provides that the Government be responsible for full exploitation of inventions for the public benefit. This statement of policy seeks to protect the public interest by encouraging the Government to acquire the principal rights to inventions in situations where the nature of the work to be undertaken or the Government's past investment in the field of work favors full public access to resulting inventions. Specifically, the statement calls for the Government to normally acquire the principal or exclusive rights to inventions resulting from research which directly concerns the public health or public welfare.

On the other hand, the policy recognizes that the public interest might also be served by according exclusive commercial rights to the contractor in situations where the contractor has an established nongovernmental commercial position and where there is greater likelihood that the invention would be worked and put into civilian use than would be the case if the invention were made more freely available.

The HEW patent regulations in effect since 1955 specify that the results of research supported by grants shall be used in the manner which will best serve the public interest. The HEW patent regulations as contained in the Code of Federal Regulations (42 CFR, pts. 6 and 8) provide:

> "* * * in some cases it may be advisable to permit a utilization of the patent process in order to foster an adequate commercial development to make a new invention widely available. Moreover, it is recognized that inventions frequently arise in the course of research activities which also received substantial support from other sources, as well as from the Federal grant. It would not be consistent with the cooperative nature of such activities to attribute a particular invention primarily to support received from any one source. In all these cases the Department has a responsibility to see that the public use of the fruit of the research will not be unduly restricted or denied."

HEW policies governing the treatment of inventions are designed to afford suitable protection to the public while giving appropriate recognition to the legitimate interests of others who have contributed to the invention. The regulations require that all inventions arising out of activities supported by the grants be promptly and fully reported to the agency. The regulations require further that each grant contain a provision that ownership of inventions and disposition of all rights be determined by either the responsible agency official or, except for foreign rights, the grantee institutions whose established policies and procedures have been approved by the agency.

[1] The terms screening and testing are often used interchangeably. In subsequent sections of this report, the terms are used in accordance with the usage made by investigators and by others interviewed by us.

As a condition of each research grant, the Surgeon General was responsible, in accordance with HEW regulations, for determining the ownership and disposition of all rights to any invention resulting either directly or indirectly from PHS grants; in October 1966, this responsibility was transferred to the Assistant Secretary for Health and Scientific Affairs, HEW.

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FINDINGS AND RECOMMENDATION

Need To Provide Improved Means To Facilitate Screening And Testing Of Compounds Prepared Under Grants For Research In Medical Chemistry

Our review of the administration of medicinal chemistry research grants showed a need for providing improved means to facilitate the screening and testing of compounds prepared under the grants and to assist in obtaining optimum benefits from the research in the form of new drugs.

We found that many grantee investigators had been unable to obtain the screening and testing services necessary to determine the usefulness of compounds prepared during their research. Although these research efforts tend to provide useful scientific information in the area of health-related chemistry, the usefulness of such research would be greatly enhanced if the compounds received the timely screening and testing necessary to determine their potential medicinal value in the treatment and cure of human diseases.

Grantee investigators at eight of the 10 universities at which our review was made have encountered difficulties in obtaining the screening and testing services which they believe are essential to the development and practical application of new compounds. They told us that previously these services had been obtained from the pharmaceutical industry but that since 1962, when PHS revised its patent procedures and required a formal patent agreement, this cooperation had no longer been forthcoming and no adequate substitute services had been available.

Prior to 1962, pharmaceutical companies had routinely made tests, at no charge, on compounds developed by grantees. The companies received several benefits in return for providing the test services. In general, they acquired certain rights to the development and marketing of promising compounds, without incurring the cost of synthesizing the compounds to be screened and tested.

Grantee investigators advised us that generally screening and testing by Government facilities, by commercial or nonprofit testing laboratories, and by academic institutions had been adequate for determining a specific activity or effect but that these sources had been found unsatisfactory as they had not provided the broad-scale screening which the investigators considered necessary for developing synthesized compounds into potential new medicinal drugs. Some investigators advised us that they were redirecting their research by concentrating on more basic chemistry studies while others were directing their research around the need for screening and testing.

We found that the difficulties encountered in obtaining screening and testing services were related to certain problems in the administration of the Department's regulations concerning invention rights which needed resolution. Involved here is the determination of ownership and disposition of inventions conceived under HEW grants, which was a factor contributing to the reluctance of industry to provide services to grant-supported investigators.

On the basis of our observations, we proposed that the Department direct its efforts toward timely determination of rights to potentially patentable inventions, in order to reduce uncertainties as to the status of invention rights. We proposed also that the Department clarify the intended use of institutional patent agreements of which only limited use had been made but which appeared to be a useful device for assigning ownership rights while protecting the public interest.

Our findings on the difficulties encountered in obtaining screening and testing services for NIH-supported grants in medicinal chemistry and in the administration of HEW regulations concerning invention rights, together with the views of cognizant Government and non-Government officials, are further discussed in the following sections. The Department's comments on our findings, which were furnished to us by letter dated March 20, 1968, from the HEW Assistant Secretary, Comptroller, are summarized starting on page S-42 and are included in full as appendix II to this report.

Difficulties Encountered In Obtaining Screening And Testing Services

We discussed with 38 investigators the results of their NIH-supported research efforts. Many of these investigators informed us that the cooperation of the pharmaceutical industry generally ended in early 1962 when PHS required the use of a formal patent agreement which was a part of the investigator's application and part of the terms and conditions of the grant whenever a commercial organization became involved in the research. The agreement provided that any invention which arose or which was developed during the course of the work aided by the grant would be referred to the Surgeon General for determination as to whether patent protection should be sought and for the disposition of rights under any patent issues thereon.

The provision regarding determination of invention rights has been a part of the investigator's application since the 1940's. We were advised by the Assistant Secretary, Comptroller, of HEW that the amended patent agreement of 1962 did not involve any change in PHS policy but that it merely formalized in writing the relationship and respective rights of the parties in light of the investigator's obligations to the PHS under the grant agreement. Also, in 1962 PHS strengthened its procedures for the required reporting of inventions.

The agreement contained a number of conditions governing the submission of chemical compounds to pharmaceutical companies for screening purposes, including a provision that the Government shall reserve a nonexclusive, irrevocable, royalty-free license with the power to sublicense for all Government purposes. One condition specified that:

> "The pharmaceutical company shall be permitted to obtain patent rights to new uses of compounds developed at its own expense, except where the grantee contributed or participated in the conception or reduction to practice of such new use . . . , or where such new use is within the field of research work supported by the grant."

Representatives of the Pharmaceutical Manufacturers Association (PMA) advised us that, because of uncertainty concerning the interpretation of new use rights, its members had declined to sign the patent agreement and had discontinued screening and testing services for compounds prepared under NIH-financed research. Officials at two pharmaceutical firms, with whom we met to discuss problems involved in providing screening and testing services for NIH-supported investigators, informed us that they had considered exclusive invention rights to be necessary to permit recovery of research and development costs and that assurance of invention rights was not provided in the 1962 patent agreement.

We found that during recent years HEW has considered a number of changes in its patent agreement adopted in 1962 for use by grantees in connection with compounds to be submitted for screening and testing. During fiscal year 1967, while our review was in progress, HEW prepared a revised patent agreement which was intended to clarify the rights of the contracting parties. This agreement differs significantly from that originally required in 1962 in that it does not restrict the tester's rights of ownership to new uses of compounds which it may discover at its own expense without the participation or suggestion of the PHS investigator even "where such new use is within the field of research work supported by the grant."

Representatives of the PMA advised us that, although recognizing that the proposed agreement would not solve all problems in this complex area, they endorsed it as a progressive measure. They pointed out, however, certain ambiguities which they believe require further clarification, in particular with respect to the rights of a tester who develops at his own expense a first utility completely unrelated to the subject matter of the grant and with respect to the interpretation of the term "co-inventor" as it applies to the relationship between tester and grantee, when the latter asserts a right because of his prior suggestion of possible medicinal value of large fields of compounds.

Because of the reluctance of pharmaceutical firms to sign the patent agreement adopted in 1962, a review was made by the NIH committee on Biological Testing which in its May 1962 report stressed the urgency of developing biological testing facilities in academic institutions.

The report of the NIH committee stated that the patent regulation was "depriving medicinal chemists of the most important source of help in determining biological activity." The committee agreed to compile a list of testing facilities and, as a result, an NIH booklet "Biological Testing Facilities" was published in

September 1963. The booklet contained only names of academic institutions, commercial and nonprofit laboratories, and Government facilities. Representatives of several pharmaceutical firms advised NIH that, because of the provisions in the patent agreement concerning the determination of invention rights, it would not be advisable to include the names of their firms in the booklet.

In commenting on Government-supported testing facilities, such as those that exist for cancer or malaria, grantee investigators generally agreed that they provide adequate screening and testing services in their particular disease area but pointed out that they do not provide for the necessary broad-scale screening. For example, an official of the National Cancer Institute has stated to us that the Cancer Chemotherapy National Service Center (CCNSC) does not send left-over compounds received from grantee investigators to other laboratories for testing in other disease areas but relies on the grantee investigators to obtain such services. Moreover, Government facilities are not available in all disease areas, and one which had been included in the NIH booklet, the Psychopharmacology Service Center of the National Institute of Mental Health, discontinued its services in 1964.

Commercial and nonprofit testing laboratories offer screening and testing services both directly to grantee investigators and indirectly as contractors for Government testing facilities. Direct testing services are usually limited to the tests requested. A letter from a commercial laboratory to one of the investigators we interviewed indicates that broad screening is available but that only limited tests on humans are performed as the laboratory is basically a service organization not concerned with drug development.

Grantee investigators may also obtain screening and testing services from academic colleagues in other health-related disciplines, such as pharmacology and physiology. However, 10 of the investigators contacted told us that these services were limited in scope and that there were delays in receiving the results; limitations result from the fact that their testing needs do not always correspond to the independent research programs of their colleagues. We also have been informed that academic testing services do not provide the screening and testing necessary to develop promising compounds because their emphasis is on scientific knowledge and not on utilization.

* * * * * * *

Change In Direction Of Research

We found that, within the broad terms of the grants, several grantee investigators have redirected their research efforts away from the objective of developing compounds having potential new medicinal value in the prevention and treatment of human disorders. Some investigators are concentrating on basic chemistry studies even though they had originally proposed to prepare compounds with potential medicinal value in several areas of health. We were advised by other investigators that, because of their awareness of testing problems encountered by others, they intentionally directed their research around the need for testing. The following cases illustrate the changes being made in the direction of the research effort in certain medicinal chemistry grants as a result of the difficulties being encountered in obtaining adequate screening and testing services.

1. At one university an investigator received grants of about $49,000 during the period 1962-66 from NIGMS. The investigator was preparing various kinds of potential medicinal agents when he applied for the PHS grant. In his application the investigator stated that he planned to obtain screening and testing from a pharmaceutical firm.

   Subsequently, he received a commitment from the firm for these services. However, in May 1962, the firm advised him that it was opposed to the signing of the patent agreement required by PHS. The investigator made alternate testing arrangements with a commercial testing laboratory and later with a university pharmacologist for specific types of tests, but not for broad screening. The investigator has informed us that he is currently interested in the study of how drugs work and that he is studying specific drugs whose medicinal value is already known, rather than concerning himself with developing new drugs.

2. Another investigator, who received grants of about $66,000 for the period 1962-66, proposed in his initial grant application to submit his compounds to routine screening in order to obtain as broad an evaluation as possible.

The investigator stated that his attempts to obtain screening and testing from the pharmaceutical industry were unsuccessful and that he finally made arrangements with a university pharmacologist who provided limited services. The investigator informed us that his current research goals were limited and that his testing needs were also limited. He said that the broad testing proposed in the original grant application was still valuable and that, if it had been obtained from industry, the direction of his research might not have changed.

On the basis of the several grants reviewed by us and of discussions with grantee investigators, it appears to us that the difficulties encountered by grantee investigators in obtaining adequate screening and testing of compounds have adversely affected the achievement of important objectives of research grants in medicinal chemistry. These difficulties, which many of the investigators attributed to the inability to obtain the cooperation of the pharmaceutical industry and the unavailability of adequate alternative sources of screening and testing, also seem to be related to certain problems in the administration of HEW regulations concerning invention rights, which are discussed in the subsequent section of this report.

Difficulties In Administration Of Regulations Concerning Invention Rights

We noted certain difficulties in the administration of regulations concerning invention rights which needed resolution to facilitate the development of grantee investigators' discoveries of potential new drugs. These difficulties involved the determination of ownership and disposition of inventions conceived under PHS grants for research in medicinal chemistry, which we found was a factor contributing to the reluctance of the drug industry to provide screening and testing services to NIH-supported investigators.

It is the general policy of HEW that the results of Department-sponsored research should be made widely, promptly, and freely available to other research workers and to the public. At the same time, the policy recognizes that in some situations, and particularly where commercial development of inventions will be costly, the public interest can best be served if a developer is granted some exclusivity for a limited time. However, we were advised by HEW officials that, in view of an opinion of the Attorney General (34 Op. Atty. Gen., 320,328 (1924)), HEW could not guarantee exclusive licensing of inventions. HEW officials told us that this opinion generally had been interpreted as holding that agencies may not grant exclusive licenses under Government-owned patents without specific statutory authority.

HEW regulations (45CFR8) require that all inventions arising out of activities supported by grants shall be promptly and fully reported to the agency. The regulations, as quoted on page S-34, permit a utilization of the patent process in order to foster adequate commercial development to make new inventions widely available to the general public. The regulations specify that determination of ownership and disposition of invention rights may be made by either the responsible official on a case-by-case basis (sec. 8.1(a)) or, except for foreign rights, under blanket "institutional agreements" by grantee institutions whose policies and procedures have been approved by HEW (sec. 8.1(b)).

The regulations (sec. 8.2) provide four criteria for use by the responsible HEW official in determining disposition of rights under section 8.1(a). One of the criteria (sec. 8.2(b)) states that an invention may be assigned by HEW to a "competent" organization if it will be more adequately and quickly developed for widest use, providing there are adequate safeguards against unreasonable royalties and repressive practices.

In accordance with the general policy concerning publication or patenting of inventions, we found that HEW generally followed the practice of disseminating the results of PHS-sponsored research to other research workers and to the public through publication. Publication has the effect of making the results of research freely available to all interested parties and, subject to existing patents, permits nonexclusive exploitation of the discovery. However, we have been advised by representatives of the pharmaceutical industry that, since commercial development of new drugs is generally costly, the industry will not undertake this development unless some form of exclusivity can be obtained.

During our review, several grantee investigators informed us that, in their opinion, publication of the results of their research was not an adequate means to ensure development of promising compounds into new drugs. In addition, we noted that in April 1962 the Director of the National Cancer Institute advised the Surgeon General that it was doubtful that the policy of emphasizing dedication of inventions to the public

through publication would make inventions available or that such a policy would always serve the public interest. He stated that a no-patent concept delayed the marketing of inventions because there was no protection for the investment of the developer.

Assignment Of Invention Rights By HEW

Our review showed that HEW had not taken timely action to determine the disposition of rights to certain inventions and that only limited use had been made by HEW of the authority provided in the regulations to assign invention rights to "competent" organizations, such as grantee institutions. We found that, at the time of our fieldwork in January 1967, HEW had not acted upon several petitions which had been received from grantees for assignement of rights. We found also that, from 1962 through June 30, 1965, HEW had assigned invention rights to grantees in only one situation. NIH records showed that, during the 1962-65 period, grantees had reported a total of 682 inventions resulting from NIH-sponsored research and that numerous requests had been received for assignment of rights.

Subsequent to reporting inventions, grantee organizations may petition HEW for assignment of invention rights on an individual case basis. In such instances pursuant to section 8.1(a) the responsible HEW official, in accordance with section 8.2(b) of the regulations, may assign the invention rights to the grantee for a limited period.

HEW officials provided us with a list of nine petitions received by HEW from grantees that were pending determination as of January 1967. Two of these petitions had been submitted in 1963, one in early 1965, and three others were at least 6 months old.

University and industry officials advised us that they were dissatisfied with the determination of rights provisions by the agency because the provisions did not provide criteria and guidelines for determining rights; there were uncertainties as to the determinations to be made. The following case illustrates the delays and uncertainties involved in resolving a petition for patent rights made by a university we visited during our review:

In January 1966 a university petitioned PHS for assignment of domestic rights to inventions covering steroid compounds conceived under a PHS grant. Prior to the petition the Surgeon General had permitted the university to file six patent applications. At least 14 companies expressed interest in licenses for development of the university's inventions.

We were advised, however, by a university official that no company would develop the inventions without exclusive rights to protect its investment in the development of the inventions. He stated that, as of May 1967, no development work had been done on the inventions by any of the 14 companies. The investigator informed us that he had lost interest in development of the inventions, because of the long delay. In July 1967, 18 months after the petition, the Assistant Secretary for Health and Scientific Affairs assigned domestic rights to the university and stated that the public interest would best be served by expeditious development of the inventions.

Statements made in 1965 by two organizations representing university administrators stress the importance of assigning invention rights to universities at the time of awarding research grants or contracts. The Patent Policy Subcommittee of one organization[1] stated in a position paper that the public interest could best be served by encouraging educational institutions to assume the responsibility of furthering public use of the inventions of their faculties and recommended that universities be permitted to establish the licensing arrangements necessary to encourage private companies to invest in the development of pharmaceutical discoveries.

The Chairman of the Subcommittee in commenting on the position paper adivsed the organization's executive secretary that the necessity to petition the sponsoring agency for the right to patent an invention, and to justify each such petition on an individual basis, introduces substantial delay and a prolonged period of uncertainty.

[1] Committee on Government Relations, The National Association of College and University Business Officers.

In 1965 the other organization[1] submitted statements to the Senate Subcommittee On Patents, Trademarks, and Copyrights, Committee on the Judiciary, which stressed that granting invention rights to universities at the time of contracting would eliminate delays in the development of discoveries and the dissemination of research knowledge and would assist the sponsoring agency charged with the task of promoting the fruits of research. This organization also recommended that universities be premitted to use licensing incentives to attract industry investment in product development. (Hearings on Government Patent Policy, pt. 2, p. 645.)

During our review, we requested HEW to provide us with information concerning the current status of its determinations under section 8.2(b), including the nine pending cases shown in its January 1967 listing. This information, provided to us in November 1967, showed a marked increase in departmental actions, inasmuch as HEW:

1. Had signed section 8.2(b) determinations, assigning invention rights to the grantee for a limited period, in seven cases.

2. Had decided to dedicate the invention to the public in one case.

3. Was evaluating additional information received on the remaining case.

The information provided to us also showed that, since January 1967, 17 other proposals had been submitted to HEW for 8.2(b) determinations; HEW had made determinations in four cases and was evaluating the proposals received in the other 13 cases.

On the basis of our observations, we proposed to the Secretary that HEW, in line with its responsibility, should direct its efforts toward timely determination of rights to, and the appropriate disposition of, potentially patentable inventions resulting from research in medicinal chemistry reported by grantee investigators. We believe that such action would serve the public interest by reducing the uncertainties of the status of invention rights.

Use Of Institutional Agreements

Our review showed that HEW had made only limited use of the regulation permitting the assigning of the determination of invention rights to grantee institutions whose patent policies had been approved by HEW (45 CFR. 8.1b). This regulation has been applied through the use of institutional agreements between PHS and individual universities, and 18 such agreements, entered into between 1953 and 1958, are now in existence. At least 34 other universities have submitted requests for these agreements; however, in March 1967, we were advised by HEW officials that no additional agreements had been approved because opinions of responsible agency officials differed concerning the value of such agreements.

We found that HEW, in addition to placing limitations on the number of institutional agreements being approved, placed limitations on the institutions' administration of the agreements now in existence, because it required use of the PHS patent agreement. Some agency officials have expressed the opinion that the use of patent agreements should not be required at grantee institutions which are holding institutional agreements and that greater use of institutional agreements would help alleviate problems in obtaining screening and testing services by pharmaceutical companies.

Information obtained during our review shows that investigators from at least seven of the universities holding agreements with PHS encountered difficulties in making screening and testing arrangements with pharmaceutical companies, becuase of the required use of the PHS patent agreement. The following case illustrates problems encountered when screening and testing arrangements were sought:

> In November 1962 the chairman of the patent board at a university holding an institutional agreement advised an investigator, as well as university administrators, that PHS preferred to have investigators obtain screening and testing for their compounds from commercial laboratories not

[1] American Council on Education.

engaged in the manufacturing business. Testing fees were to be charged to the grant. The chairman pointed out that he had:

> "*** protested this and other recent actions of the USPHS in issuing directives requiring compliance on matters contrary to established procedure within the university and the university's institutional agreement with that agency ***."

On two occasions the university advised the Deputy Surgeon General that fees for the required testing would amount from about $30,000 to $50,000 and would consume nearly all the funds of the grant. The university recommended action to permit the use of the free services of the pharmaceutical industry. The Deputy Surgeon General replied that although there was merit in this argument, PHS had no alternative but to use the amended patent agreement clause on screening compounds.

On the basis of our observations, we proposed to the Secretary that H-E-W clarify the intended use of institutional agreements and review the necessity for requiring the use of patent agreements by grantee institutions whose patent policies had laready been approved by H-E-W.