REGIONAL PRIMATE RESEARCH GENTERS

THE CREATION OF A PROGRAM

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Cover: Young Japanese macaques in the outdoor corral Oregon Regional Primate Research Center Beaverton, Oregon

REGIONAL PRIMATE RESEARCH

CENTERS

The Creation of a Program

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE National Institutes of Health

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INTRODUCTION

A. The Purpose of this Report

The purpose of this report is to bring together in one document a record of events that transpired in the creation of a definitive program of regional primate research centers. The report is intended as a historical statement and reference document relative to the development of the concepts, policies, procedures, and limitations of this program.

B. Summary Statement

Events of this world have no precise beginning or ending, except as they are arbitrarily designated for purposes of convenience. The more precisely one attempts to identify such points in time, the more difficult it becomes to do so. So it is with the Regional Primate Research Centers Program. For purposes of this report, this program is considered to have begun at the time the Director of the National Heart Institute (NHI) and the National Advisory Heart Council¹/ agreed to initiate the efforts that ultimately brought the program into existence. But the development period is not over, for characteristics of the program are still being evolved, and the program does not yet reflect the full intent of its creators.

There is something dramatic about the creation and development of a program such as this one. In the present case, prior to the raising of the curtain on the first act in February 1957, there were separate events that together constituted a kind of prologue.

Important among these was the fact that several different groups expressed concern over the lack of long-term primate research facilities in the U. S. At least two NIH committees, associated with the Division of Research Grants, proposed the establishment of national primate colonies. These efforts were ineffective.

In 1956, Dr. James Watt, NHI Director, and Dr. K. F. Meyer, separately visited the Russian primate research colony at Sukhumi on the Black Sea. The Regional Primate Research Centers Program began in February 1957 when the National Advisory Heart Council, stimulated by Dr. Watt's report of his visit, recommended to the National Heart Institute that a committee be set up to plan for a single national primate research colony, of the "Woods Hole" type, to meet a national need. The Council recommended that the colony be planned for longterm cardiovascular research, and that in time it should be broadened to include any other biomedical research areas. It was implicit in the Council's thinking that the grant or grants supporting the colony would eventually be transferred from the NHI to an appropriate noncategorical part of the NIH. The colony would be for primate research, not merely a primate supply resource.

An initial <u>ad hoc</u> committee commenced the planning and laid down the foundations for the concept of a national colony, later called a national primate research station. The planning was continued by a second committee composed of several members of the Heart Council. This committee, referred to hereafter as the Organization Committee, soon began to work with a third NIH committee from the Division of Research Grants. This latter committee, which was called the Primate Research Study Section, not only reviewed initially the center applications that were submitted, but helped in the detailed planning that led to the present Regional Primate Research Centers Program.

Although the initial plans were for a single large national primate research station, it shortly became obvious that this plan would not succeed. Congress considered the proposal of one national station against the alternative of several regional primate research centers, geographically distributed on the mainland of the U.S. In Fiscal Year 1960, the Congress appropriated an initial \$2 million to the NHI for the establishment of one or two regional centers for broadly conceived biomedical research not limited to the cardiovascular field or to other categorical areas. This money awarded in the form of two grants2/, was used to establish the first center at Beaverton, Oregon, near Portland. Congress appropriated additional funds in Fiscal Years 1961 and 1962; in 1962 the NHI awarded the last of the grants for the establishment of the center at Davis, California. Altogether seven centers were established, six of them designated as regional and one national. The national center was not, however, of the type first planned by the Heart Council and its committees. All centers, were established on a long-term continuing basis ("for the next hundred years")³/. It was agreed that to establish such a regional organization and activity on a short-term basis was inadvisable. Because the centers were regional, the Federal Government assumed a special obligation to provide full direct maintenance costs and as much of the indirect costs as it could⁴. "Regional"came to mean "more than local."

The distinction between the regional centers and the national center is not clear-cut, for all the centers are organized according to the same general

 $\frac{2}{2}$ A pair of grants, one for construction and one for the operation of the center.

3/ At the first meeting on September 25, 1957, of the Advisory Committee on the Establishment of a Cardiovascular Primate Colony (see reference (6) page 20, lines 2-4 of the minutes of its meeting), a committee member stated: "'I would think in terms of not less than fifty years, maybe several times that, but I don't think we can--should, think of it in terms of something done on a basis of two or three or ten years. It would be a waste of money. It would not be justified on a ten-year basis, but as a fifty-year project it might be worthwhile." This position, accepted by the committee and by the Director of the National Heart Institute, continued to be basic to the thinking and planning of the National Advisory Heart Council, of its committees, and of the National Advisory Committee on Primates (later designated the Primate Research Study Section) of the Division of Research Grants. This position was so taken for granted that, although the words "for fifty years or more", "for fifty or a hundred years" and "for the next hundred years" were used in discussions from time to time, it was not at the time thought to get them into the records. Instead such terms as "on a long-term basis" were used, meaning the same thing. The "on a long-term basis" is to be found repeatedly in the records, including

pattern: 1) They have the same functional features represented by the words "core staff," "visiting scientists," and "collaborative activities". 2) Each center is more than local in its activities, although each is sponsored by a local "host institution". 3) Each was established with local concurrence and local assumption of responsibility for the continued welfare of the center. 4) Each center is headed by a director administratively responsible to an appropriate official of the host institution. 5) Each is supported by grants made to a local organization, usually the host institution in which is located the "principal investigator," a person different from the director of the center. 6) Each center differs from the others in the details and main orientation of its research program.

The national center differs from the regional centers chiefly in its commitment to carry on investigations of animal breeding and husbandry with respect to various species of primates. It was partly for this reason that the national center was located on a large tract of land at Davis, California, in close association with a planned medical school and a well-established school of veterinary medicine.

The following table provides some information on the seven primate centers. The numbers for staff and for animals in the primate colonies are approximate. Subsequent paragraphs give additional information about the centers:5/

the Congressional testimony. For example, in the minutes of the joint meeting of the Heart Council Organization Committee and the NACP in San Francisco on November 23, 1959, page 9 (see reference (15) and (20)) is the phraseology "(a) to carry on long-term institutional research programs requiring more than one generation of investigators and more than one generation of animals." Phraseology such as "long-term" and "research-wide in scope" and "of long-term nature" are in the Congressional testimony records (see (27), House, 1960, p. 684 and House, 1964, p. 204). The minutes of the June-16-18, 1958 Heart Council meeting page 11, under section "IX Report of the Subcommittee on Organization of a Primate Research Station" states: "Dr. Andrus reported on the meeting, held on May 9, in Bethesda. It met to deliberate about various organizational patterns which might be suitable for the Primate Research Station. It was agreed that the station should be established on a long-term basis, similar to research centers with specific programs such as the National Heart Institute, Brookhaven National Laboratory, etc." This concept of a long-term basis (fifty or a hundred years) was held consistently throughout and did not change when the decision was made favoring multiple regional primate research centers, rather than a single, very large national station. (This footnote applies to other places in this document, for example to the first paragraph on page 10.) 4/ See page 26, footnote 47.

5/ For other details, see Fiscal Year 1967 Hearings before the Subcommittee of the Committee on Appropriations, House of Representatives, 89th Congress, 2nd Session, Part 4, DHEW, NIH(<u>27</u>). Also see the article "Scientific and Administrative Concepts Behind the Establishment of the U. S. Primate Centers" by Willard H. Eyestone, reprinted from "Some Recent Developments in Comparative Medicine," Symposia of the Zoological Society of London, Nov. 17, 1966, Academic Press, London and New York; (28) also in J. Am. Vet. Med. Assoc. <u>147</u>: 1482-7, 1965.(<u>28</u>)

	Area (Acres)	(gross s	q. ft.)	Primates	Prin. s Species	Fresent Start	1
Oregon Regional Primate Research Center Director: Dr. William Montagna	160	70,500	Beaverton, Oregon (nr. Portland)	1200	Rhesus	Professional Supporting 1	40 174
Primate Research Dr. Theodore Ruch camp	snc	36,000	Univ. of Washington campus (Seattle)	198	Pig Tail Macaques, <u>M. Nemestrina</u>	Professional Supporting	15 57
Wisconsin Regional Primate Research Center Director: Dr. Harry Harlow 1,	1/2	30,000	Univ. of Wisconsin campus (Madison)	1100	Rhesus	Professional Supporting Student Aids	15 125 70
Yerkes Regional Primate Research Center Director: Dr. Geoffrey Bourne 20	a ay annar - martunan	56,000	Emory Univ. campus (Atlanta) Georgia	325	Rhesus and Greater Apes	Professional Supporting	23 55
Delta Regional Primate Research Center Director: Dr. Arthur Riopelle 500	•	75,500	Covington, La. (nr. New Orleans)	650	Chimpanzees, Rhesus, Tree Shrews	Professional Supporting	22 138
New England Regional Primate Research Center Director: Dr. Bernard Trum 100		55,500	Southborough, Mass. (nr. Boston)	250	New World, Squirrel, Wooley, Marmosets	Professional Supporting	33
National Center for Primate Biology Director: Dr. Leon Schmidt 300	0	60,800	Univ. of Calif. campus (Davis)	2340	Rhesus	Professional Supporting	15 56

(1) <u>The Oregon Regional Primate Research Center</u>: Located at Beaverton, Oregon, on 160 acres of land about 10 miles from the University of Oregon Medical School, the host institution in Portland. Initial grant award in 1960; formal dedication in 1962. Main research orientation: reproductive physiology, especially perinatal physiology. Other research areas: anthropology, cardiovascular physiology, cutaneous biology, immunology, neurophysiology, biomathematics, radiology, pathology.

(2) <u>The Regional Primate Research Center at the University of Washington</u>: Located at Seattle, Washington, on the campus of the University, the host institution. Initial grant, 1961; dedication in 1964. Main research orientation: heurophysiology and gastrointestinal physiology. Other research areas: skeletal and dental development, infectious diseases, nutrition, cardiovascular disease. Has a computerized bibliographic service on medical research utilizing nonhuman primates and a literature collection on nonhuman primates throughout the world.

(3) <u>The Wisconsin Regional Primate Research Center</u>: At Madison, adjacent to the primate laboratory of the psychology department at the University of Wisconsin, host institution. Initial grant in 1961; building dedicated in 1964. Main research orientation: infant developmental behavior and emotional conditioning. Other and related areas: brain function, biochemical mechanisms of learning, pregnancy, radiation, leukemia, low-level toxicity, mental retardation, venous occlusion disease.

(4) <u>The Yerkes Regional Primate Research Center</u>: At Atlanta, Georgia, on the campus of Emory University, the host institution. Initial grant in 1961; dedication in 1965. The former Yerkes Laboratory of Primate Biology at Orange Park, Florida, established by Professor Robert M. Yerkes in 1928, was moved to Atlanta and absorbed into the new primate center. Main orientation: behavioral studies on anthropoids. Other research areas: anatomical and physiological studies of the brain, studies of blood.

(5) <u>The Delta Regional Primate Research Center</u>: At Covington, Louisiana, on 500 acres of land, 35 miles from downtown New Orleans and the host institution, Tulane University. Initial grant in 1962; dedication in 1964. The large land area was designated because of the southern climate and need for large all-year outdoor caging of a variety of species. Main research orientation: infectious diseases. Other research areas: genetics, developmental disorders, behavioral studies, environmental health and chronic, metabolic, and degenerative diseases.

(6) <u>The New England Regional Primate Research Center</u>: On 100 acres at Southborough, about 30 miles from Boston, Massachusetts. Host institution is Harvard University. Initial grant in 1962; dedication in 1966. Main orientation: infectious diseases. Other research areas include endocrinology of growth, nutrition, animal behavior, neurophysiology.

(7) The National Center for Primate Biology: On 300 acres of land at the Davis campus of the University of California, the host institution. Initial grant in 1962; construction completed in 1966. Main orientation: studies

on primates per se, including studies on methods of procurement, transportation, housing, breeding, maintenance, disease and, in general, animal husbandry of primates. Other research includes: studies on cancer, infectious diseases, diabetes, and drug toxicity. Other activities include: dissemination of information, materials, and animals for special research purposes to qualified investigators in other institutions, including the regional primate research centers; contribution of materials to a registry of comparative pathology to be a part of the American Registry of Pathology at the Armed Forces Institute of Pathology, Washington, D.C.; and establishment of a primate biological storage and retrieval program as a central information function. This center provides a facility for a large number of special studies supported by research grants from most of the NIH institutes and from some other agencies.

In July 1962, administration of the Regional Primate Research Centers Program was transferred to the Animal Resources Branch of the newly formed Division of Research Facilities and Resources. The DRG abolished its Primate Research Study Section in 1964, and DRFR established an initial application review group, the "Primate Research Centers Advisory Committee." The program is now administered entirely by DRFR's Animal Resources Branch.

The efforts that led to the creation and development of the primate centers program were filled with truly cooperative participation of persons involved but with often strongly divergent and conflicting concepts. Details will be presented in the following portions of this report, which also will delineate some of the problems and principles that emerged.

Chapter I. EARLY INDICATIONS OF CONCERN

In 1947 and in 1949, concern at NIH about the lack of subhuman primates for research in the United States resulted in an attempt by the Division of Research Grants (DRG)¹ to establish and finance a program for the "procurement of chimpanzees for medical research, to make available to all research workers in this country an adequate supply of chimpanzees²." Prior to and during 1953 and 1954, the NIH Committee on Radiation Studies held three conferences on the effects of radiation on animals, including monkeys; in 1955, it held a conference on "The Use of Primates for Studies of Radiation Effects and Aging."(2)In 1953 and 1954, a subcommittee² developed a proposal for a

1/ Unsuccessful.

2/ Letter of July 24, 1947, Vander (DRG) to Nissen (Yerkes Laboratories); memorandum of August 16, 1949, Culbertson (DRG) to Topping (NIH).(1)

3/ See (3) for minutes of meeting of "Subcommittee of the Committee on Radiation Studies on Long-Term Primate Program." Dr. Howard Curtis was chairman of this subcommittee.

primate colony in the U. S. for use in a "national long-term primate radiation program." Discouraged in 1954 by the reception the proposal received, the committee asked its subcommittee to reevaluate the proposal. The result was that in January 1955 the Committee on Radiation Studies said "new methods of handling primates and the newer drugs for controlling tuberculosis seem to have eliminated the necessity for having one large central laboratory with monkeys kept under ideal conditions for a long period of time * * *." Instead, support for existing "excellent primate laboratories" was urged. The committee asked that the proposal of its subcommittee be presented to the National Advisory Councils.

In May 1955, the attention of the Committee on Radiation Studies was directed to a Public Health Service (PHS) memorandum4/ about a nationwide survey, requested by the State Department, of the actual need for rhesus monkeys for medical and biological purposes for the fiscal year beginning July 1, 1955. In June 1955, the Institute of Laboratory Animal Resources, under the auspices of the National Academy of Sciences-National Research Council in Washington, D. C., held a conference on "The Procurement and Production of Rhesus Monkeys."(4) In 1955, a National Advisory Committee on Rhesus Monkey Requirements (NACRMR) was established in the DRG with Dr. E. Cowles Andrus as chairman. $\frac{5}{2}$ Throughout its history, this advisory group was concerned with the importation and certification of monkeys from India. Later, when it became the NACP and still later the PRSS, it worked closely with the Heart Institute and its Advisory Council in the development of the Regional Primate Research Centers Program. In 1956 and 1957, at its regular meetings, the Human Embryology and Development Study Section discussed the need for pregnant monkeys for research and appointed a subcommittee to look into the matter. This subcommittee recommended "support of both central and independent colonies of monkeys" (September 1956) and requested that the proposal be brought to the attention of advisory councils and the institute directors of the several Institutes. Upon learning of the interest of the Heart Institute in the establishment of monkey colonies to facilitate research, this study section in April 1957 again set up a small subcommittee to advise on the matter. It recommended that the NIH Councils consider ways and means of meeting this need.⁶ Nothing came of these efforts.

Thus a number of groups and individuals had recognized the need for development of additional primate research facilities and additional research programs. They had expressed their concern repeatedly. In view of the continued expression of concern and the proposals by committees and study sections, it is interesting that a national program of primate research facilities was not

4/ Dated May 13, 1955.

5/ See (15) for a concise history of this committee. In 1958, Dr. K. F. Meyer succeeded Dr. E. Cowles Andrus as chairman. In 1959, the committee's name was changed to "National Advisory Committee for Primates" (NACP), and in 1961, to "Primate Research Study Section." (PRSS). The Study Section was abolished in 1964 when DRFR established a Primate Research Centers Advisory Committee for the initial review of applications.

6/ Subcommittee Report of August 23, 1957.

actually brought into being prior to the establishment of the present program by the National Heart Institute. It would seem that concern on the part of a study section and a council was not enough. To create such a program, it was necessary to have concerted action on the part of a national advisory council and institute staff on the one hand, and study section and DRG staff on the other. Without strong concerted efforts by a national advisory council and institute staff (or the equivalent) the delivery of a new program conceived at a study section level was extremely difficult or impossible. This is particularly the case when no interest or enthusiasm for the program exists at higher administrative levels.

Chapter II. <u>THE NHI PERIOD</u>^{1/}

A. Origin of the idea in the National Heart Institute

In 1956, Dr. James Watt, the Director of the National Heart Institute, and Dr. Paul D. White, then a member of the National Advisory Heart Council, visited Russia. Dr. Watt had long been interested in and supported the use of primates in research. When he learned of the Russian work on hypertension with the subhuman primate, he arranged to visit the primate colony at Sukhumion the Black Sea, where subhuman primate research had been carried on continuously since the 1920's.

Prior to coming to the Heart Institute, Dr. Watt himself had been involved with primate research for about two years in Puerto Rico, working with a colony of monkeys on the small island of Santiago. Upon the return of the mission from Russia, Dr. Watt discussed his visit with Heart Council members. Then, at the Council's February meeting, he gave a report of his trip to Sukhumi and talked with the Council and its Planning Committee. about the need for more effective primate research facilities in the United States. The Council, in line with advice from its Planning Committee, recommended that a primate colony be developed on the mainland of the United States, near a university, to "serve as a site for a long-term, multiuniversity, multidisciplinary approach to cardiovascular problems." The Council charged its

<u>1</u>/ See Chart, page 50: <u>Groups Involved in Development and Administration</u> of Regional Primate Research Centers Program relative to committees referred to in this document.

2/ Dr. K. F. Meyer had also visited Sukhumi in 1956. Upon his return, he advocated the development of a primate research colony in the U. S. in a letter to Dr. Shannon.(1)

3/ The words "Planning Committee" will always refer to the Heart Council's Planning Committee.

- 4/ February 1957 meeting.
- 5/ January 1957 meeting.

Planning Committee with initiating plans for the establishment of the primate colony. The Council also recommended that individuals selected by the Planning Committee explore the possibility of establishing a colony primarily for research in cardiovascular diseases. However, representatives of other fields of research would be invited to participate in the planning and use of the colony as opportunities arose. The Planning Committee Chairman's grant was to provide funds needed for planning.

At this meeting, a guiding principle was established: that the primate colony should be planned initially as a cardiovascular research colony, but would allow for expansion to include other research areas. The alternatives of "cardiovascular" versus "general" research became a point of issue later among those participating in the planning of the colony.

B. From the development of NHI interest to the initial appropriation by the Congress

At its May 1957 meeting, the Heart Council's Planning Committee asked its chairman, Dr. E. Cowles Andrus, to work with staff to set up an <u>ad hoc</u> steering committee for planning, which would in turn call together a varied group of consultants knowledgeable about primate research. "The steering committee, working under the general auspices of the Heart Council's Planning Committee and with continuous staff assistance, would be given the task of looking into all aspects of the problem and developing a definite plan to establish the colony, including estimates of the initial capital maintenance." Dr. Andrus reported to the Council⁶ that the National Advisory Health Council had recommended that funds be made available to the National Research Council for a survey on the needs and supply of primates throughout the United States. This survey would be helpful to the Heart Council's <u>ad hoc</u> committee in looking into the establishment of a primate center for cardiovascular research.

Dr. Andrus and the NHI staff set up an <u>ad hoc</u> Advisory Committee for the Establishment of a Cardiovascular Primate Colony, $\frac{1}{2}$ with Dr. George Burch (then a member of the Heart Council) as chairman. (5) The first meeting of this group was held on September 25, 1957 at the Dupont Plaza Hotel, Washington, D. C.⁸

6/ June 1957 meeting.

7/ A group the Council had referred to as "Steering Committee."

8/ Members were provided written information on the "Cayo Santiago Primate Colony" in Puerto Rico, "Large Scale Primate Production in a Caged Colony" and "Breeding and Care of Monkeys." For documents, the agenda of the meeting, and a report of the meeting see (6). It is interesting that on the same day, September 25, the NACRMR met in Bethesda to discuss problems of procuring rhesus monkeys from India, particularly the problem of avoiding large losses during shipment. The general discussion at this meeting, $\frac{9}{}$ the report of its subcommittee, and the subsequent report by Dr. George Burch (as committee chairman) to the Heart Council, represent a struggle of conflicting ideas as to the nature of the colony to be developed. These also brought out some interesting information as well as policy issues in an early stage of formation.

At this meeting $\frac{10}{}$, the following issues were raised: (a) whether or not the proposed monkey colony should constitute a cardiovascular research colony or more broadly a general primate research colony, and (b) whether it should be primarily for research, for breeding and supplying monkeys to researchers in the United States, or for both. In general, committee members favored unrestricted primate research but were interested in working closely with the Heart Institute to bring the national primate colony into being. committee members remembered that the earlier proposals for national primate research facilities made by the Committee on Radiation Studies to the National Advisory Councils had gotten nowhere. Dr. Watt emphasized that, if the ad hoc committee wanted the Heart Institute and the Heart Council to move effectively to bring the proposed colony into being, it would have to be focused in the categorical area of the Institute. This was admitted by the committee, for the members recognized that too many cooks spoil the broth. Although this particular question of cardiovascular versus general research arose at this meeting, it became a more critical issue at the next meeting of the committee.

In regard to the question of the over-all purpose of the proposed colony, Dr. Watt pointed out that in order to receive the full support of the Heart Institute, it would have to be primarily a research facility and not simply a resource for the supply of monkeys.

This meeting also pointed up the importance of establishing the contemplated colony as a long-term facility, for fifty or a hundred years. All agreed that to set up such a colony on a five to ten year basis would be shortsighted and inadvisable.

Another principle brought out at this meeting was that such a primate research colony should have a "core group," that is, a group of scientists in residence, which would not include visiting scientists. The activities of this group would be supported by a basic budget "which would maintain the colony and provide research opportunities for those who are responsible for the continued maintenance of the colony."¹¹/₁₁ The amount of money needed for such a colony was considered to include "an initial investment of a \$5 million initial appropriation with \$100,000 annually for maintenance for each of fifty years years..."¹²/₁₂ At the end of the meeting the chairman agreed to appoint a

9/ September 25, 1957.

- 10/ September 25, 1957.
- 11/ From the minutes of the meeting.

12/ At the second meeting of the Committee (February 10, 1958) it was pointed out that \$100,000 was an unrealistically low estimate.

subcommittee to propose recommendations and plans for the colony for presentation to the committee at its next meeting on February 10, 1958.137

Dr. Burch reported in November to the Heart Council on his September 25th committee meeting.

The subcommittee appointed by Dr. Burch consisted of Dr. Howard Curtis (chairman), Dr. Leon Schmidt, Dr. Harry Harlow, and Dr. Theodore Ruch. They visited Okatie Farm, 14' the Yerkes Laboratories, the monkey colony of the National Institute for Neurological Diseases and Blindness at the University of Puerto Rico, and the caged primate colony at the Institute for Medical Research, Christ Hospital, Cincinnati. The subcommittee members were already familiar with the Balcones Primate Laboratory of the Air Force at Austin, Texas, and Dr. Harry Harlow's Laboratory at the University of Wisconsin. The subcommittee then wrote "A Proposal for a National Primate Institute"(7) which set forth the concepts, objectives, needed facilities, staff requirements, costs, and type of site for the location of the "Institute." However, this carefully thought-out document was destined for a difficult time and, as written, for elimination. The members of the subcommittee were outstandingly competent and experienced research scientists. They were not government administrators whose administrative world bore down upon them with somewhat different semantic forces. An interplay of different approaches developed fully at the February 10, 1958, meeting of the full committee which was to have later consequences.

The February 10th meeting(8) of the committee was devoted entirely to a discussion of the subcommittee's document which was, as originally intended, considered to be a preliminary proposal subject to modification. There were two different ways of thinking about the development of a primate colony: that reflected by the words "National Primate Institute" in the subcommittee's proposal, which described a general primate research facility but did not focus upon the categorical area represented by the National Heart Institute; and the view presented by Dr. Watt that, if the Heart Institute and Heart Council were to try to bring the primate colony into being, the proposal must be for a primate research colony or research facility that would be focused primarily upon the cardiovascular research area. He emphasized that to propose a general non-categorical primate research facility would be to take it out of the hands of the interested Heart Institute and Heart Council. Furthermore, to designate the facility as a National Institute or even as a National Laboratory would confuse it semantically with existing organizations in a way that would be detrimental. It was suggested that the term "Primate

13/ Reference to the minutes of this September 25 meeting and the documents supplied the members will provide detailed information regarding (a) the monkey colony in Puerto Rico (which received some support at one time from NIH), (b) the primate research activity in Puerto Rico of the Institute for Neurological Diseases and Blindness, and (c) the primate colony of the Soviet Union at Sukhumi.

14/ The conditioning center for the National Foundation for Infantile Paralysis.

Research Station" be used, and this was accepted. It was also agreed 15/ that the proposal would be rewritten by NHI staff, which would take into consideration all of the discussions of the matter and would word the proposal so that it would be in line with the responsibilities of the Heart Institute and Heart Council as established by the National Heart Act. The proposal would be written to be used by the Director of the Heart Institute to "get the green light" from those administratively above him in order to implement the Council's recommendations.

The committee recognized the wide scope of the Heart Institute's program responsibility, and further recognized that perhaps later on the proposed primate research station could be broadened still further. The committee thought this should be the first and not the last primate research station or center to be established and reiterated that such a station or center should be undertaken only on a very long-term basis. The committee discussed other aspects of such a center or station, for example, the need for the training of scientific and ancillary personnel in the field of primate research, the need for the development of a "standard animal," and the need for the procurement and supply of monkeys. While still recognizing the need for a supply of primates, the committee agreed that the primary mission of the station should be research. The committee was in favor of: 1) research at all life stages of the primate, 2) a minimum amount of 30 acres of land for the station, and 3) an initial outlay of about \$9 million. The amount was expressed in 1957 dollars because the committee anticipated a decrease in the purchasing power of the dollar due to inflation.

It was understood that it would not be necessary for this <u>ad hoc</u> committee to meet again, as the staff would revise the proposal document on the basis of the discussions and would follow through with its presentation to the Heart Council.(8)

Subsequently Dr. Burch, the chairman, presented to the Heart Council^{16/} a "Report on the Meeting of the Committee on the Establishment of a Cardiovascular Primate Station, "(9) based upon the subcommittee proposal as modified in the committee discussions. He had already reported verbally to the Planning Committee.^{17/} This report proposed a "Primate Research Station" with focus in the cardiovascular field. The initial costs were estimated at 9,250,000 (facilities) and 2,475,000 (annual operation) expressed in terms of 1957 dollars. At its meeting the Council agreed with the Planning Committee, accepted Dr. Burch's report and, in line with the Burch committee suggestions, recommended that two committees be set up, one for exploring a location for the station and one for planning its organization. However, the Council had not yet been presented with the subcommittee document ("A Proposal for a

- 15/ Somewhat reluctantly.
- 16/ February 27, 1958 meeting.
- 17/ February 11, 1958 meeting.

National Primate Institute") either in its original form or as revised by staff.

The Heart Council then set up a "Committee on Organization of a Cardiovascular Primate Research Station" consisting of Dr. George Burch, Dr. Michael E. DeBakey, Mr. David Robertson, and Dr. William P. Shepard, all members of the Heart Council. This group met in Bethesda on May 9, 1958. Dr. Andrus, Chairman of the Council's Planning Committee, called the group together and temporarily served as chairman. It was decided to ask Dr. Burch (who was absent) to be chairman (which he subsequently agreed to do). At this meeting the group agreed that the Primate Research Station should be established on a long-term basis, as previously recommended, in one of several ways that should be considered: namely, 1) as a direct operation of the National Heart Institute in Bethesda, 2) as a direct operation of the Heart Institute at another location, 3) as an operation under contract from the Heart Institute, located at a university and under a university's administration, 4) as an operation under contract from the Heart Institute and under control of a group of universities, or 5) as a separate contract operation independent of a university or other institution. Later, when the Regional Primate Research Centers Program came into existence the centers were set up according to alternative three, but supported by research grants rather than by contracts. The committee also proposed that: "a qualified individual $\frac{18}{18}$ with intimate knowledge and experience in the use of primates for research programs be delegated to develop a definite organization plan or pattern;" that he "be provided with an assisting staff as necessary to proceed effectively;" "that this person work closely with Dr. George E. Burch;" that "sufficient funds should be provided for planning;" and that "the results be presented to the committee for further consideration and action." The committee also urged that a program of training additional personnel in the area of primate research be started, and that two or three persons be sent to the Sukhumi Primate Station for training.-

The subcommittee document "Proposal for a National Primate Institute" was revised by staff. This revised document, "Report of the Subcommittee to the Cardiovascular Primate Committee,"(<u>11</u>) dated April 3, 1958, was provided to the Heart Council at its June 1958 meeting along with a "Report of the

 $\frac{18}{}$ At this time the committee and NHI staff had in mind Dr. Willard H. Eyestone who later joined the NHI to head up the new primate program.

<u>19</u>/ This Council group, initially called the "Committee on Organization of a Cardiovascular Primate Research Station," was the one that worked closely with the DRG Primate Research Study Section group in the development of the present program. It continued in existence until, by request of the chairman (Dr. Burch), it was dismissed with thanks on the basis that the committee had completed its function, as of the June 1962 Heart Council meeting. (<u>10</u>) No one was sent to the Sukhumi colony for training. This committee's name will be abbreviated to "Organization Committee" in this report. Cardiovascular Primate Committee" submitted by Dr. George E. Burch, Chairman. (11 The revision was based upon the estimates of the subcommittee, but differed from the original subcommittee document in designating the proposed research facility as a "Primate Research Station" with a non-exclusive focus in the cardiovascular research field, in line with the discussion at the February 10, 1958 meeting.

Also at the June 1958 Council meeting, Dr. Andrus reported on the May 9th meeting of the Council's new Organization Committee, the suggestions of which were accepted by the Council. At the same time the Council dismissed the previous <u>ad hoc</u> (Burch) committee with the following expression of appreciation:

"As an initial stage in the development of plans for a cardiovascular primate research station, the National Advisory Heart Council asked one of its members Dr. George Burch, to serve as chairman of an ad hoc committee to provide the Council with preliminary advice. The committee consisted of Dr. George Burch (Chairman), Dr. E. Cowles Andrus, Dr. Howard J. Curtis, Dr. Harry F. Harlow, Dr. Theodore C. Ruch, Dr. Leon H. Schmidt, Dr. Irving S. Wright, and Dr. Glenn Finch. Several members of the committee had had experience with the use of nonhuman primates in research and constituted a subcommittee to look into the problem in considerable detail. The Council appreciates the work of the committee and its subcommittee and the well-considered advice given to the Council in the committee's report. This is of great assistance in enabling the Council to enter now into a second stage of planning. The Council wishes to have this expression of its thanks conveyed to the members of the committee and particularly to the subcommittee, who expended so much of their valuable time and effort in the initial stage of planning. Although the work of the ad hoc committee is completed, the Council hopes that those who have served on the committee may be called upon for additional assistance from time to time as the need arises."

The members of the first committee, $\frac{21}{}$ particularly its subcommittee, were much distressed that the push being made was for a categorical (cardiovascular) primate research facility, rather than simply a primate research facility (institute). It was most difficult for them to accept the categorical approach, even for tactical purposes. Although recognizing that the initial categorical focus could be broadened to a general biomedical approach, they evidently feared this would not take place. There was much off-the-record discussion

20/ Mrs. Edgar G. Tobin, a member of the Heart Council, was added after the first meeting of the group. Mrs. Tobin was interested in the development of primate research facilities and was closely involved with the development by the Southwest Foundation for Research and Education of a baboon research colony at San Antonio, Texas. Although not supported through the RPRC Program, this colony under the Directorship of Dr. Harold Vagtborg has developed into a true regional primate research center, with the baboon as the main animal.

21/ The "Steering Committee," Dr. Burch, Chairman, whose "subcommittee" wrote the "Proposal for a National Primate Institute." outside of the meeting and verbal expressions, both in person and by telephone, of intense concern over this issue. But the Heart Institute and Council were adamant on this point--that it had to be a cardiovascular research approach if the Institute were to move to bring the program into existence. It was partly because of these strong differences of viewpoint that the Heart Council requested some of its members to serve as a Heart Council "Committee on Organization of a Cardiovascular Research Station." Some of the members of the initial committee continued to play an important role as members of the Primate Research Study Section group in the development of the primate program. It is interesting to see that these and other members of this study section later elected to have scientific attainment as the basis for their recommendations, rather than base their recommendations on that plus other factors of a broader administrative character on which decisions had to be made.

The Planning Committee, at its July 24, 1958, meeting was told that Dr. Willard H. Eyestone had agreed to assist in preparing more detailed plans for the Primate Station and that the new Council Committee would meet again soon.

The Organization Committee met on October 16, 1958. Several criteria were developed for the selection of a site for the Station. The Committee asked the staff and Dr. Eyestone (who was present) to develop a more definitive set of criteria, and asked the chairman to propose an application for funds to cover the cost of planning. The members reiterated the view that the cardio-vascular primate research station should "look toward broad utilization of its facilities in the future, but at the present stage the focus should be cardiovascular." The Committee suggested that Dr. Eyestone be allowed to devote at least half his time to this extramural activity (which arrangement Dr. Eyestone said would be satisfactory to him). Dr. Watt discussed the timing that would help make the committee's work most helpful. He explained that the Heart Institute had received a Congressional mandate, expressed in the Senate fiscal 1959 report,^{22/} also accepted by the House Committee, to investigate the desirability and feasibility of a primate research colony. A report to be completed by December 1958 had to be prepared for the 1960 Congressional appropriation hearings.

22/ From Senate Report relative to Fiscal Year 1959: "3. Experimental production of atherosclerosis in animals and other basic studies of this disease. The desirability of establishing a monkey colony, in which heart disease could be studied over the life span of animals and even from the hereditary point of view, was stressed by citizen witnesses. The committee wishes the Institute to investigate the desirability and feasibility of establishing such a colony." All that had happened is not indicated in the written records, but something like the following occurred: prior to October 16, written information about the Heart Council and Planning Committee meetings, including their consideration of the proposed primate program, had been sent routinely to the Office of the Director of the NIH, but evidently there had not been a special conference on the subject between the Directors of the NHI and NIH. However, about this time, such a conference or conferences took place.^{23/} At these conferences, the Office of the Director, NIH, demonstrated little enthusiasm for the proposed primate program and none for a single major primate station. The only basis on which the primate program could get acceptance and backing at the NIH level would be for a plan to be developed for several regional centers rather than a single major national station as was being proposed. This was at a time when the NIH was attempting to develop a program of regional centers (e.g., computer and animal resource centers), in which Dr. Shannon had become much interested.

As indicated above, the Senate Appropriations Subcommittee had asked the Heart Institute for a statement documenting the nature of the proposed primate colony. Subsequently, the Institute was asked to prepare a similar statement for the House Appropriations Subcommittee for presentation at its hearings on the Fiscal Year 1960 budget. This is the "Congressional mandate" mentioned by Dr. Watt to the Council's Organization Committee.

At the Heart Council's November 1958 meeting, Dr. Burch reported on the October 16 meeting of his committee, stating that the committee had "definitely concluded, in response to a question from Congress, that such a station is both feasible and desirable." Also that "the committee has in the past and will continue in the future to receive favorable advice from Dr. Eyestone (a veterinarian), Chief, Laboratory Aids Branch, DRS,²⁴ at the NIH, on the organization of a primate station. The committee feels that to facilitate progress at this stage of planning, the station should primarily be a Heart activity, and that at some later date other interests could be included."

The Council accepted this report and the committee's suggestions. It recommended a grant $\frac{25}{}$ in the amount of \$67,275 for the first year and \$65,550 for the second year to Dr. Burch, chairman, to implement the planning of the organizational structure, physical plant, and geographic location of a primate research station. By this action, the Heart Council charged this one committee with the two functions of geographical and organizational planning for which two separate committees had been suggested earlier.

Dr. Watt informed the Heart Council (June 1959 meeting) that although the Council in response to a request from the Senate Appropriations Subcommittee

23/ There was also a meeting on March 12, 1959, of Drs. Burch, Watt, Eyestone, and Yeager with Dr. Shannon, who favored multiple regional primate research centers rather than a large national primate research station.

24/ Division of Research Services.

25/ Fiscal Year 1959 funds.

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had determined that there was a national need for primate facilities and had recommended the establishment of a single, large, national station, it had become evident through discussions with other NIH staff that perhaps multiple primate facilities would be just as desirable as a single facility. He said the Heart Institute's report to the Senate reflected both approaches. The Council then asked its Committee on Organization of a Primate Station to continue planning and to consider the merits of both approaches.

The document prepared by Heart Institute staff for the Senate Appropriations Subcommittee was dated April 23, 1959, and had the title "Feasibility and Desirability of Primate Research Centers."(12) This document proposed an initial outlay of \$10 million and an annual operating cost of \$3.5 million for a "single large center;" or for each of a number of "smaller national primate research centers...approximately \$2 million capital outlay and approximately \$700,000 annual operating costs." Four to six "smaller national centers" were suggested. The objectives of a center or centers were to be focused on cardiovascular research but with gradual expansion to include "other disease categories and other disciplines, until, ultimately the function of the station or centers is the full and complete investigation of the primate (s)."²⁶ This document may have been influenced by another one that had been prepared by staff for administrative and Council purposes which contained a brief historical review, reflecting the views of consultants and estimating \$9,650,000 for capital outlay and \$3,460,000 for annual operation.(<u>13</u>)

All indications pointed to the strong probability that the Congress would appropriate some funds to the Heart Institute for this proposed program, but more likely for regional primate research centers than for a single major primate station. In anticipation of this, Dr. Burch called a meeting of his committee on July 17, 1959, at the Roosevelt Hotel in New Orleans, at which Dr. Eyestone and Dr. Yeager represented the Heart Institute staff. The entire meeting was devoted to the issue assigned to the committee by the Council: whether it would be best to have a single major national research station, or several regional research centers, or both. Taking all factors and viewpoints into consideration, the committee decided that a coordinated, integrated system should be developed, consisting of a central large national primate research station plus several small subsidiary national research centers, each of which would get its support through the national station. The station itself should be supported through direct appropriations from the Congress and these appropriations should include funds for the several centers. The station would be a part of the PHS in an organizational position, comparable to that of the recently created National Library of Medicine.27/ It would have an appropriate relationship to the NIH although it would not necessarily be located in the Bethesda or Washington area. Under the Director of the Station would be a Board of Directors composed of directors of the subsidiary centers plus outstanding, knowledgeable persons from various parts of the United States.

<u>26</u>/ The statement prepared for the House Appropriations Subcommittee said essentially the same thing.

27/ Established in October 1956.

These latter Board members would be appointed by the President of the United States upon advice of the Surgeon General of the Public Health Service. This integrated system of centers should be complementary to and not competitive with the National Institutes of Health.

The purposes of the national station would be: 1) to conduct research on primates in conjunction with other basic and clinical studies, 2) to investigate the usefulness of various species of primates in research, 3) to serve as a national reservoir of information on primates and for primate research, and 4) to provide facilities for visiting scientists as well as for researchers coming from the subsidiary centers for training. The visiting scientists would get the bulk of their research support from sources other than the station's budget. The committee emphasized that, although this system of centers was the ultimate goal, initially only the station and one or two centers would be established, others being added later. The subsidiary centers should be connected with appropriate universities or research institutions and should have a maximum of local and institutional participation and support. It was considered less desirable that the national station be tied closely to any institution, since it should have national direction and guidance and relate to all institutions in the country. Although the main support would come from Congress, additional support from other sources should be permissible and welcomed. The site for the station should include not less than 1,000 acres and should be in a location attractive to the permanent staff and visiting scientists.

The committee asked Dr. Burch and Dr. Eyestone $\frac{28}{}$ to get the help of an architect, to obtain from an appropriate management-consultant firm information on criteria for the selection of a suitable site for the station, and to see that fact-finding visits were made to potential sites by persons provided with a checklist of items. The items on the checklist should include: 1) local interest, enthusiasm and potential backing (both financial and functional), 2) potential scientific support and utilization of station by local institutions and personnel, 3) appropriateness of the site for a national station, 4) amount of land available and possible cost, 5) favorable and unfavorable physical characteristics of the site, 6) proximity to a city, 7) attractions the city could offer the station staff and their families, 8) unfavorable characteristics of the city, 9) other attractions the site would offer, such as natural scenery, climate, weather, sports, entertainment, schools, cultural activities, housing, etc., 10) accessibility of the site (available public transportation), 11) proximity to a suitable university, research institution or other educational institution, 12) views of various categories of personnel at or near the site regarding the station possibility, 13) possible functional relationship of a neighboring university or college to the station (or, in the case of a regional center, the professional, administrative and scientific roles in the center of the personnel of the local university or college), 14) names of local persons to be contacted, and 15) a detailed map of the locality. Those persons making these site visits were

28/ Dr. Eyestone joined the staff of the Heart Institute, October 27, 1959, in charge of the Regional Primate Research Centers Program. to present a full report of their findings to the committee immediately on their completion of the visits.

The committee requested that NIH staff discuss the committee's plan with appropriate officials in the NIH and the PHS and convey back to the committee any reasons why it should not proceed according to these plans. The committee said it did not wish to waste time and effort trying to carry through plans that would not be acceptable or practicable.

The committee decided to meet again on September 5, 1959, in Bethesda if funds were appropriated in Fiscal Year 1960.29/ It was agreed to try to make site visits and have reports available by the September date. If funds were not appropriated for Fiscal Year 1960, the site visits were to be made and completed for a meeting of the committee on November 4th.

At the meeting of the committee on July 17, 1959, $(\underline{14})$ the members did not know that Congress would decide not to establish a national station of the kind the committee wanted, but only an as yet undetermined number of regional primate research centers. But the planning ideas of the committee were such that the bulk of them could be put to use in the development of regional centers. It was at this meeting that agreement was reached as to who would visit which potential site.

During this period, events were leading to the first appropriation of funds by the Congress in support of the new primate program. The House and Senate Appropriations Committee conferees agreed on an appropriation of \$2 millionto the NHI: "To Establish two primate colonies during the year 30' as authorized by section 433(a) of the Public Health Service Act. The funds may be used for such construction as may be required to establish the two colonies."31/The Senate committee appropriation language included the following:

"The committee notes the testimony of several witnesses in connection with the need to establish within the continental limits of the United States one or more primate colonies which would permit heart disease to be studied over the lifespan of the animals, including studies related to heredity. Based on such testimony, it is the committee's judgement that such primate colonies would be most useful to medical science if there were several such colonies geographically distributed and created as a part of a university environment. Under these circumstances, the colonies could serve the purposes of several programs and could be more economically administered than would be true if they were established as separate resources. The committee will provide increases

29/ The Fiscal Year 1960 began July 1, 1959.

- 30/ Fiscal Year 1960.
- 31/ From "Congressional Record-Senate, 13443," July 30, 1959.

over the House allowance to permit the Heart Institute to proceed with the establishment of one such facility during Fiscal Year 1960, assuming that this will serve as a prototype for the creation of similar resources elsewhere in subsequent years."32/

The appropriation was such, however, that the funds could be and were used to establish primate research centers on a broad basis of research on primates without the categorical restrictions so feared by the advisors to the Heart Council and Heart Institute.

The Congress thus appropriated funds for the beginning of a program of primate research centers, and the Heart Council's Committee on "Organization of a Cardiovascular Primate Station" changed automatically into the Heart Council's "Committee on Organization of Primate Research Centers,"<u>33</u>/ shedding its categorical constraints without losing any momentum whatsoever. The committee held its next meeting on September 5, 1959.

C. From the initial appropriation to the establishment of seven centers

Up to this point, the Division of Research Grants had not been brought into the development of the primate program, although informal communication had occurred. However, after the July 17th New Orleans meeting, the Executive Secretary (Miss Katherine Parent) of the NACP $\frac{34}{}$ helped to make the initial exploratory site visits. These were carried out by members of the Organization Committee, Dr. Eyestone, Dr. Yeager, and Miss Parent.

At its meeting on September 5, 1959, in Bethesda, the Organization Committee persistently reaffirmed its preference for a major national research station.35/ The committee agreed to work towards the establishment of two centers this year (one of which they hoped might evolve into a station), but feared that a center closely allied with a nearby university would become absorbed as a part of the university, whereas a national station would not. The committee recommended that the chairman (Dr. Burch) use his grant funds to convene a carefully selected group to advise on the best means of organizing and financing a station. This group should include a university administrator, a business accountant, a businessman, a lawyer, a primate research man, and one or two staff representatives. Advice would be obtained from this group in advance of the next meeting of the committee on November 4.

32/ From Senate Report, p. 32, Fiscal Year 1960 appropriations.

 $\frac{33}{}$ This group will continue to be referred to by the abbreviated name "Organization Committee."

34/ Formerly the National Advisory Committee on Rhesus Monkey Requirements.

<u>35</u>/ The persistent efforts to bring a national station of the "Woods Hole" type into existence failed, but undoubtedly they helped to achieve a national conditioning center (National Center for Primate Biology).

At this same meeting, the Organization Committee discussed the results of the initial exploratory visits, thirteen of which were made after the July 17th committee meeting. The sites visited were Orange Park (Florida), New Orleans, San Antonio, Madison, Cincinnati, New Haven, Boston, Seattle, Portland, San Francisco, Palo Alto, La Jolla, and Denver. Each locality was evaluated as a possible site for a center or for a station through thorough discussion. The committee agreed that seven of these were potential center sites and designated one of the seven as a possible site for a station.

Speaking for the Heart Institute staff, Dr. Yeager described the following procedure for obtaining primate center applications and the mechanism for supporting the centers through grants: 1) initial exploratory site visits (thirteen already made), 2) subsequent negotiation visits, mainly by staff, to advise on the formulation of grant applications, 3) submission of applications to the NIH, 4) initial review of applications by the NACP in the DRG, 5) transmission of the NACP's recommendations to the Heart Council through the Council's Planning Committee, 6) final review and recommendation by the Heart Council and final recommendation by the Council of the two centers to be established with the available funds, 7) center grants to be made with a formal (written) promise of nine additional years of support in specified annual ceiling amounts, $\frac{36}{8}$ annual negotiations between Heart Institute staff and the Primate Center administrative staff as to the amount of operational funds needed for each next succeeding two years, and 9) timing of these annual budget negotiations so that anticipated needs could be reflected in the Heart Institute's own annual budgetary requirements. The committee agreed to the proposed procedures.

These procedures were also agreed to by the Heart $\operatorname{Council}^{37/}$ and its Planning Committee.^{38/} The Council again emphasized the desirability of developing a national primate station and emphasized its view that neither centers nor station should be developed as only breeding colonies or monkey supply resources. It also stated that unsolicited primate center applications should be accepted and any possible site applications be allowed to compete. The Planning Committee and Council suggested that there be a close working association between the Council Committee, the Planning Committee, the initial application review group (NACP) and the staffs of the NHI and DRG.

The Organization Committee met briefly on November 4, 1959, in conjunction with the Planning Committee meeting held the same day; in fact, the membership of the Organization Committee and that of the Planning Committee were almost the same. The Organization Committee discussed the relative roles of the Council Committee and the NACP, as well as a joint meeting of the two groups then being planned. Miss Parent, NACP Executive Secretary, explained the

- 36/ Beyond the first year, making ten years.
- 37/ November 5, 1959, meeting.
- 38/ September 20, 1959, meeting.

history and composition of the NACP, which was to provide the initial review of applications. She then reported on primate center grant applications received and anticipated. It was agreed that all the project site visits made as a part of the review procedure should be by members of the initial review group, but that professional members of the Heart Council should be included. Applications for two primate centers selected for establishment might acceptably add up to more than the \$2 million appropriated, but the \$2 million could be used to get the centers started. Although two regional centers were to be established, the committees still viewed a "station" as a goal.

The joint meeting of the Heart Council's Organization Committee and the NACP was held in San Francisco on November 23, 1959. Dr. K. F. Meyer presided. The joint group reviewed the history and activities of the NACP, considering the function of the NACP and its relation to the Heart Council. They reviewed the historical development of the primate research center program and discussed the concept of and support of the primate research centers. Provided with information on anticipated applications, they discussed primate research support needs which could not be met by the regional centers. Early plans were made for project site visits.

At this meeting the NACP drafted $\frac{39}{}$ several resolutions to the Heart Council that were later put into final form.(15) The following is quoted from these: "The National Advisory Committee on Primates is willing (a) to accept the responsibility to function as a study section in providing initial scientific review of applications for grant support where the primate is of major consideration and to make recommendation to the appropriate National Councils; (b) to proceed with all dispatch to recommend to the National Advisory Heart Council suitable locations for two or more primate centers; (c) to consider especially the possibility that one of these centers may develop into a national primate research station; and (d) to investigate the desirability of encouraging primate research projects and recommending their support to the appropriate Council." The committee also urged the establishment of training programs in the field of primate research.

The following, quoted from the minutes of the committee meeting, indicates the concept of a center as agreed upon by the committee: "The concept of a center as contrasted with a large station would be a more local or regional kind of establishment, closely associated with a university locality or region. It would perform a local function and in addition a regional or possibly a national function. The local function means that a research program would be carried on by a professional staff in the center, working in cooperation with the people in the various departments of the medical school or university, financed either directly by the government or some special mechanism in which the university is involved. The center would have a director, and the research staff

<u>39</u>/ The reader is referred to the minutes (<u>15</u>) of this meeting for details other than those given here.

would have, ideally at least, university appointments. The regional or national function means that the center would provide space and certain basic equipment to visiting scientists from the region, the country, or even outside the country. The center might use only one or two prime species of primates, although the center would not be limited as to the variety of species it might use. The director of the center would have the advantage of an advisory board made up of people from the university with which the center is associated, and people from nearby universities and/or universities throughout the country."

Also, it was pointed out that the funds in Dr. Burch's chairmanship grant had not been used to plan a national primate research station, as recommended by the Council, because of the development of the regional "center" concept.

The NACP, at its meeting on January 30, 1960, reviewed eleven applications for regional primate research centers. Only three<u>40</u>/ "met the criteria which were established as a basis for review of applications this year."<u>41</u>/ The committee recommended two of these three for support from the \$2 million available; the third was recommended for deferral. Five others were recommended for reconsideration in the future, should additional funds become available. Orders of priority were indicated for the two recommended and also for the others. The committee also recommended that support for primate resources, within existing research institutions, be encouraged, particularly with regard to non-matching construction grants. This was in addition to the committee resolutions drafted in San Francisco.

At this time the difficult problem of decision-making emerged. Although the written records of meetings indicate this, they do not reflect the soul-searching and differences in viewpoints that existed. The problem was essentially that the final decision on the establishment of regional primate research centers had to be based upon a number of considerations other than the scientific merit of the primate research already being carried on by an investigator or investigators at the site selected. The question was whether the study section (NACP), the Council, or the Heart Institute staff would bring into consideration these other factors, e.g., geographic distribution, limitation on the number of centers to be established, etc. After considerable discussion of the problem, the NACP decided to base its recommendations to the Heart Council essentially on scientific merit evaluations. The Heart Council, having been strongly indoctrinated with the view that it should accept study section scientific merit evaluations, was very resistant to the idea of changing the committee's recommendations or its priority arrangements. The Heart Institute Director (Dr. Watt) and his staff were under considerable pressure to make decisions involving a number of factors in addition to scientific merit, if the primate center program were to continue to be palatable to the Congressional appropriation subcommittees. The following were among

the factors that had to be considered: the program had to be finite, as only a stated number of centers could be established; one of these could not be or become a station of the "Woods Hole" type as urged by the Heart Council and the several comittees; there would have to be a geographical distribution of the centers at named sites in different parts of the country, etc. Only after earnest and persistent persuasion by the Heart Institute Director did the Heart Council make the recommendations that were needed to obtain continued Congressional support.

At its February 20, 1960, meeting the Planning Committee "discussed the recommendations of the National Advisory Committee for Primate Research that two centers be established this fiscal year, west of the Rocky Mountains and geographically adjacent." The opinion of some 42' of those present was that a factor of geographic distribution of centers should be taken more fully into consideration. The Committee recognized, however, that the two sites recommended by the Committee on Primates represented the best judgment of that Committee on a purely scientific basis. After considerable discussion the Planning Committee voted to concur with the recommendation of the National Committee on Primates--that is, two centers established by means of the \$2 million appropriated this first year should be located at Seattle, Washington (first choice), and Portland, Oregon (second choice), "in the amounts and for the time recommended by the Committee on Primates."

At this same meeting the Planning Committee reviewed in detail and evaluated nine primate center applications, six of which it arranged in a priority order, and recommended to the Council that any additional funds in the next fiscal year be used to establish some or all of these centers in that priority order. Any further negotiations with the applicants were to be carried on by the staff. The Planning Committee then recommended that four other applications be deferred for further negotiation and review should yet more funds become available in the future.⁴³ Other than the changes mentioned, the Planning Committee concurred with the report of the initial review committee, including its resolutions to the Council.

The Council, at its March 1960 meeting, said: "The Planning Committee of the Council accepted the recommendations of the National Advisory Committee on Primates that this fiscal year two primate research centers be established, one at Seattle, Washington, and one at Portland, Oregon. The Council recognized that these recommendations were made only on the basis of scientific merit and, on this basis, concurred with the recommendations of the National Advisory Committee on Primates and the Planning Committee of the Council. The Council then took into consideration the other factors of geographical distribution of centers and the species of primate that would serve as the chief

42/ Chiefly Heart Institute staff.

<u>43</u>/ These total to twelve instead of eleven recommendations on eleven applications, because one application involved two geographical areas which were given separate recommendations. subject of study within a center. From this broader standpoint, the Council did not concur with the recommendations of the National Advisory Committee on Primates and the Planning Committee and, on the basis of a presently active primate research program of high quality, considered Portland, Oregon, to be the number one choice." Thereupon the Council made the following recommendations:

"(1) That the application, H-5129, from Drs. Pickering and West, University of Oregon, Portland, Oregon, be selected as number one choice for the development of a regional primate research center in which the rhesus monkey would be the principal experimental animal; that the staff of the Heart Institute negotiate with the applicants, their advisory board, and others at that institution and in that region to insure that the center would, in fact, be a regional one concerned with the rhesus monkey in any of its aspects and at any stage in its life span, and that it be not merely an expansion of the research on the younger animals now being carried on so competently by Dr. Pickering; that the Council recommend that this application be supported in an amount not to exceed \$2 million this fiscal year, with nine additional years of committed support not to exceed \$2 million per year (this is in accordance with the accepted plan for supporting long-term centers through the grant mechanism).

"(2) That, if the above conditions cannot be met in Portland, Oregon, the same conditions apply to the negotiation of the application, H-5396, from Dr. Theodore Ruch, University of Washington, Seattle, Washington, and that the Council recommend this grant accordingly, as an alternative center, in which the rhesus monkey would be the principal research animal."

The Council also recommended that the Yerkes Laboratory be accepted as the basis for a regional center in which the chimpanzee would be the chief experimental animal. A suitable site was to be worked out with Emory University. In the interim, support would be provided the Yerkes Laboratory through a research grant at a \$150,000 level. They also recommended the Southwest Foundation for Research and Education at San Antonio, Texas, be explored as a possible site for a center in which the baboon would be the chief experimental animal. The Council further recommended that the other favorably recommended applications be deferred for additional review in the next year; that still other possible sites be explored; and that in general primate research in the United States be encouraged and supported by regular research and training grant funds.

Thus, at this meeting, the Heart Council recommended the establishment with Fiscal Year 1960 funds of one regional primate research center instead of two, the recommended one at Portland, Oregon. The NACP at its May 12 meeting accepted the Heart Council's decision, although with some concern, and agreed to continue to provide initial review and evaluation of the center applications.

Subsequent to the March Council meeting, staff negotiations (April 4) proceeded relative to the primate center to be established at Oregon. Heart Institute staff, including the Institute Director (Dr. Watt) who played a leading role

in the negotiations at this stage, met with representatives of local institutions. These included the University of Oregon Medical School, the University of Oregon 44/, the Medical Research Foundation of Oregon, Inc., and the Oregon State System of Higher Education. As a result of these negotiations it was agreed that a Director of the Center would be designated 45/, that a "Statement of Responsibilities and Relationships"(16) would be prepared and signed 46', and that these would be accomplished before a grant would be awarded by the Heart Institute. The "Statement of Responsibilities and Relationships: Primate Research Center in Oregon" refers to "the grant applications dated April 15, 1960 and the memorandum dated April 8, 1960 summarizing Portland meeting of April 4, 1960 as basic documents." The "Statement" contained sections on the "Purpose of the Center," "Administrative and Academic Relationships," the "Scientific Advisory Council," and "Signatures. Under "Signatures," was a section relative to the representatives who signed the "Statement." At the end of the statement is an acknowledgment of the receipt of the document by the National Heart Institute, and this is signed by Dr. James Watt, the Institute Director47'.

Dr. Watt's foresight in requiring this signed statement prior to the award of the construction and operational grants for the establishment of the center was fully demonstrated later when serious difficulties developed relative to the administrative, academic, functional responsibilities, and role of the Director of the Center. The "Statement," reinforced by subsequent communications from the Heart Institute staff, served as a sound basis for the maintenance of the primate center operation according to the initial understanding. The difficulty which occurred at this Center brought into effect another principle pertaining to the Regional Primate Research Centers Program: that a center's operational difficulties are to be considered local problems so long as they do not jeopardize the existence and welfare of the regional center as originally established. The Federal Government will intervene only when the difficulty is of sufficient magnitude to seriously jeopardize the center and when local attempts to solve the problem fail. This principle was the basis of the statement in a letter from the Heart Institute to the University of Oregon School of Medicine (the "host" institution) which included the following: "It is our understanding that the conditions under which the center has been established will be the conditions under which it will continue to operate. Any attempt on the part of the Director of the center or any other

44/ The Medical School was not a part of the University of Oregon; the Medical School Dean was not administratively responsible to the President of the University.

45/ Dr. Donald Pickering, University of Oregon Medical School, was selected.

46/ The "Statement" is dated April 17, 1960.

 $\frac{47}{16}$ The "Statements" prepared and signed at the other center sites were similar. (16)

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person to change these conditions or to operate contrary to them will necessitate a complete review of the entire situation by the granting agency and the institutions whose representatives signed the 'Statement of Responsibilities and Relationships.'"(<u>17</u>)

The following are the main points of interest relative to the primate center program during the rest of the 1960 calendar year. (1) The original plans for the Portland, Oregon center called for the establishment of five units, only the first of which was assured through the construction and operational grants awarded. An additional (supplemental) request for the construction of the second unit was turned down by the Council. (2) The Council and committee still urged development of a national primate station. (3) A visit was made to Africa by a group which included Dr. Meyer and Dr. Eyestone, to explore with Belgian scientists the possibility of developing a breeding colony of monkeys in the Belgian Congo $\frac{48}{48}$ and also to evaluate the baboon colony and laboratory at Kwębezi, Kenya, developed by the Southwest Foundation at San Antonio, Texas 49/. (4) A manual on "Policies and Procedures Governing Grants Awarded for Construction of Primate Research Facilities"(18) was prepared by staff, with concurrence by committees and council. Brief "Guidelines for Organization of Primate Research Centers"(19) were prepared as well. (5) A larger amount (\$7 million) was appropriated by the Congress for the primate center program, an unspecified portion of which could be used as necessary for non-matching construction.

The "Guidelines" stated: "In general, a primate research center would have these characteristics: (a) A distinct organizational entity with a stated mission^{50/} to carry out research using the subhuman primate. It might operate independently or as a semiautonomous part of a university or a medical school; (b) A director with clear responsibility and authority for administration of the center and its scientific program; (c) A basic corps of full-time scientific, technical and administrative staff of such character and of sufficient numbers for the successful accomplishment of its stated mission; (d) A scientific committee or board advisory to the director of the center with respect to the research program of the center and its scientific standards; (e) A document which provides assurance that a parent institution or other organization(s) will maintain a responsibility for the continuing administrative and scientific functioning of the center; (f) A facility will be supported by providing construction funds, and long-term support of operational costs. Construction of a facility outside the territorial limits of the United States is not permitted."

48/ This came to naught, partly because of political upheavals in the Congo.

49/ This colony, later moved to Darajani, Kenya, never received direct support from the Heart Institute, but did get some indirect support through the Southwest Foundation at San Antonio.

50/ The mission desired and intended was that of research on primates.

The Organization Committee held a meeting on September 24, 1960, at the Park Sheraton Hotel in New York City. Several additional persons were present to advise the committee on the development of a primate research station. They advised that a national primate research facility be established, though it need not be called a "station," that as much as 2,000 acres of land would probably be needed; and that the facility should be coordinated with smaller centers.(20)

The following is taken from the minutes of the October 1960 meeting of the NACP: "Although the term 'regional' was not defined $\frac{51}{}$, it is being interpreted as 'non-intra-institutional.' None of the money can be spent for construction outside the United States, but can be used to support operations outside the United States."

After the October meeting, the name of this committee was changed to "Primate Research Study Section" (PRSS).

In calendar year 1961, the following events of special interest occurred. (1) The Primate Research Study Section, the Heart Council Planning Committee, and the Heart Council itself again urged the establishment of a national primate research station at a capital cost of \$11 million on a ground area of 1,000 acres. (2) The establishment in Fiscal Year 1960 of two additional primate research centers, one at Seattle, Washington, the other at Madison, Wisconsin, was recommended by the Heart Council (March meeting). (3) The Heart Council (April meeting) recommended that a "conditioning center for subhuman primates which are to be scientifically prepared and tested for special studies in medical research by scientists throughout the country" be established at an appropriate site. The Council also recommended that the Primate Research Study Section look into the needs in this country for the procurement, conditioning, and supplying of primates for research needs. The Primate Research Study Section (May 8th meeting) concurred with the Council in the need for a facility in this country to develop techniques for procuring, conditioning and maintaining various species of primates for study, but did not agree that such a facility should or could supply the country with monkeys 53/. (4) At its June 1961 meeting the Heart Council recommended that in Fiscal Year 1961 three additional primate centers be established at Atlanta, New Orleans, and Boston, the amount per center not to exceed \$2.5 million. The New Orleans center site would consist of no less than 1,000 acres "because of special opportunities for the study of arboreal primates in that region." The Council further recommended that a study be undertaken immediately to develop "reliable techniques for procuring, conditioning and maintaining healthy primate colonies"

51/ i.e., by the language of the appropriation.

52/ As for example, at the Darajani baboon colony and laboratory.

<u>53</u>/ The Study Section formulated a resolution to the Council on these points in the terms of a primate research station.(21)

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(staff to negotiate a contract at San Antonio for an initial study); $\frac{54}{}$ and that a national station be established as a central coordination point for research and for training in primate research.

The members of the Primate Research Study Section were so very disturbed by these recommendations of the Heart Council(22) that the Director of the National Heart Institute (Dr. James Watt) and the Deputy Director of the National Institutes of Health (Dr. David Price) were invited by the chairman of the Study Section to meet on September 7th with the Study Section in executive session⁵⁵. The Study Section wanted to "hear some of the reasons why certain actions were taken by the Heart Council."(23) The matters the Study Section wanted to have explained(24) included: (a) Why had a decision been made earlier, contrary to the advice of the committee of technical experts, to establish several regional centers rather than a national station? (Answer: The Senate and the House of Representatives made the decision to put money into regional centers rather than a single national station.) $\frac{56}{(b)}$ Why did the Heart Council make recommendations at the June 1961 meeting that were not in line with the advice of the Study Section group? (Answer: Someone had to make recommendations at this time relative to a definitive formulation of the broad characteristics of the regional center program. The Council, in its advisory capacity, acted in compliance with the intent of the Congress in appropriating the funds, taking into consideration the Study Section's advice on scientific merit and other factors the Study Section did not use as a basis for its recommendations.) (c) Why did the Council recommend that the particular contract be negotiated for an initial study on methods of procuring and conditioning primates? (Answer: The Council had expressed its belief that a primate conditioning center or compound ought to be established and had asked the Study Section whether it thought this should be done. The Study Section advised against the establishment of a conditioning center at this time, because additional information was needed. Consequently, the Council recommended that a contract be negotiated for an initial study to help get such information.) (d) Why did the Council recommend that a regional center be established at a site not yet selected by the Study Section? (Answer: Because that site provided a unique opportunity for a center focused on a particular species of primate that should be included in the regional research centers program.) Various other matters were discussed at this session, but the above were the main issues brought out.

It is the considered opinion of the writer that the basic issue that bothered the Study Section members was that, although they represented the most knowledgeable and experienced group of primate researchers in the country (and probably in the world), their opinions and advice did not finally determine the decision involved in the creation of a primate research center or primate research

54/ This was attempted but did not work out.

55/ Dr. Eyestone and Dr. Yeager were present at the executive session.

56/ These answers are here expressed in the words of the writer of this report, not in the words of Dr. Watt, who carried on the discussion with the Study Section.

station program. Had the advice and recommendations of the groups of experienced and outstanding research consultants been followed completely from the beginning, neither the present program of regional primate research centers nor the desired national primate research station (or "Institute") would have become established at all. It was essential that some decisions be made, based on other than scientific research reasoning; these were made by the staff of the National Heart Institute backed by the Heart Council's recommendations. It is a wonderful commentary on the high caliber of these individuals, holding such diverging viewpoints, who continued their collective efforts to bring this program into being.

Three other events of special interest occurred in 1961. (1) The Heart Council (November meeting) recommended that the Southwest Foundation baboon colonies at San Antonio, Texas, and Darajani, Kenya, be partially supported by the Heart Institute until the Foundation had had time to demonstrate whether or not the baboon would continue to be useful in medical research. (2) The Council recommended that a "tag" for a conditioning center be put upon a land area (government property) in the Sacramento Valley near San Francisco. (3) The Council recommended that the word "regional" be used in the official titles of all the regional primate centers supported by this program.

At their meeting of January 25-26, 1962, (<u>25</u>) members of the Primate Research Study Section were joined for a time by members of the Virus and Cancer Board of the National Cancer Institute to discuss the use of primates in virus and cancer research. Representatives of the Cancer Institute's Laboratory Animal Panel were also present. The Laboratory Animal Panel urged the establishment of a primate conditioning center, having formulated a resolution to this effect in December 1961.

Also at this meeting the Study Section joined in executive session with Dr. Ralph Knutti, who had succeeded Dr. Watt as Director of the Heart Institute, Dr. Dale Lindsay, Chief of the Division of Research Grants, and Dr. Ernest M. Allen, Associate Director of the National Institutes of Health, to discuss the problems involved in establishing a Primate Conditioning Center at Davis, Somewhat earlier (December 15, 1961), Drs. Meyer, Knutti, Yeager, California. Eyestone, Price, and Allen had had a staff meeting (26) at which agreement was reached that efforts would be made to establish and finance a conditioning center for primates on what at that time was Federal Government property (about 2,000 acres). It was possible that this land could be sold to the University of California. It was clearly understood that this would not constitute a phase-one move toward a primate research station, and that any research to be done would be on the procurement, transportation, care, breeding, etc., of primates. Information on this and on subsequent steps was provided the Study Section at its January 25th executive session. Approval had been obtained from the Director of NIH for a single university, the University of California, to serve as host institution. Conferences had been held with University

President Kerr and Chancellor Mrak of the Davis campus, which had been selected because of the immediate availability of land in a climate suitable to free-ranging primates 57/.

Dr. Allen, speaking for NIH, asked the Study Section whether it would advise setting up a primate conditioning center at this time; if so, whether a single university should act as host institution; and what principles and plans should be used for setting up, financing, and operating such a center. Dr. Allen said that \$2.5 million was being considered for the establishment of the center that fiscal year, to cover cost of land, construction of facilities, and first year of operation 58'. The Study Section thereupon reaffirmed the recommendation made at its May 8, 1961, meeting in favor of establishing a conditioning center. The Study Section's May 8th recommendation included the "It $\frac{397}{100}$ is of the opinion that such a facility should be established following: at the earliest possible moment. Whereas the major function of such a unit would be the development of techniques for procuring, conditioning and maintaining various primate species, it is almost certain to produce special experimental primates for use by qualified investigators and the opportunity to explore the diseases of primates easily transmissible to other animals and man, and vice versa." After suggesting that 300 acres would be the amount of land needed, the Study Section agreed to meet at Davis to determine what other recommendations it should make to the Heart Council relative to a conditioning center there. It met at Davis on February 17, 1962, and recommended to the Council the establishment of the conditioning center at that location.

The Heart Council at its March 1962 meeting recommended that a construction grant and an operations grant "be awarded to the University of California for the establishment of a national primate conditioning center at an appropriate site adjacent to the Davis campus, or at another appropriate site should the Davis site not remain available, the site to be negotiated by the staff of the National Heart Institute with appropriate persons in the university at a facility cost not to exceed \$2.5 million and at a fully developed operations cost not to exceed \$1 million annually; and that in the site negotiations, the National Heart Institute staff is to obtain advice as necessary from members of the Primate Research Study Section."

Thus, the last of the primate research centers became a reality. At the June 1962 Heart Council meeting the members were informed that the Division of Research Facilities and Resources had been created and that, effective July 15, 1962, the Primate Research Centers Program would be transferred from the Heart Institute to that Division. The work of the National Advisory Heart Council, its committees, and its staff was completed <u>60</u>[/].

57/ Dr. K. F. Meyer played an important role in bringing about this establishment of the National Center for Primate Biology at Davis, California.

58/ It was hoped to obtain Bureau of the Budget approval to use \$2 million of the funds that had been appropriated for the primate center program but which had been held in reserve. These funds were not released. The NHI, however, was permitted to transfer \$2.5 million from another NHI program for this purpose.

59/ The Study Section.

60/ Or rather almost completed, for a few more things had to be done in connection with the transfer of the program.

Chapter III. LEGISLATIVE HISTORY 1/

A. Introductory Legislation

When Congress recognized the importance of establishing in this country a national program of primate research facilities, it made the decision that the program would take the form of an as yet undetermined number of regional primate research centers. Because these would be regional in character, the initial amount of two million dollars was appropriated with authorization to use the money for non-matching construction, including purchase of land, as well as for the operation of the centers. These initial funds were for the establishment of one or two centers, and were used to establish one.24Although this was the basis of the initial appropriation, the conviction that a larger national center (later called a "station") should be established persisted in the minds of the members of the Heart Council, the Heart Council committees and the National Advisory Committee for Primates (later the Primate Research Study Section). This conviction was reiterated at the hearings before the House and Senate Appropriation Subcommittees by Dr. Watt and others. The result was that the seventh and final center to be established $\frac{3}{\text{was}}$ a national primate conditioning center, different from the others and later called the "National Center for Primate Biology."4/ These seven centers (six regional and one national), taken together, were to constitute a national resource not only for research using subhuman primates as experimental animals in the various disciplines of medical research, but also for research on subhuman primates themselves. These seven centers were to constitute a national network of coordinated research facilities, the elements of which need not be identical, yet which would function as a coordinated whole.

This national research resource was established to meet needs in the United States that would otherwise involve inordinate expense in primate colony maintenance, needs not being met by other educational institutions, research laboratories, or commercial companies. The new program was directed toward meeting the needs of biomedical research on subhuman primates which could serve as experimental subjects in certain types of studies in which humans could not be used. In these centers, several different species of primates could be used for research in any scientific or clinical discipline, without any implied categorical restrictions. Particularly mentioned in the hearings were the rhesus monkey, the chimpanzee, and the baboon. It was expected that the rhesus monkey would be used most extensively but that as time went on the usefulness of a variety of other species would be explored. Each center would develop its own research orientation and species focus. Under these circumstances, the animals would be studied throughout their life span. Some of

 $\frac{1}{2}$ Some of the more pertinent sections of the hearings of the House and Senate appropriations subcommittees are included in reference($\frac{27}{2}$).

- 2/ At Portland, Oregon.
- 3/ With Fiscal Year 1962 funds.
- 4/ Located at Davis, California.

the investigations would be directed to problems particularly relevant to diseases of the human, and all the research would provide basic biomedical information important to problems of human health.

The regional centers would be appropriately distributed geographically throughout the continental United States in areas where climatic conditions were acceptable. The centers would provide good care for animals, working space and facilities for qualified research scientists from areas other than the local region, and facilities generally not within the scope of the usual research grant. The centers would not constitute a resource for supplying monkeys to all researchers in the United States, from time to time they would provide a limited number of animals for special research purposes to qualified investigators at qualified institutions.

The national center (National Center for Primate Biology) was to differ from the others in that it would focus on the study of the subhuman primate as itself an object of study (just as man is an object of study for his own sake), in comparative studies on different species of primates and on investigations to improve the breeding, handling, maintenance, raising, and nutrition of primates. $\frac{5}{}$ This center was particularly intended to extend the utility of primates as experimental animals in biomedical research. The national center, like the regional centers, would provide space for visiting scientists from other areas, and would cooperate appropriately with the other centers and with qualified institutions.

B. Testimony on status of the centers and on program development (27)

At successive annual congressional hearings the current status, or stage of development, of the program and of the individual centers was reported to the subcommittees. The first indication of NHI interest in primate research and in comparative cardiovascular research was indicated at the Fiscal Year 1959 House Hearings. At the Fiscal Year 1959 Senate Hearings⁶/the subcommittee was told that the NHI was seriously studying the formation of a "colony of primates, of apes and monkeys, a population which can be controlled, in a facility at which studies can be made and to which scientists from all over the world can come to carry out investigations." Dr. K. F. Meyer's earliest visit to "a similar colony . . . in the Crimea" was mentioned. In the record was the NHI proposal for the "Establishment of a Primate Colony for Research Related to Atherosclerosis, Hypertension and other Cardiovascular Diseases." In this way began the legislative moves that led to the Regional Primate Research Centers Program.

5/ Primate Animal Husbandry

6/ Senate and House appropriations subcommittee hearings take place within the six months preceding the beginning of a particular fiscal year, which starts July 1. Usually the House subcommittee hearings take place prior to the Senate. In the House Fiscal Year 1960 Hearings, the desirability and feasibility of developing "a center or centers" for primate research was again stressed, with emphasis on multiple centers rather than a single station. The NHI statement, requested by the House subcommittee, is a part of this record. The corresponding report 7/ of the NHI staff to the Senate subcommittee is a part of the record of the Senate Hearings.

In the House Fiscal Year 1961 Hearings, it was made clear that the Congressional authority to use the primate center appropriations for nonmatching construction and purchase of land as well as for center operational costs was legal and not in conflict with the terms of other authorizations.⁸/ Here also it was clearly understood that the non-matching authority was provided by Congress "on a basis that the Centers were to be regional in nature and not just local." The testimony indicated that eleven million dollars "would be enough in 1961." A little later, the Senate subcommittee was told at their hearings that a "tentative award" had been made to establish a center in Oregon and that the University of Oregon Medical School would be the "host institution." The testimony also indicated that thirteen possible sites had been visited by a special committee of the Heart Council and ten applications⁹/

Testimony at the House hearings for Fiscal Year 1962 brought out that construction of the center facilities at Portland, Oregon, were nearing completion, and that "it may also be desirable to construct at least one center large enough to permit comparative studies on various species of primates, and the increasing difficulty of obtaining suitable primates for research suggests that it may at some future time become necessary to establish breeding colonies for certain species in this country." At the Fiscal Year 1962 Senate Hearings the points brought up in testimony included: (1) Eight or nine key sites were planning to compete for primate center grants, (2) Four major species of primates (the rhesus monkey, the chimpanzee, the baboon and a South American species) plus several

"Feasibility and Desirability of Primate Research Centers" 7/ 8/ NIH had obtained the advice of the HEW General Counsel whose opinion was NIH could do this because "in this case the legislative history indicates the Congressional intent to use funds under the regular appropriation for construction authorized by section 433(a) in addition to funds appropriated for matching grants for construction under Title VII. Should the legislative history be developed through instructions in the House report to use the general authority in section 433(a) for facilities such as we are now discussing, then, I believe it would be appropriate to apply our General Counsel's advice and utilize the general authority in section 433(a) for construction on a non-matching basis without new legislation." (Dr. Shannon speaking). "The advice we got was that the authority provided in the matching funds program (Title VII) did not rescind the provisions of Section 433(a) but rather made that authority lie dormant except where the legislative record indicated that it was the intent of Congress to make the authority of Section 433 (a) active for a specific purpose." (Mr. Richard Seggel, Executive Officer, NIH, speaking.)

9/ Actually eleven applications were reviewed. See Chapter II, footnote 43.

other less well-known species were worthy of study in the centers' programs. (3) Grants had been recommended by the Heart Council for establishment of two more centers, one at Seattle, Washington, and one at Madison, Wisconsin. (4) A question was raised and answered regarding the geographical proximity of the centers at Portland and Seattle. (5) Collaborative visiting scientists would represent one aspect of center program activity. (6) Six to eight regional centers were being planned, four east of the Mississippi and three west, "with the possibility of a supply center being one of these three." That is the general thinking at this time. The original idea, as you will recall, of having a central station^{10⁷} from which a series of these small centers would develop is still one that the group feels very strongly about."11/ (7) There was a need to have non-matching construction grant authority extended to include non-regional, local, institutional primate research facilities. (8) "Regional" was defined: "... 'regional' implies that such facilities should, unless there is a compelling reason to the contrary, be located in different regions of the country. It should not imply that primate centers must serve primarily institutions in a specific region." (9) Ten million dollars should be made available for the primate centers. (10) The Heart Council had asked the Council's Primate Committee, i.e., Organization Committee, for recommendations about: (a) geographical spread of the regional centers; (b) possibility of one of the centers "assuming certain central functions such as keeping census records and other data which would permit the use, for example, of an animal 20 years old, which had grown up in a particular center, in a study of aging;" (c) the question of supply of primates and a breeding colony;127 (d) the need to develop laboratory resources for groups who were particularly interested in specific categorical disease areas but whose activities were local (institutional) rather than regional.

At the Fiscal Year 1963 House Hearings, the testimony indicated that: (1) Three centers were being established (Portland, Seattle, and Madison) and three others projected (Atlanta, Boston, and New Orleans.) (2) Future needs included (a) "a center for the study of the subhuman primates themselves, not as a laboratory animal for studies directed to other purposes, but as the primary subject of investigation," and (b) "a production facility . . . to develop known genetic strains . . ."

10/ "...one large primate station, somewhat comparable to the world-renowned marine biological laboratory at Woods Hole in Cape Cod" was proposed in another part of these Senate Hearings.

11/ From Dr. Watt's testimony before Senator Hill's subcommittee; "the group" refers to Heart Council and committees.

12/ "One center in one location which would carry on a supply function including research on standards of care. It would be a conditioning center to see to it that the animals themselves were in good condition, free from diseases, before they were introduced into any of these colonies." The testimony at the Fiscal Year 1964 House Hearings included these points: (1) In July 1962 the NIH formed the Division of Research Facilities and Resources, which included an Animal Resources Branch to which the Regional Primate Research Centers program was transferred from the National Heart Institute. (2) Of the seven primate centers in the program, one was a national conditioning center and six were regional, "the term 'regional' relating to an integrated scientific community without geographical limitation." (3) "Though each center has its own program orientation, the six regional centers are committed to providing facilities for a broad scope of disciplines using primates in research. The seventh center, a national primate conditioning center, is committed to investigations on the primate itself, including capture and transportation, maintenance under laboratory conditions, and breeding and rearing in captivity. This center will also supply scientists in regional centers and institutions animals that have unique characteristics and that would be unobtainable from any other source." (4) Reports were presented on the status of each individual center.13/

In the Fiscal Year 1965 House Hearings, the Regional Primate Research Centers program was said to have had a slow but "well-grounded" start. This was reiterated at the Senate Fiscal Year 1965 Hearings, and the "slowness" was attributed to the fact that "highly specialized institutions" (centers) had to be developed. The uniqueness of the conditioning center at Davis, California, was emphasized, as was the fact that it was associated with a campus having a Veterinary College and a developing new medical school.

During the Fiscal Year 1966 House Hearings, the following points were included in the testimony: (1) Of the seven primate centers, four, (Oregon, Madison, New Orleans, Seattle) were completed, and all had initiated research programs. (2) Because the centers were regional in character, the NIH was doing its best "to provide the full direct costs and as much of the indirect costs as are permitted under present regulations."¹⁴ Further, "We do not look upon the state university as an equal partner with us in the financing of this resource, because this resource will meet the needs of many people outside the state--and this is the way we wish it."¹⁵

Testimony at the Fiscal Year 1967 House Hearings included: (1) Of the "seven primate centers, six regional and one national," construction of five had been completed and the other two "will be completed before summer. All have their research programs under way." (2) A report was made of some results of the research in the established centers.16' (3) The essential components of a

13/ See Summary Statement, pages 1-6.

14/ Dr. Shannon's testimony, at the moment referring to the Oregon Center.

15/ Dr. Shannon's testimony, at the moment referring to the Oregon Center.

 $\frac{16}{a}$ These need not be detailed here. The important fact is that here began a feedback to the Congress of research results.

primate center were considered to be (a) the core research program, (b) a visiting scientist program, and (c) collaborative research wherein core staff members cooperate with other scientists. (4) The official names of the seven centers were given as follows:

Oregon Regional Primate Research Center Wisconsin Regional Primate Research Center Primate Research Center of the University of Washington<u>17</u>/ Delta Regional Primate Research Center Yerkes Regional Primate Research Center New England Regional Primate Research Center National Center for Primate Biology<u>18</u>/

C. Tabulation of annual appropriations and obligations

The following tabulation shows the Congressional appropriation figures for Fiscal Years 1960 through 1967 and the amounts used ("obligations") for each of the years excepting 1967. In Fiscal Year 1962, \$2 million of the \$9 million appropriated by the Congress was held in reserve and not made available. In order to establish the National Center for Primate Biology, \$2.5 million was transferred from another Heart Institute program. The NHI financed the centers with Fiscal Years 1960, 1961, and 1962 funds. After Fiscal Year 1962 none of the appropriated funds could be used for construction. The \$9 million in Fiscal Year 1967 was not sufficient to implement all previous recommendations or to develop the program fully.

<u>Fiscal Year</u>	Appropriation	<u>Obligation</u>				
1960	\$2,000,000	\$1,917,000				
1961	7,000,000	6,881,242				
1962	9,000,000	9,494,972				
1963	6,000,000	4,443,600				
1964	5,700,000	6,194,484				
1965	7,000,000	7,000,000				
1966	7,000,000	7,000,000				
1967	9,000,000	9,000,000				

Chapter IV. THE DRFR PERIOD

The DRFR period began in July 1962 when the Regional Primate Research Centers Program, together with Dr. Eyestone and staff who were administering the program in the NHI, moved from NHI to DRFR. Since then the number of centers has remained the same, six centers being designated as "regional" and one as

17/ Subsequently "Regional Primate Research Center" (University of Washington).

18/ A status report on these individual centers was put in the record, the one on the National Center being much longer. It is not necessary to give details here. The important point here is that detailed reports did go back to Congress. "national." The difference between "regional" and "national" is not clear-cut, for all of the centers are organized according to the same general pattern. The "national" center differs from the "regional" centers chiefly in its commitment to carry on investigations of breeding and animal husbandry with respect to various species of primates.

Although the overall characteristics of the primate centers have in general remained the same during the DRFR period, various administrative problems arose that are inevitable in any program still in the developmental stages. Some of them are local, requiring local solution by the center director and staff alone, or in cooperation with appropriate representatives of the host institution, particularly with the "Principal Investigator." Some of the problems are such that their solution requires cooperative consideration and action between the center director and/or principal investigator on the one hand, and representatives of the DRFR staff administering the primate center program.

The staff of DRFR's Animal Resources Branch remains continuously in touch with the directors of the centers in order to maintain an effective working relationship, to be continuously aware of significant developments, to be in the best position to provide necessary administrative services, and to help resolve mutual problems when they arise. The ARB staff also arranges periodic site visits to each center by a group of knowledgeable consultants (usually the committee that initially reviews the applications.) Members of the staff arrange periodic meetings of the center directors to discuss problems requiring solution, and to encourage exchange of information between the centers.

A number of these meetings of the center directors have been held1[/]. Various subjects were discussed: high standards of animal care, workshops and symposia, procurement of primates, primate holding facilities, fiscal relationships of center base grant to other grant support, accreditation of centers by American Association for Accreditation of Laboratory Animal Care, cost-sharing, availability of Federal excess property to the centers, usage of computers by centers, need for better communications to and from and between centers, "time and effort" requirements, the meaning of "regionality," and the kind and amount of "commitments" NIH has made to support center development and operations.

The following are examples of problems of special concern to the staff:

(1) Outstanding is the problem of adequate financial support. The grants for establishment of the seven centers were not awarded at the same time and therefore the construction of facilities and the beginning of program operations

1/ Meetings of the center directors were held October 11, 1963 (in Bethesda, Md.); July 1964 (Beaverton, Ore.); November 20, 1964 (Covington, La.); April 1, 1965 (Bethesda, Md.); October 28, 1965 (Atlanta, Ga.); April 27, 1966 (Davis, Cal.); and November 13, 1966 (Southborough, Mass.). At other times Workshop meetings were held at Tulane University, New Orleans, La., and at the national center, Davis, Cal. started at different times. Consequently, centers that began early had early access to available funds² and were well along in their development when later centers were still putting up their buildings. As the level of the annual appropriations did not rise in the years 1963, 1964, 1965, and 1966, it was not possible for NIH to provide sufficient funds for the full development of the centers, particularly those that were started later. Additional operational funds appropriated in fiscal 1967 were not sufficient to implement earlier recommendations, causing some local problems at the center sites.

(2) Because of the character of the research program at the National Center for Primate Biology, with its emphasis on animal husbandry, additional construction is needed to provide outdoor housing for the primates. The absence of authority for construction and the unavailability of non-matching construction funds in the primate center program constitute impediments to the full development of this center. The same problem of needed construction also prevails at some of the other centers, for example at New Orleans (Covington, Louisiana).

(3) A financial problem stems from the impact upon a center by the addition of research projects supported by grants to members of the core staff or the addition of special projects carried on in a center by visiting scientists. In either case, certain costs of providing necessary facilities and services, such as animals and animal caretaker services, may be paid for by funds in the center's basic grant. A problem is created when these demands upon the base grant exceed what that grant can provide. The administrative problem is to increase the base grant, when necessary, if appropriations are insufficient³/.

(4) A problem exists with regard to the national scientific advisory boards^{4/} that, according to initial agreements, were to be set up to periodically review the broad aspects of a center's program and advise the principal investigator. Not all of these advisory boards have been established; however, when one is set up, there is a question concerning its usefulness. A "rubber stamp" committee is of little use and a hypercritical one is not most effective. The specific role of such a group has not been worked out. A pertinent question is whether the advisory function might be performed more effectively by periodic evaluation visits by members of the Primate Research Centers Advisory Committee. To a considerable degree this committee has been providing advice that ultimately goes to the director of a center and to the principal investigator.

 $\frac{2}{1}$ These could not be held over past the fiscal appropriation year for the use of the centers beginning later.

 $\frac{3}{1}$ The Animal Resources Branch, DRFR, has found it necessary to establish a limitation of 25 percent of the total operational budget on the amount of additional grant support; to exceed this PHS approval is required.

4/ Committee, Board, Council--the name varies.

(5) It is possible that a difficulty may arise in regard to the relationships between a director of a center and the principal investigator or others in the host institution⁵. Depending upon the seriousness of the problem, it may be solved locally by the host institution or its solution may require the intervention of the Federal granting agency. Federal intervention can take place, but this is regarded as undesirable unless absolutely necessary. However, the staff stands ready to assist in a local solution when asked to do so.

(6) Primary control of a center and its activities rests with the director of the center, the principal investigator in the host institution, and the NIH (DRFR) staff. There is a problem in regard to the most appropriate distribution of this control and the inter-relationships involved. The goal is to attain communication and mutual understanding. Most of the center directors were selected because of their recognized research accomplishments; it is expected that their research experience and interests would strongly influence the initial orientation of the center programs. Their goals may or may not be identical with Congressional intent. To what extent and by what means is DRFR to exercise influence or pressure upon a center if its program is not completely fulfilling Congressional intent?

(7) What should be the policy position of NIH with respect to funds from another agency or private source being used for the construction of additional facilities at a center site to expand the program of the center? What responsibility does the NIH have to see that such additions will not change the purposes of the center from those intended by Congress? A policy position on this point has not been clearly worked out and probably will become well defined only when required by actual developments.

(8) The "regional" or "national" role and responsibilities of a center are yet to be clearly defined or widely understood by potential users of a center, including those wishing to be accepted as visiting scientists, whether they are from the local region or from far away. This is largely a matter of mutual education and understanding between the center director and staff and the potential users. A problem does exist as to the best mechanism for deciding whether to provide facilities and animals to near or distant applicants. Ultimately, the responsibility for the decision must rest upon the director of the center. Should he make these decisions alone as director or should he have an advisory group for this purpose? What responsibility does DRFR have to see that any particular desision-making mechanism is set up at the center?⁶

(9) The respective roles of the "regional" centers and the "national" center and the functional relationship between them have not yet been clearly defined.

5/ A problem of this type did arise once and was resolved locally with great difficulty.

6/ Experience thus far has indicated that some persons have assumed that because a center is "regional" and government-supported they can obtain facilities and animals practically on demand, which is not the case.

It is expected that these will be worked out with further operational experiences. To what extent are the centers to form an integrated coordinated whole? To what extent and by what means is the "national" center to serve as a focal point in the total centers program for communications, information, and coordination?²/

(10) The ARB has had difficulty in establishing clear-cut communications on steps leading to sources of support for additional activities at a center from other NIH or PHS supported programs, other public or private granting agencies, or private individuals or organizations. An attempt is made by the staff to obtain such information early from the directors of the centers. It is more difficult to obtain early and complete information from the many support programs of the NIH and PHS. These communications problems have yet to be satisfactorily resolved.

(11) There is the question of the interrelationship of the Regional Primate Research Centers Program and the Animal Resources Branch staff on the one hand, and NIH grant applications for support of projects involving subhuman primates on the other. The ARB staff is in a favorable position to provide or to obtain expert advice relative to the procurement and maintenance of primates for research. Should the ARB staff serve as an additional source of advice to NIH review groups not in DRFR? If so, by what communication mechanism should they do so?

(12) The regional centers are still in a relatively early period of development and are not at a stage at which one should expect "startling discoveries." A problem arises as to if and when such "discoveries" are expected and demanded in return for the financial investment in research. The maximum usefulness of these centers, as a national resource, lies not in infrequent "startling discoveries" but in a steady, continuous and highly competent level of research and training activity.

(13) One problem, related to that just mentioned, is inherent in the human tendency to want to know quickly what the financial investment in the centers has bought in terms of program activity and research results. This tends to lead to attempts at early evaluations. Those who first conceived the program envisioned a project that would be established on a very long-term basis (for a hundred years or more). The staff sees to it that periodic evaluations are made of developmental progress. But full development of these centers probably will take not less than five and perhaps as many as ten years. Attempts to evaluate a completed center very likely would be premature before at least five years after the completion of construction.

7/ As indicated in some of the legislative language of the Congressional hearings relative to the establishment of a national "primate conditioning center."

Chapter V. PROGRAM POLICIES AND PROCEDURES

The development of some of the policies and procedures for the Regional Primate Research Centers Program has been described in the preceding sections. It is unnecessary here to go into all of their details. The reader will find these in the most current brochures for construction grants1/ and operational grants2.

Early in the development of this program, long before the appropriation of any funds by the Congress, consideration was given to the problem of how best to finance the primate centers, whether by grant or by contract. It was recognized that if financed through a grant, whether for construction or operations, or both, the large size of the grant and the character of the project would necessitate special handling by the administrative staff. The staff would have to play a continuing role not only during the development of a center but also after the center had been completed and was operating. As such a grant would be midway between a regular research grant and a contract, the responsibilities of the NIH staff would be similar to those if the contract mechanism were used. The decision to use one or the other of these two support mechanisms, therefore, came to rest largely on the way the one used would affect the recipient of the award. Because these centers were to be established on a very long-term basis, and because the recipient institutions would want (and did want) an overt expression of the long-term commitment of the Federal Government to the continued support of the centers, it was decided to use the grant mechanism and to award the operational grants for an initial ten-year period3!

A. Construction of Facilities

Although at first the intent was to provide both construction and operations funds through a single grant, it soon became necessary to support construction by one grant and the operations by another, and to award the construction grant for a two-year period.

Conditions for the award and utilization of construction grant funds were developed, based almost entirely on those that had been developed for the NIH matching construction grant programs^{4/}. The construction grant funds for primate

1/ "Policies and Procedures Governing Grants Awarded for Construction of Primate Research Facilities," Grants and Training Branch, National Heart Institute.(18)

2/ A "Guide to the Policies and Procedures Governing Grants Awarded for Operation of Regional Primate Research Centers," still in preparation, although a draft is in actual use.

3/ i.e., initial year plus nine years of promised support at specified annual ceiling amounts. This was done in the first award (Oregon) but NIH policy limitation to not more than seven years for a "grant period" forced a gradual reduction from ten to seven years.

4/ Administered by the Health Research Facilities Branch, DRFR.

centers could be used for purchase of land, architectural fees, and construction costs. They could not be used for operational costs. The performance of construction had to comply with a number of conditions. It was the responsibility of the grantee (host) institution to supervise and inspect the construction in progress and to determine when the construction had been completed in compliance with the conditions, to accept the completed facility, and to make final payment to the contractor. Inspection visits could also be made by members of the National Advisory Heart Council and the NHI staff. The grantee institution had to keep appropriate accounting records suitable for audit and to provide the granting agency (NHI) with the necessary expenditure report(s). Construction grant funds were released to the grantee institution, upon appropriately timed requests, in suitable installment payments as construction progressed. At least 5 percent of the grant funds were withheld by the granting agency to satisfy any possible claims or adjustments at the final audit. Upon completion of construction and acceptance by the grantee institution, inspection of the primate research facility could be made by the Surgeon General of the PHS or his representative(s).

To assist in the handling of the construction aspects of the Regional Primate Research Center program, Dr. Eyestone called upon the services of the intramural NIH architects and added an architect-engineer to his staff. Although, for one reason or another, some of the construction took longer than was at first anticipated, the program moved along without particular difficulty. The first construction began in 1960 in Portland, Oregon, and the last was finished at Davis, California, in 1966. In practically all of the centers, investigative programs began prior to completion.

B. Operation of Centers

Operational grants to the centers are subject to the PHS regulations for research project grants⁵, to the extent that they apply⁶. In line with the initial agreements made before each grant was awarded²⁷, every center director was to have a scientific advisory board including member scientists with broad experience in a variety of disciplines from various parts of the country. The board members, who were to be selected and appointed by the host institution (the principal investigator being responsible), would meet at the center at

5/ Title 42, Chapter I, Subchapter D, Part 52.

 $\frac{6}{100}$ An informal policy guide was developed in 1963 to supplement the regulations for research project grants and has been used as a guide in the operation of the program.

7/ "Statement of Responsibilities and Relationships."

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least once a year to review the activities, status, and accomplishments of the center. It would then make its report to the principal investigator⁸. As the recommendations of the board are not binding, there is some question as to how effective and helpful to the centers the boards will be.

Each center is to provide space, facilities, and animals to visiting scientists on a selected basis, so that they may carry on discrete studies for a limited time.⁹. The base-operating grant of the center can provide the salary and traveling expenses of a visiting scientist. Other costs are generally not allowable¹⁰. Other research expenses may come from other sources, such as individual research grants.

The centers were not established to provide facilities and animals to researchers merely on demand. Each center must make a decision according to certain criteria, to accept or reject a request. The responsibility for the decision rests with the center director, whether he makes the decision alone or with advice from others. The most appropriate criteria for arriving at the best decisions have yet to be fully determined.

Budget negotiations between the ARB staff and each center director and staff are carried on annually at an appropriate date prior to a forthcoming grant period. The negotiations are to determine the amounts to be included in the application for continued support. The amounts determined take into consideration other sources of support, such as other grants, contracts, or fees for services to outside investigators. The total budget may include, as direct costs, complete support of (a) the core research program, (b) maintenance, (c) administrative activities carried on at the center, (d) a fixed cost fee to the grantee institution for payroll, purchasing, library, and other appropriate services $\frac{11}{}$. Each center was designed for a scientific program not to exceed \$2 million when fully operational; this may not be exceeded without PHS approval, or without convincing evidence that adequate facilities are available. Outside funding is limited to about 25 percent of the total operating budget; the centers advise the PHS when the support from other sources exceeds this limit. This percentage may not be exceeded without PHS approval.

The host institution is a university which has accepted responsibility for providing an academic environment of high quality for the center's director and staff. In accordance with NIH policy, the host institution also provides

- 8/ An official of the host institution.
- 9/ Not to exceed two years without PHS approval (policy limitation).
- 10/ PHS approval required for other costs.

11/ A proposed policy was not implemented. The grantee institutions have been reimbursed for indirect costs not to exceed actual indirect costs.

a principal investigator $12^{/}$ who is responsible to the PHS for the conduct of the operation of the center. Administratively under the principal investigator, the director of the center has scientific responsibility for the conduct of the operations of the center and its research program. The core staff is responsible to the director of the center.

Before the initial grants were awarded by the NHI a "Statement of responsibilities and Relationships" had to be signed by the designated director of each center, by the designated principal investigator, and by other appropriate representatives of the host institution and any other institution willing to provide formal backing to the proposed center.

The "Statement of Responsibilities and Relationships" is an important document that, at least in one instance, has served as an effective compass in helping a center maintain a steady course even in rough weather. The "Statement" charts this course by indicating the purpose of the center, the administrative and academic relationships (particularly between the director of the center and the principal investigator or other responsible official of the host institution), the appointment procedures and the role of the Scientific Advisory Board, and the reasons for locating the center in the area. The "Statements" for all centers are similar(16).

Chapter VI. SOME GENERALIZATIONS

During the development of the Regional Primate Research Centers Program, some generalizations and principles emerged and at times formed bases for the development of policy or procedure. The following are examples:

(1) Such a program as this is necessarily a "closed" rather than an "open" one. By this is meant that it makes good sense to establish only a limited number of regional centers in the country. The number of centers along with the average cost per center determines the size of the program.

(2) Decisions as to the number of centers and the size of the program must be made by the NIH staff, taking into consideration the advice of knowledgeable, experienced consultants.

(3) Factors other than "scientific merit" must be taken into consideration in deciding on the size and form of a regional center program. Factors not brought into consideration by consultants in formulating their recommendations must be considered by the staff.

(4) The development of a regional center program requires the know-how both of scientific consultants and administrative staff. Neither can do the job alone. Their teamwork is essential, as in the case of the present program.

12/ At Portland, Madison, and Seattle, for a limited initial period, a single individual was both director of the center and principal investigator, but this is no longer the case.

(5) Financial support for the construction and operation of a regional center is best provided by a pair of grants (or a pair of contracts), one to support construction, the other the operation of the center.

(6) Instead of making a general announcement and invitation to the public to submit applications, it is better for the granting agency, with the advice and assistance of consultants, to seek out the most qualified potential host institutions and negotiate with them grant applications or pre-contract proposals. Applications from unsolicited sites would also be accepted and allowed to compete for available funds.

(7) The centers need not be identical in their program orientations or in the pattern of their facilities; however, there should be certain basic similarities to their organizational structures. There should be an optimum balance between constraint and flexibility.

(8) A considerable amount of overlapping in research program activities should be acceptable, avoiding only unproductive and useless duplication.

(9) The "regional" or "national" aspects of a center should be interpreted broadly; in general, narrow, restrictive definitions should be avoided.

(10) Each "regional" center must be welcome in the locality and have responsible local cooperation and backing from institutions in the area.

(11) A regional center should be established only an a long-term basis. Only under special and exceptional circumstances would it be reasonable to make large investments in a regional center on a short-term basis.

(12) A regional research center would, in general, be better located if it were closely associated with and geographically near a qualified academic institution.

(13) Multiple sources of support should be available to regional centers, but limitations and conditions of support must exist if the original purpose of the center is to be maintained and the "control" of the center is to remain unified.

(14) Initial agreements and understandings should be incorporated into a document signed by the appropriate parties, in order that future misunderstandings may be avoided.

(15) The granting agency should not interfere in the local solutions of local difficulties; it should intervene only as a last resort to resolve a problem. However, the granting agency should work at all times with the center director and principal investigator (or others) and be ready to render assistance.

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(16) Continuing communication efforts should be made to maintain maximum understanding on the part of all concerned relative to the various interlocking responsibilities of the agency staff, the center staff, the principal investigator, the host institution and others involved in the operation of a center.

Chapter VII. OUTLOOK

These regional primate research centers not only are sites of research, but also should be centers for the special training of future primate researchers and supporting personnel involved in the maintenance and handling of primates. It is to be expected that at the beginning the major effort in these centers would be to develop active research programs; these would then provide the setting for training programs. There are signs that this phase of center activity is already beginning.

Was there something particularly significant about the number seven, that seven and only seven regional primate research centers were established? The answer is no. Time and chance, not magic, brought about the decision to establish seven centers. At the time when it was sensed administratively that Congress had to be presented with the image of a definitive, but limited program, the "sites" that appeared most ready to accept local responsibility and support the establishment of regional centers numbered seven. At that point in time and in the prevailing scheme of things an administrative decision was made to "close" the program¹. The temporary Congressional authorization to use appropriated funds for non-matching construction was terminated2/; but not necessarily irrevocably, for Congress can give and Congress can take away such authorization when in its good judgment the giving or taking away is in order. When the funds were made available for the non-matching construction of the seventh and last center and the program became "closed," it was but natural to think the job done. Actually it was not. The 300 acres of land at Davis and the 500 at New Orleans, for example, were purchased to develop outdoor colonies of primates with outdoor housing and runways. These have not yet been built. Until they are somehow provided, the centers cannot develop their full and intended capabilities, but will remain underdeveloped resources.

Additional funds are required not only for construction but also to implement operational developments in the centers. Some of the recommendations made earlier by the present Council have not been carried out.

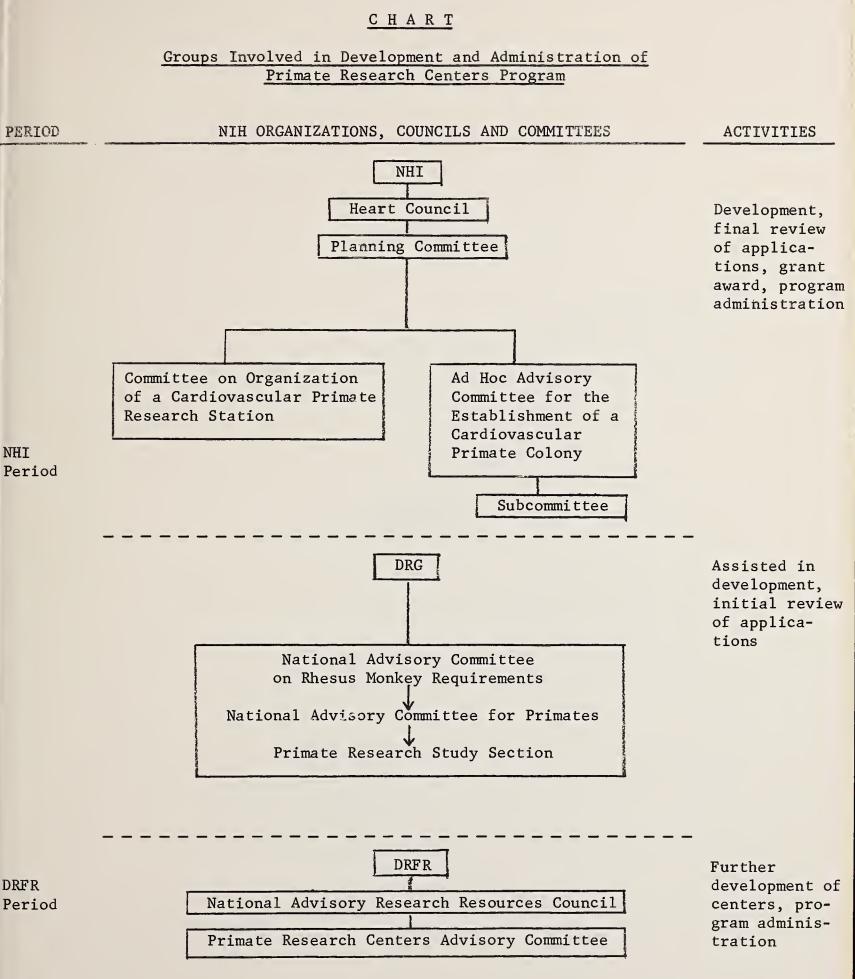
It was unrealistic to consider the program complete when the decision was made to limit the number of centers to seven. Hardly had that decision been made when the program was transferred from one part of NIH to another. Although the

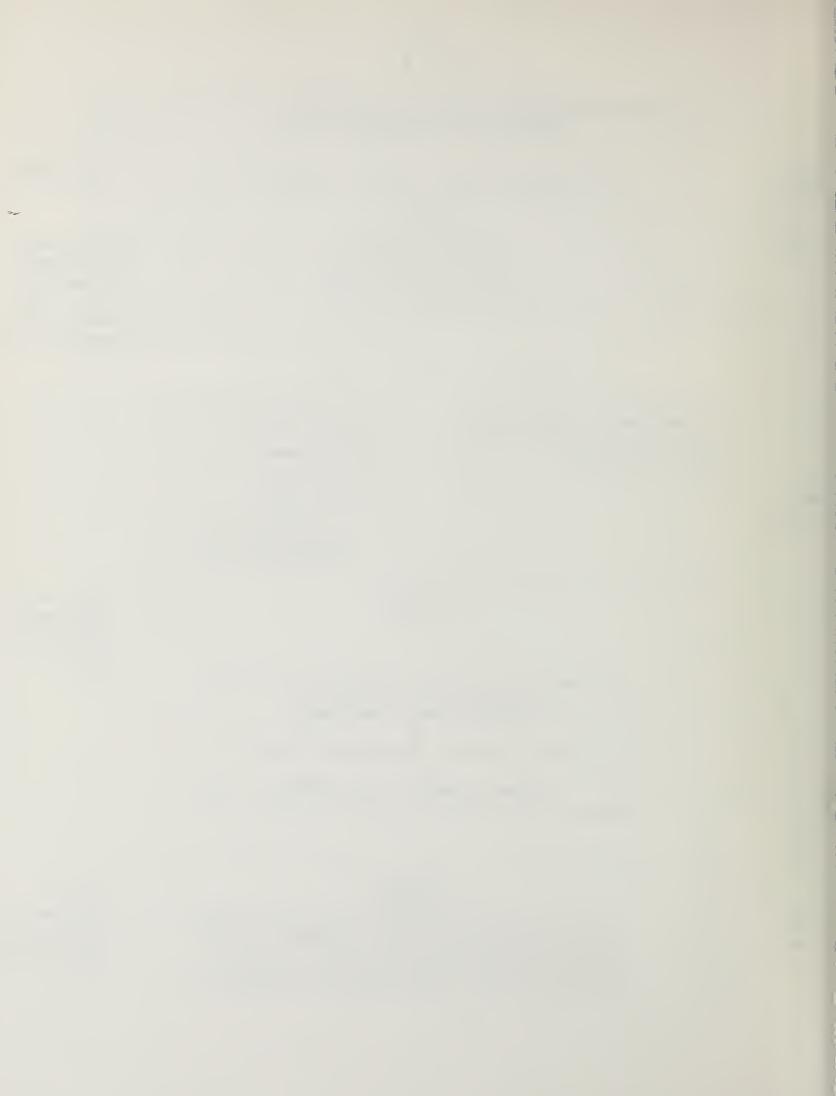
1/ Congressional testimony had indicated an intent to establish six to eight primate centers.

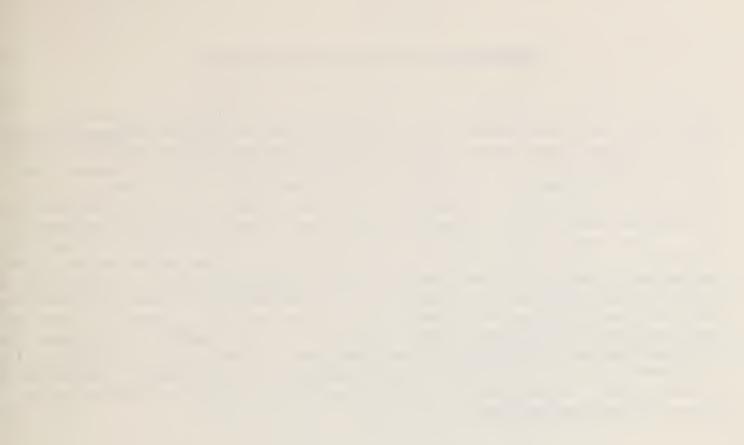
2/ The authorization had been made available because and only because the centers were to be regional, not merely local.

staff moved with the program and continued to administer it, much of the momentum of the program development was lost. To make up for this loss will require vigorous and concentrated efforts by staff and scientific consultants, particularly those constituting the Study Section and Council.

The seven centers are still in their infancy, requiring tender administrative love and financial care. It will be interesting to see them grow and develop during the next ten years to physical and operational maturity. The direction of their development will be greatly influenced not only by each center director and host institution, but also by the DRFR staff and its consultants on the initial review committee and Council. In the final analysis, the success of the program now underway will determine its future course. A sound program well executed will do much to gain the continued interest and support of appropriating bodies of the Congress.







Chronology

Explanation of Chronological Listing

Events are listed only if they are pertinent to the text of this report. Meetings of the Heart Council, its committees and the Primate Research Study Section group (formerly committee) are not listed unless something transpired that was significant to the Regional Primate Research Centers Program. The letters "FY" preceding a year indicate that the fiscal year is meant. One should bear in mind that the Federal fiscal year begins on July 1 and runs through the next June 30. Thus one fiscal year stands astride two calendar years. Furthermore, the item listed relative to a fiscal year will have been discussed at the Congressional Hearings about six to nine months prior to the beginning of the fiscal year indicated. For example, in calendar year 1958, the Senate appropriations subcommittee was informed by a witness that the Heart Institute was planning the formation of a primate colony. However, since the testimony was in the hearings for the Fiscal Year 1959 budget, it is shown in this listing for "FY 1959." A fiscal year can be approximately translated into a calendar year by subtracting a number of months from the July 1 beginning of a fiscal year: subtact nine months in case of House Hearings and six months in case of Senate Hearings.

CHRONOLOGY

1947	DRG	tried	to	establish	a	chimpanzee	supply	program.	(p.	6)1/	

- 1949 DRG again tried to establish a chimpanzee supply program. (p. 6)
- 1954 (September) Committee on Radiation Studies recommended development of a proposal to establish a national primate laboratory and set up a subcommittee to develop the proposal. (p. 6)
- 1954 (November) Subcommittee of the NIH Committee on Radiation Studies held a conference on the need to procure primates for a long-term primate research program. (p. 7)
- 1955 (January) Committee on Radiation Studies held "Conference on the Use of Primates for Studies of Radiation Effects and Aging." (p. 6)
- 1955 (January) Committee on Radiation Studies said one large primate laboratory was not necessary but existing excellent primate laboratories should be supported. (p. 7)
- 1955 (May) State Department requested survey of need for rhesus monkeys for fiscal year beginning July 1, 1955. (p. 7)
- 1955 (May) Membership of "<u>ad hoc</u> Committee on Needs for Rhesus Monkeys Dr. E. Cowles Andrus (Chairman), Dr. Harry Harlow, Dr. Theodore Ruch, Dr. Leon Schmidt. Shortly thereafter in 1955 the name was changed to "National Advisory Committee on Rhesus Monkey Requirements." (p. 7)
- 1955 (June) Under auspices of NAS-NRC conference held on procurement of rhesus monkeys by the Institute of Laboratory Animal Resources. (p. 7)
- 1956 (January) Human Embryology and Development Study Section appointed subcommittee to look into needs for pregnant primates for research. (p. 7)
- 1956 (February) Heart Council considered letter of Dr. George Burch on need for better experimental animals.
- 1956 (August) Dr. K. F. Meyer by letter expressed need for primate research colony in the U. S., after visiting Russian primate colony at Sukhumi earlier in the year. (pp. 1 and 8)
- 1956 (August) First NHI exchange group visited Russia; Dr. James Watt, NHI Director, visited Russian primate colony at Sukhumi. (pp.1 and 8)

1/ Page numbers refer to this report.

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- 1956 (September) HED Study Section subcommittee recommended support of both central and independent colonies of monkeys. (p. 7)
- 1956 (from September on) Dr. Watt discussed with members of Heart Council the Sukhumi visit and the need for primate research facilities in the U.S. (p. 8)
- 1956 (October) National Library of Medicine established. (p. 17)

1957 (January) Heart Council Planning Committee meeting. Primate colony in the U. S. urged. (p. 8)

- 1957 (February) Dr. Watt reported informally to Heart Council at its regular meeting on the Sukhumi visit. Council charged its Planning Committee to initiate planning for long-term cardiovascular primate research colony on the mainland of the U. S. (p. 8)
- 1957 (May) Heart Council Planning Committee asks its chairman (Dr. Andrus) and NHI staff to set up an <u>ad hoc</u> committee to develop definitive plans for a national primate colony. (p. 9)
- 1957 (May-June) NHI ad hoc Advisory Committee for the Establishment of a Cardiovascular Primate Colony (Dr. Burch, Chairman) appointed to work with Heart Council Planning Committee. (p. 9)
- 1957 (June) Heart Council meeting. Dr. Andrus tells Council of an NRC survey on primate needs and supply in the U. S., for which the National Advisory Health Council had recommended support. (p. 9)
- 1957 (August) HED Study Section, hearing of NHI interest in primate colonies, again set up subcommittee to advise in the matter and recommended that the NIH Councils consider ways and means. (p. 7)
- 1957 (September) First meeting of "ad hoc Advisory Committee for the Establishment of a Cardiovascular Primate Colony," Dr. George Burch, Chairman, at Dupont Plaza Hotel, Washington, D. C. A subcommittee was appointed to develop detailed initial plans: Dr. Howard Curtis (Chairman), Dr. Leon Schmidt, Dr. Harry Harlow, and Dr. Theodore Ruch. (p. 9)
- 1957 (November) Dr. Burch reported to Heart Council at its regular meeting on the September meeting of the <u>ad hoc</u> committee. (p. 11)
- 1957 (September 25 to May 10) Period in which the <u>ad hoc</u> committee's subcommittee (Dr. Curtis, Chairman) visited a number of sites and prepared a report "A Proposal for a National Primate Institute." (p. 11)
- 1958 (January) Dr. K. F. Meyer succeeded Dr. E. Cowles Andrus as chairman of the National Advisory Committee for Rhesus Monkey Requirements. (p. 7)

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- 1958 (February) Second meeting of the Burch ad hoc committee. Discussion of the subcommittee's report, "A Proposal for a National Primate Institute." (p. 11)
- 1958 (February) Dr. Burch reported to Heart Council on the February 10 meeting of the <u>ad hoc</u> committee. Council appointed a new Heart Council "Committee on the Organization of a Cardiovascular Primate Research Station,"1/ consisting of Dr. George Burch (chairman), Dr. Michael E. DeBakey, Mr. David Robertson, and Dr. William P. Shepard, all Heart Council members. (p. 13)
- 1958 (April) NHI staff revision of the subcommittee document "A Proposal for a National Primate Institute," now given the title "Report of the Subcommittee of the Cardiovascular Primate Committee." (p. 13)
- 1958 (May) First meeting of the Organization Committee, which was temporarily chaired by Dr. Andrus. Dr. George Burch was made permanent chairman. (p. 13)
- 1958 (May) Planning Committee meeting. Dr. Burch reported on the May meeting of the Organization Committee.
- 1958 (June) Heart Council at its regular meeting accepted the staff version, "Report of the Subcommittee of the Cardiovascular Primate Committee," of the subcommittee report, a "Report on the Cardiovascular Primate Committee" by Dr. Burch, Chairman, and a report by Dr. Andrus on the May meeting of the Council's Organization Committee. The Council dismissed the <u>ad hoc</u> committee with expression of appreciation and thanks. (p. 14)
- 1958 (July) Planning Committee told that Dr. Willard H. Eyestone had agreed to assist in the planning for a primate station. (p. 15)
- 1958 (October) Meeting of Organization Committee. Dr. Watt told the committee of a Congressional mandate to NHI. (p. 15)
- 1958 (November) Heart Council meeting. Dr. Burch reported on October meeting of the Organization Committee. Council recommended a planning grant to Dr. Burch, Chairman. Council was informed Dr. Eyestone had agreed to assist. Council reiterated that national station was feasible and desirable. (p. 16)
- 1959 (February) Planning Committee meeting. Primate research station favored.
- 1959 (March) Doctors Burch, Watt, Eyestone, and Yeager met with Dr. Shannon on

1/ The abbreviated title "Organization Committee" will be used hereafter to designate this committee.

question of primate research station; Dr. Shannon favored regional centers rather than a national station. (p. 16)

- 1959 (April) NHI staff document, "Feasibility and Desirability of Primate Research Centers," prepared for Senate Appropriations Subcommittee. (Note: a similar statement was prepared for the House Appropriations Subcommittee.) (pp. 17 and 34)
- 1959 (June) Heart Council meeting. Dr. Watt reported that multiple regional centers should be considered. Council concurred and advised its Organization Committee to consider both a national station and regional centers. (p. 16)
- 1959 (July) Name of "National Advisory Committee for Rhesus Monkey Requirements" changed to "National Advisory Committee on Primates." (p. 7)
- 1959 (July) Third meeting of Organization Committee at Roosevelt Hotel in New Orleans. Committee recommended that both a central national station and regional centers be established. (p. 17)
- 1959 (July 17 to
September 5)Period in which Organization Committee members and NHI and DRG
staff made 13 exploratory site visits. (pp. 19 and 20)
- 1959 (September) Organization Committee meeting in Bethesda. Site visit reports discussed and sites evaluated. Procedures for obtaining applications and supporting centers proposed by NHI staff. (pp. 19,20, and 21)
- 1959 (September) Planning Committee meeting. Close teamwork with National Advisory Committee for Primates favored. (p. 21)
- 1959 (October) Dr. Eyestone joined the staff of the Heart Institute, in charge of the Regional Primate Research Centers program. (p. 18)
- 1959 (November) Organization Committee meets with Planning Committee. (p. 21)
- 1959 (November) Heart Council meeting. Council concurred in proposed procedures for obtaining applications and supporting centers. (p. 21)
- 1959 (November) Joint meeting of Organization Committee and the National Advisory Committee for Primates in San Francisco. (p. 22)
- 1959 (November) Meeting of National Advisory Committee for Primates. Committee urges national primate research center. (p. 22)
- 1959 (December) National Research Council held meeting on primate field research, Washington, D.C.

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- FY 1959 Senate Appropriations Subcommittee informed that NHI is studying formation of a colony of primates; that Dr. K. F. Meyer visited Sukhumi; in the record is NHI document "Establishment of a Primate Colony for Research Related to Atherosclerosis, Hypertension and Other Cardiovascular Diseases." (p. 33)
- 1960 (January) Meeting of National Advisory Committee for Primates. Reviewed 11 applications, of which two were recommended (Seattle and Portland); drafted a resolution to Heart Council for support of primate research other than in regional centers, including funds for construction. (p. 23)
- 1960 (February) Planning Committee meeting. Concurrence with NACP recommendation of two out of eleven applications for centers at Seattle and Portland. (p. 24)
- 1960 (March) Heart Council meeting. The Council recommended one of the two center applications that had been recommended by NACP and Planning Committee for Fiscal Year 1960 support. The application recommended was from Portland, Oregon. (pp. 24 and 25)
- 1960 (April) Meeting in Portland, Oregon, of NHI staff with local representatives, leading to formulation of "Statement of Responsibilities and Relationships." (p. 26)
- 1960 (April) The Oregon "Statement of Responsibilities and Relationships" signed. (p. 26)
- 1960 (May 1) Beginning of grant period for establishment of first regional center at Portland, Oregon. (p. 5)
- 1960 (May) Meeting of National Advisory Committee for Primates. The committee chose to function chiefly as a scientific advisory group. Heart Council recommendations of concern to the committee. (p. 25)
- 1960 (September) A meeting of the Organization Committee with special consultants to advise on plan for primate research station, held at the Park Sheraton Hotel, New York, New York. (p. 28)
- 1960 (October) Meeting of National Advisory Committee on Primates. "Guidelines for Organization of Primate Research Centers" were being developed and were reported on to the committee. "Regional" was interpreted as "non-intra-institutional;" funds could support operations but not construction outside the U. S. (p. 28)
- 1960 (October to February 15, 1961) Sometime in this period, probably in early January 1961, name of NACP changed to "Primate Research Study Section." (p. 28)

- 1960 (October) Planning Committee meeting. "Guidelines for Organization of Primate Research Centers" reviewed; a national primate research station urged. (p. 27)
- FY 1960 House Appropriations Subcommittee told of desirability and feasibility of a center or centers for primate research. Emphasis was on multiple regional centers. Record contains NHI document "Feasibility and Desirability of Primate Research Centers." (pp. 15, 16, and 34)
- FY 1960 Congress appropriated \$2 million. (p. 37)
- 1961 (March) Heart Council meeting. Council favored establishment of additional regional centers at Seattle and Madison. (p. 28)
- 1961 (April) Heart Council meeting. Council recommended a conditioning center be established at an appropriate site; recommended grants for centers at Seattle and Madison; recommended that study section look into primate procurement and supply problems; and favored broad institutional support for primate research in addition to regional centers. (p. 28)
- 1961 (May) Primate Research Study Section meeting. Resolution prepared to Heart Council on conditioning center. (p. 28)
- 1961 (June) Organization committee meeting. Considered station site, conditioning center, and a baboon supply center.
- 1961 (June) Planning Committee meeting. Dr. Burch reported on primate center developments.
- 1961 (June) Heart Council meeting. Council recommended that additional regional centers established be at Atlanta, New Orleans, and Boston; urged establishment of a conditioning center; favored support for primate research in institutions other than centers; asked staff to negotiate contract, if possible, at San Antonio, Texas, for an initial study on techniques for procuring, conditioning and maintaining health primate colonies; and still favored establishment of a national station. (p. 28)

1961 (July) Dr. Eyestone's membership on Primate Research Study Section terminated.

1961 (September) Primate Research Study Section meeting; executive session with Dr. Watt and Dr. Price. (p. 29)

- 1961 (September) Planning Committee meeting. The Organization Committee was urged to plan a national primate station and also a procurement and conditioning center; Committee favored broad institutional support for primate research in institutions other than regional centers; suggested that the word "regional" be in the title of each regional center.
- 1961 (November) Heart Council meeting. Council recommended continued support for baboon colony at San Antonio, Texas, but not as a regional primate research center; that a "tag" be put upon a land area in California near San Francisco for a primate conditioning center; and that "regional" be in the titles of all the regional primate research centers. (p. 30)
- 1961 (December) Meeting of Dr. K. F. Meyer, Dr. Knutti, Dr. Yeager, Dr. Eyestone, Dr. Price, and Dr. E. Allen. Agreement was reached to try to finance a primate conditioning center at Davis, California. (p. 30)
- FY 1961 House Subcommittee hearings clarified the authorization to use appropriation funds to buy land and construct buildings on nonmatching basis; \$11 million said to be sufficient for the program in fiscal 1961. Senate Subcommittee was told that a tentative award had been made to establish the center at Portland, Oregon. (p. 34)
- FY 1961 Senate Subcommittee hearings indicated a tentative grant award had been made for a center in Oregon. (p. 34)

FY 1961 Congress appropriated \$7 million.

- 1962 (January) Primate Research Study Section meeting. Joined by Cancer Institute Virus and Cancer Board to discuss use of primates in cancer virus research; and by representatives of Cancer Institute's Laboratory Animal Panel which urged the establishment of a primate conditioning center. Study Section met in executive session with Dr. Ralph Knutti, Dr. Dale Lindsay, and Dr. Ernest Allen, relative to a conditioning center at Davis, California. (p. 30)
- 1962 (February) Meeting of Primate Research Study Section at Davis, California. Establishment of conditioning center recommended. (p. 30)
- 1962 (February) Planning committee meeting. Considered and recommended conditioning center to be established at Davis, California.
- 1962 (March) Heart Council meeting. Council recommended grants for establishment of national primate conditioning center at Davis, California. (p. 31)
- 1962 (June) Planning Committee meeting. Dr. Burch requested termination of the Organization Committee. (p. 13)

- 1962 (June) Heart Council meeting. Council abolished the Organizational Committee and was informed that the Regional Primate Research Centers program was to be transferred to DRFR. (pp. 13 and 31)
- 1962 (July) The Regional Primate Research Centers program, along with Dr. Eyestone and his staff, transferred from NHI to DRFR. (p. 31)
- FY 1962 House Subcommittee was told that the Oregon Center construction was nearing completion, and that a large conditioning center was needed. (p. 34)
- FY 1962 Senate Subcommittee told that two additional centers at Seattle and Madison had been recommended by Heart Council. A conditioning center was needed; six to eight regional centers were being planned, four west and three east of the Mississippi with one of the three becoming a supply center (or conditioning center). A central primate research station was still strongly urged. (p. 35)
- FY 1962 Congress appropriated \$9 million, \$2 million of which was put in reserve, but \$2.5 million was provided by NHI from another program. (p. 37)
- FY 1963 House Subcommittee hearings indicated that three centers were being established (Portland, Seattle, Madison) and three others projected (Atlanta, Boston, New Orleans) and that a primate station and conditioning center was needed. (p. 35)

FY 1963 Congress appropriated \$6 million. (p. 37)

- 1964 (September) The DRG Primate Research Study Section was abolished and an initial review committee, "Regional Research Centers Advisory Committee," was established by DRFR. (p. 7)
- FY 1964 House Subcommittee hearings included progress report on program development. (p. 36)
- FY 1964 Congress appropriated \$5.7 million. (p. 37)
- FY 1965 House Subcommittee hearings indicated that, although the start had necessarily been slow, the program was developing. (p. 36)
- FY 1965 Congress appropriated \$7 million. (p. 37)

House Subcommittee hearings indicated that the construction of four of the seven centers were complete and all seven had initiated research programs. (p. 36)

FY 1966 Congress appropriated \$7 million. (p. 37)

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FY 1967 House hearings indicated construction of five of the seven centers was complete, that the two others were nearing completion, and that all had research programs underway. (p. 36)

FY 1967 Congress appropriated \$9 million. (p. 37)

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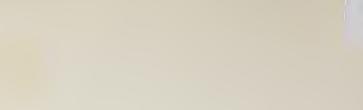
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- (1) Correspondence relative to NIH (DRG) interest in procuring primates (chimpanzees) for research in the United States. Letter of July 24, 1947, Vander (DRG) to Nissen (Yerkes Laboratories); memorandum of August 16, 1949, Culbertson (DRG) to Topping (NIH) and other related correspondence. Also letter of August 7, 1956, K. F. Meyer to James A. Shannon suggesting establishment of primate colony in the U. S.; and related correspondence. (pp. 6 and 8)
- (2) January 5, 1955, "Conference on the Use of Primates for Studies of Radiation Effects and Aging," sponsored by the Committee on Radiation Studies, DRG, held in Bethesda, Maryland. (p. 6)
- (3) November 15, 1954 meeting of "Subcommittee of the Committee on Radiation Studies on Long-Term Primate Program." (p. 6)
- (4) June 7, 1955 "Conference on the Procurement and Production of Rhesus Monkeys," Institute of Animal Resources, NAS-NRC, Washington, D. C. (p. 7)
- (5) Membership lists of National Advisory Heart Council 1956-1962; the NHI's ad hoc Advisory Committee on the Establishment of a Cardiovascular Primate Colony; the Heart Council's "Organization Committee;" the DRG's National Advisory Committee on Rhesus Monkey Requirements; DRG's National Advisory Committee on Primates; DRG's Primate Research Study Section; DRFR's Primate Research Centers Advisory Committee. (p. 9)
- (6) Agenda and minutes of the "Meeting of the National Advisory Heart Council Advisory Committee on the Establishment of a Cardiovascular Primate Colony," September 25, 1957, Dupont Plaza Hotel, Washington, D. C. Also documents sent to the committee members prior to the meeting: (1) "The Cayo Santiago Primate Colony" by José Guillerno Frontena, University of Puerto Rico School of Medicine; (2) "Breeding and Care of Monkeys" by Gertrude van Wagenen, Yale University School of Medicine; and (3) "Large Scale Primate Production in a Caged Colony" by Willard H. Eyestone, Division of Research Services, National Institutes of Health. (p. 9)
- (7) Report of subcommittee "A Proposal for a National Primate Institute," February 8, 1958. (p. 11)
- (8) Agenda and "Transcript of Proceedings, National Heart Institute Advisory Committee on the Establishment of a Cardiovascular Primate Colony" meeting, February 10, 1958, Bethesda, Maryland. (pp. 11 and 12)
- (9) "Report of Meeting of the Committee on the Establishment of a Cardiovascular Primate Station," by Dr. George E. Burch, Chairman, February 27, 1958.
 (p. 12)

- (10) Correspondence: (a) letter of April 4, 1962, Burch to Knutti, suggesting dismissal of the Heart Council Committee on Organization of a Cardiovascular Primate Research Station; (b) reply of July 18, 1962, Knutti to Burch; (c) letters of July 18, 1962, Knutti to committee members. (p. 13)
- (<u>11</u>) "Report of the Cardiovascular Primate Committee" submitted by Dr. George Burch, Chairman. Also "Report of the Subcommittee to the Cardiovascular Primate Committee" dated April 3, 1958, (this is a staff revision of the document "A Proposal for a National Primate Institute"). (pp. 13 and 14)
- (12) "Feasibility and Desirability of Primate Research Centers," April 23, 1959. (An NHI staff document prepared at the request of the Senate Appropriations Committee.) (p. 17)
- (13) "Cardiovascular Primate Research Station," March 12, 1959. (A staff document) (p. 17)
- (14) Agenda and minutes of the July 17, 1959, meeting in New Orleans of the Heart Council "Committee on Organization of Primate Research Centers" (actually at this time still the "Committee on Organization of a Cardiovascular Primate Research Station"). (p. 19)
- (15) Minutes of Joint Meeting of National Advisory Committee on Primates and the National Heart Council's Committee on Organization of Primate Research Centers, held in San Francisco on November 23, 1959. Also "Resolutions of National Advisory Committee on Primates," November 23, 1959. (pp. 7 and 22)
- (16) "Statement of Responsibilities and Relationships: Primate Research Center in Oregon," April 17, 1960. Also similar "Statement" for each of the other six centers. (pp. 26 and 45)
- (<u>17</u>) Letter, September 24, 1962, from Dr. J. Franklin Yeager, National Heart Institute, to Dr. D. W. E. Baird, Dean, University of Oregon School of Medicine. (p. 27)
- (<u>18</u>) "Policies and Procedures Governing Grants Awarded for Construction of Primate Research Facilities," September 16, 1960. (pp. 27 and 42)
- (<u>19</u>) "Guidelines for Organization of Primate Research Centers," September 29, 1960. (p. 27)
- (20) Minutes of Meeting of an "Ad Hoc Committee for Primate Research Station," September 24, 1960, Park Sheraton Hotel, New York, New York. This was the Heart Council's Organization Committee plus several specially interested consultants. (pp. 3 and 28)
- (21) Primate Research Study Section Resolutions on "National Primate Research Station" and "Holding and Conditioning Compound," both May 8, 1961. (p. 28)

- (22) "Recommendations of Heart Council Planning Committee Approved by National Advisory Heart Council, June 22, 1961." (This document was considered by the Primate Research Study Section on September 7-8, 1961.) (p. 29)
- (23) Letters of July 24, 1961, from Dr. K. F. Meyer, Chairman of the Primate Research Study Section, to Dr. James Watt, Director of the National Heart Institute, and to Dr. David E. Price, Deputy Director of the National Institutes of Health. (p. 29)
- (24) Verbatim.record of discussion at the "Executive Session" of the Primate Research Study Section on September 7, 1961. (p. 29)
- (25) Minutes of meeting on January 25 and 26, 1962, of the Primate Research Study Section. (p. 30)
- (26) Memorandum of December 15, 1961, from Dr. Ernest M. Allen to the Director, NIH, on "National Conditioning Center for Primates." (p. 30)
- (27) Copies of some of the more pertinent sections of the hearings of the House and Senate Appropriations Subcommittees and reports in the record. (pp. 3, 32-37)
- (28) "Scientific and Administrative Concepts Behind the Establishment of the U. S. Primate Centers" by Willard H. Eyestone, in Recent Developments in Comparative Medicine, Symposia of the Zoological Society of London, November 17, 1966, Academic Press, London and New York; also same article in J. Am. Vet. Med. Assoc. <u>147</u>: 1482-7, 1965. (p. 3)

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