NIH GUIDE for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

No. 7, June 14, 1971

SUBMISSION OF SALARY INFORMATION IN GRANT APPLICATIONS (NIH 4305)

POLICY CHANGE

1. *PURPOSE* This issuance states the NIH's policy on submission of individual salary items on grant applications which are made available to reviewing consultants.

2. *APPLICABILITY* This policy is applicable to all NIH grant programs which (1) require applicant organizations to submit information on salary rates or amounts for individuals in connection with the budgets of grant applications, and (2) use outside consultants in the review of grant applications. The policy does not apply to applications for support of individuals such as research career development awards, fellowships, traineeship awards, Health Science Scholars, and Fogarty International scholarships, nor does it apply to noncompeting applications which do not receive review by outside consultants.

3. *POLICY* Applicant organizations shall have the option to omit specific salary rates or amounts for individuals from those copies of grant applications which are made available to NIH's reviewing consultants. Data concerning specific salary amounts for individuals will be included in copies to be used administratively by the NIH. This salary information shall not routinely be divulged in the review process, but will be available for use by regular NIH employees.

4. *IMPLEMENTATION* Until such time as all affected application forms are revised and until experience has been gained to indicate the most efficient method of obtaining salary information for NIH staff use while eliminating it from copies provided for reviewers, the following procedures will be used:

a. The new policy and instructions will be widely distributed and a copy will be inserted in all competing application kits sent out from the NIH.

b. If the applicant exercises the option allowed by this policy, information on individual salaries may be omitted on the original of the application but must be included on all copies submitted. The total amount for the personnel category will be shown on the original and all copies of the application.

c. The original of the budget page will show the name of the individual (if known), his position or job title, and a percentage of time or effort he is expected to devote to the grant-supported activity.

d. When salary information is being omitted from the original, the applicant will place asterisks in the salary column to identify each of the individuals for whom salary is being requested.

e. The original will be the one used for duplicating purposes, and only copies of the original may be provided to reviewers. The additional application copies with individual salary information will be used only by NIH staff.

5. *EFFECTIVE DATE* This change is effective July 1, 1971.

References

(1) DHEW Grants Administration Manual, Chapter 1-470, Submission of Salary Information in Grant Applications, September 5, 1970.

CARE AND TREATMENT OF LABORATORY ANIMALS (NIH 4206) **POLICY**

1. *PURPOSE* This issuance describes the responsibilities of institutions receiving NIH grant, award, or contract support for demonstrations or studies involving tests or experiments on live warm-blooded animals, and the responsibilities of the NIH awarding units for implementing policies and procedures described herein.

2. *BACKGROUND* The National Institutes of Health has a long-standing commitment to the principle that animals used in activities supported by NIH must receive appropriate care and humane treatment. With support from NIH, the National Academy of Sciences developed a "Guide for Laboratory Animal Facilities and Care." The first edition of the Guide was published in March 1963, and to date it has been revised twice. The Public Health Service "Grants for Research Projects; Policy Statement" (PHS Publication No. 1301 and "Grants for Training Projects; Policy Statement" (PHS Publication No. 1302) state that the criteria established in the "Guide for Laboratory Animal Facilities and Care" (PHS Publication No. 1024) should be followed. In addition, these publications state that "It is the responsibility of each person assigned or appointed to a project receiving any Public Health Service support to exercise every precaution to assure proper care and humane treatment of research animals."

Public Law 89-544, The Laboratory Animal Welfare Act of August 24, 1966, and amendments as of December 24, 1970, outline legal requirements for the proper care and humane treatment of laboratory animals.

3. *POLICY* It is the policy of the National Institutes of Health that institutions and organizations using warm-blooded animals in projects or demonstrations supported with funds from NIH grants, awards, or contracts shall assure the NIH that they will evaluate their animal facilities in regard to the maintenance of acceptable standards for the care, use, and treatment of such animals. Grantees and contractors will:

a. provide assurance of accreditation by a recognized professional laboratory animal accrediting body or of the establishment of a committee, at least one of whose membership is a Doctor of Veterinary Medicine, to evaluate the care of all warm-blooded animals held or used for research, teaching, or other activities supported by NIH grants, awards, or contracts; and

b. follow the guidelines prescribed in PHS Publication No. 1024, applicable portions of PL 89-544 as amended, the appended NIH Guidelines for Use of Experimental Animals,and the procedures described in this issuance.

In addition, as a part of the continuing evaluation process, awardees will keep a record of committee activities, including its recommendations and determinations.

4. *IMPLEMENTATION: GRANTEES OR CONTRACTORS* Institutions and organizations receiving NIH grant, award, or contract support shall provide the Director, NIH, or his designated representatives, with one of the following assurances over the signature of a responsible official of the awardee institution, as applicable:

"The (name of institution) does not use or intend to use warm-blooded animals in demonstrations, research and/or teaching supported by NIH grants, awards, or contracts."

or

"The ___(name of institution)___ uses or intends to use warm-blooded animals in activities supported by NIH grants, awards, or contracts. This institution is accredited by a recognized professional laboratory animal accrediting body [or has established a committee, at least one of whose membership is a Doctor of Veterinary Medicine,] to evaluate the care of all warm-blooded animals held or used for research, teaching, or other activities supported by NIH grants, awards, or contracts for meeting the criteria described in Public Health Service Publication No. 1024 'Guide for Laboratory Animal Facilities and Care.'

"The evaluation committee will periodically inspect the animal facilities of this institution and report its findings and recommendations to the institution's responsible officials on a schedule it determines necessary; but in no case will these reports be issued less than annually. Records will be kept of committee activities, recommendations, and determinations of the accrediting body. These records will be available for inspection by the Director, NIH, or his authorized representatives."

5. *REVIEW BY NIH ADVISORY GROUPS* NIH advisory groups responsible for the review of applications for grants or contracts will continue to review research protocols, with the requirements of the NIH policy on warm-blooded animals in mind. Special attention should be given to those protocols which suggest procedures or reflect institutional conditions or policies which are outside the limits of the NIH Guidelines for Use of Experimental Animals. Where procedures, conditions, or policies of applicant institutions are not within the NIH Guidelines, they shall be brought to the attention of awarding unit program staff by means of a "special note" on the advisory group's summary statement. It is the responsibility of the staff of the awarding units to resolve such questions as are raised by advisory groups. The implementation of this policy will be reviewed by the NIH after one year to determine whether modifications or strictures are necessary.

6. *IMPLEMENTATION: NIH STAFF*

   a. The Director, NIH, has designated the Institutional Relations Section (IRS), Division of Research Grants, to carry out the terms of this policy on behalf of NIH.

   b. The IRS will contact institutions and organizations receiving NIH grant, award, or contract support, to obtain the assurance required in paragraph 4 of this issuance. These assurances will be held by the NIH, which will periodically publish and circulate to all NIH awarding units a listing of those institutions that have indicated their use or intended use of warm-blooded animals.

7. *EFFECTIVE DATE* This policy is effective July 1, 1971.

References

(1) Animal Welfare Act, Public Law 89-544; 80 stat. 350, August 24, 1966.
(2) Animal Welfare Act as amended, Public Law 91-579, December 24, 1970.
(3) Guide for Laboratory Animal Facilities and Care, PHS Publication No. 1024, Revised July 1968.

GUIDELINES FOR USE OF EXPERIMENTAL ANIMALS

NATIONAL INSTITUTES OF HEALTH

The personnel

1. Experiments involving live warm-blooded animals and the procurement of living animal tissues for research must be performed by, or under the immediate supervision of, a qualified biological or medical scientist.

2. The housing, care, and feeding of all experimental animals must be supervised by a properly qualified veterinarian or other biological scientist competent in such matters.

The research

3. The research should be such as to yield fruitful results for the good of society, not feasible by other methods or means of study, and not random and unnecessary in nature.

4. The experiment should be so designed and based on knowledge of the disease or problem under study that the anticipated results will justify its performance.

5. The experiment should be so conducted as to avoid all unnecessary suffering and injury to the subject animals.

6. The scientist in charge of the experiment must be prepared to terminate it whenever he believes that its continuation may result in unnecessary injury to the subject animals.

7. If the experiment is likely to cause greater discomfort than that attending anesthetization, the subject animals must first be rendered incapable of perceiving the pain and be maintained in that condition until the experiment is ended. The only exception to this guideline should be in those cases where anesthetization would defeat the purpose of the experiment, and then the procedures must be carefully supervised by the principal investigator.

8. If it is necessary to sacrifice an experimental animal, the subject animal must be killed in a humane manner in such a way as to insure immediate death in accordance with procedures approved by an institutional committee. No animal shall be discarded until death is certain.

9. Post-experiment care of subject animals must be such as to minimize discomfort, in accordance with acceptable practices in veterinary medicine.

The facilities

10. Standards for the construction and use of housing, service, and surgical facilities should meet those described in the publication, "Guide for Laboratory Animal Facilities and Care," Public Health Service Publication No. 1024, or as otherwise required by the U. S. Department of Agriculture regulations established under the terms of the Laboratory Animal Welfare Act (PL 89-544) as amended December 24, 1970.

PROPOSED IMPLEMENTATION OF NIH COPYRIGHT POLICY (NIH 4208)

NOTICE

The NIH Policy is:

"Except as may otherwise be provided under the terms and conditions of the award, the grantee may copyright without prior approval any publications, films, or similar materials developed or resulting from a research project supported by a grant under this part, subject, however, to a royalty-free, nonexclusive license or right in the Government to reproduce, translate, publish, use, disseminate, and dispose of such materials and to authorize others to do so."

Implementation, in part, of the above policy:

Utilizing the key phrase "and to authorize others to do so," it is proposed to add to the policy the statement:

> "Communications in primary scientific journals reporting results of research supported in whole or in part by the National Institutes of Health may be copyrighted consistent with the copyright policy of the publication, with the understanding, however, that individuals are authorized to make, or have made by any means available to them, a single copy of any such article for their own use."

Anyone wishing to comment on this proposed policy change should contact Dr. Ronald Lamont-Havers before July 15, 1971, addressed as follows:

Dr. Ronald W. Lamont-Havers
Associate Director for Extramural
Research and Training
National Institutes of Health
9000 Rockville Pike, Bldg. 1, Room 118
Bethesda, Md. 20014.

PROGRAMS OF THE NATIONAL CANCER INSTITUTE

This issuance provides a summary of programs in chemotherapy, etiology, and general laboratories and clinics currently being conducted by the National Cancer Institute (NCI). The contract mechanism is used as at least a partial means of pursuing the objectives of each of the programs described below.

CHEMOTHERAPY

The objective of the Chemotherapy program is the development of drugs that are efficacious in producing complete remissions of clinical cancer at safe and tolerable dosages. This is done in laboratories and clinics in Bethesda, Baltimore, Washington, and Kampala, Uganda, by NCI scientists and at universities and commercial organizations under grants and contracts.

The Chemotherapy program at NCI started in 1955 with the establishment of the Cancer Chemotherapy National Service Center. The program was, in its early days, naturally an empiric one. In 1965 a thorough study of the 10 years' data was undertaken. As a result of that study, a linear array was developed and the logic steps from screening to clinical trial were outlined. The program was reorganized into three major segments along the lines of the linear array.

The first of these major segments is the Drug Research and Development area which is responsible for input of chemical compounds, screening, dose scheduling and drug formulation, and procurement. The second segment is Experimental Therapeutics where the toxicology and pharmacologic disposition of the drug is studied. Those compounds that pass these first two segments successfully are then studied in man under the direction of the Clinical Trials area of the program. Clinically active, safe drugs eventually are cleared by the FDA and become commercially available for use by practicing physicians for the control of cancer. Over 25 of these anti-tumor drugs are currently available. Curative activity is confined almost exclusively to the more rapidly growing tumors, but many of the drugs have some degree of activity against the slowly growing tumors.

The strategy for the future includes studies to explain the differences between rapidly growing and slowly growing tumors, and perfection of animal models for slowly growing tumors; the continuation of a broad screening operation involving randomly selected chemicals, as well as those selected because of a biochemical rationale; the use of slowly and rapidly growing animal tumor models to select the best drugs, schedules, and combinations; increased toxicologic and pharmacologic studies in animals and man; and the organization of clinical trials to study each new agent in a few representative rapidly and slowly growing tumors. Finally, there are extensive clinical studies on the natural history of cancer, and the supportive care of patients receiving chemotherapy. This includes studies of granulocyte transfusions, bone marrow transplants, and laminar flow protected environments.

ETIOLOGY

General

The Etiology area is responsible for planning and executing a broad research program on etiology and prevention of cancers. Experimental and epidemiologic research is conducted on potential and actual viral, chemical, and radiologic carcinogenic agents and on their combinations. Evaluations of carcinogenic hazards and studies on mechanism of cancer induction are included. Biometric and epidemiologic investigation of cancers are conducted in populations, and extensive

demographic data are continually compiled. The various areas of research complement each other, with data from one area providing input for another area in the planning, conduct, and evaluation of research programs. Laboratory findings provide leads that must be evaluated in human populations; observed associations of cancer with other factors determined in epidemiologic studies require further clarification in experimental investigations.

The Etiology area is divided into three main parts, each headed by an Associate Scientific Director. The Viral Oncology area is concerned with determining the significance of viruses in the induction of cancers in man and with developing means for preventing these cancers with virological, immunological, and other techniques. The Chemical Carcinogenesis area is concerned with determining the significance of chemical agents in the induction of cancer in man and with developing means of preventing these cancers. The Demographic area is concerned with continued monitoring of populations for cancer incidence, prevalence, and mortality; identification of groups with different risks of cancers and determination of associated internal and external environmental and genetic factors; conduct of observational research in situations where society or nature has provided experiments on cancer, such as studies on occupational groups, migrant populations, groups with other diseases, etc.; studies on diagnosis and therapy, including design and evaluation of therapeutic trials, end results of the therapies, diagnostic and detection studies, etc.; and collaboration in a variety of investigations requiring epidemiologic, demographic, statistical, and mathematical expertise.

The program is conducted by means of in-house research and the use of contracts for nationwide efforts within the integrated programs in the three areas. The Etiology area staff are responsible for planning, coordination, and evaluation of the contract-supported efforts as well as for the conduct of in-house investigations. Many of these efforts are done in conjunction with investigators who are also grantees of the NCI.

Viral Oncology

The Viral Oncology program is responsible for the Institute's research into the role of viruses in the causation of cancer of man and animals, intended ultimately to prevent and control neoplastic diseases of viral etiology. The three branches within the Office of the Associate Scientific Director for Viral Oncology are responsible for the planning and supervision of broad programs of basic, developmental, and applied research directed toward these objectives, as well as for the management of similarly directed special programs of national scope under the direct operations activities of the NCI.

The many disciplines and skills needed to study problems of viral causation of cancer are located in the three branches and are available for deployment in varying combinations for collaboration in problem-solving approaches to disease entities at the program and project levels. This type of collaborative utilization of research capabilities and disciplines has served to unify research efforts and to reduce unnecessary duplication to a minimum.

The Special Virus Cancer Program--Programmed research on the viral etiology of human cancer started in 1964 with a special Congressional appropriation of $10 million. Launching of the Special Virus Leukemia Program was predicated upon the underlying belief that at least one virus is causally related to human leukemia and lymphoma and persists in the diseased individual. Management of this program was under the Leukemia and Lymphoma Branch. Increased evidence of a relationship of viruses to the etiology of solid tumors led to additional funding and the launching of a Solid Tumor Virus Program in 1967, under the management of the

Viral Carcinogenesis Branch. The growth of both programs and their many common interfaces led to their merger in 1968 into the Special Virus Cancer Program, which now embraces viral etiological research on cancers of all types. The program now employs a research convergence technique to provide coordination of objectives, personnel, resources, and information under the general direction of the Office of the Associate Scientific Director for Viral Oncology.

All organizational units under the Office of the Associate Scientific Director for Viral Oncology, as well as members of other organizational units in the Etiology area, participate in the program. The resources of the Institute are strongly complemented by the numerous academic and commercial research groups collaborating in this effort. This integration has made possible the sharing of information resulting from the examination and treatment of large numbers of leukemic patients without which it would be difficult or impossible to conduct significant research programs directed to the etiology, prevention, and control of this disease. It has also made possible concurrent studies on the leukemia-sarcoma complex in animals, particularly those common to the human environment. Such studies are expected to yield answers to the possible interrelationships of these diseases to provide models for the study of the counterpart human studies.

Carcinogenesis

The Carcinogenesis area, including the Lung Cancer Task Force, together with the Biology, Chemistry, and Experimental Pathology Branches, is responsible for planning, implementing, and managing the coordinated research program of the NCI on carcinogenesis by chemical and physical factors and on cancer prevention.

Intramural research and a contract-supported collaborative program, directed by the scientific staff, encompass an integrated effort for the identification of population groups at different risks to cancers, the selection of chemical agents for bioassay with emphasis on suspected environmental carcinogenic hazards, the development and selection of biological models for carcinogenesis bioassays and studies, the identification of carcinogenic activity to selected chemicals by bioasssay, and the identification of processes required for the carcinogenic action of selected agents as target points for prevention or inhibitory measures. Processes studied include the penetration of chemicals into the organism and their molecular logistics, metabolic pathways and enzymatic mechanisms of activation, interaction with cell constituents, neoplastic transformation, growth regulation of transformed cells, and immunological control.

The Lung Cancer Unit, established on the recommendation of the Lung Cancer Task Force, will develop the Special Lung Cancer Program. The Unit conducts investigations to identify carcinogenic agents and biological factors involved in the development of lung cancer and attempts to determine means by which these factors may be inhibited or prevented. It develops, designs, and standardizes biological and chemical assay systems for testing the carcinogenic and/or synergistic effects of tobacco smoke constituents and of other chemical and physical agents involved in lung cancer causation.

Demography

The Demography area has three major functions: (a) research into the etiology of cancer in free-living populations, largely but certainly not exclusively human; (b) consultation and support in mathematics, statistics [including experiment design and analysis] and system analysis in problems of cancer research; (c) development of the basic data of cancer incidence, prevalence, and mortality in the United States sufficiently precise to permit administrators and research workers to measure their successes [and failures] in preventing, diagnosing, or treating

cancer. The two Branches [Biometry and Epidemiology] within the Office of the Associate Scientific Director for Demography supplement and support each other in these activities.

Objectives for 1972

The major objectives in the Special Virus Cancer Program are: (a) the determination of cancer-causing activity in animals by viruses already isolated from human cancers; (b) relating this activity, and other characteristics of the candidate viruses, to cancer in man; (c) the determination of the entire sequence of molecular events, including specific enzymatic activities (e.g., polymerases) in viral replication and tumor induction; and (d) relating this information to the control of cancer in man.

The Chemical Carcinogenesis area will give high priority to the identification of chemical-viral interaction mechanisms, the role of various chemicals and dusts in the induction of lung cancer, and the establishment of data collection and retrieval systems to improve efficiency in coordinating information generated by the program and disseminating it to the scientific community.

In Demography, epidemiology studies will be made in human populations of the role of viruses and chemicals in cancer initiation. In 1972, the activities of the Third National Cancer Survey will shift from the collection of data to the analysis of the data.

GENERAL LABORATORIES AND CLINICS

The General Laboratories and Clinics area is responsible for planning and directing the National Cancer Institute's general (as distinguished from specifically targeted) laboratory and clinical research activities. The objectives include obtaining information and knowledge for the understanding of the fundamental biological processes underlying cancer in man through the conduct of research in the biomedical sciences.

The research is carried out in 12 units. Five of these are in the basic sciences; namely, Biology, Cell Biology, Molecular Biology, Biochemistry, and Physiology. Seven units are engaged in clinical research programs of Surgery, Immunology, Radiation, Dermatology, Pathology, Metabolism, and Breast Cancer. There are approximately 70 hospital beds to complement these clinical programs. The Scientific Director for General Laboratories and Clinics is assisted by an Associate Scientific Director for Clinical Research to whom is delegated responsibility for the clinical programs and by a group of laboratory and branch chiefs responsible for laboratory investigations. The scientists and physicians of these 12 units conduct studies broadly described by the title of their unit. Their research is designed to add to our knowledge about the changes caused by cancer, whether they be in the biochemistry of the cell or the effect of cancer upon the patient. They include studies of the treatment of cancer by surgical, chemical, and radiological means. Studies in patients range from those designed to improve radiation therapy and surgery as therapeutic tools together with those designed to determine how a cancer affects the patient, how anemia is produced, and why host defenses to bacteria are reduced.

This broadly based program to study cancer in man and experimental animals will be vigorously pursued in 1972 to acquire new knowledge that will permit improved care of patients and a better understanding of the fundamental aberration that results in cancer. While the major effort is carried on in its own facilities, some contracts are used for obtaining specific materials or services to supplement the in-house capability.

NIH Grant and Fellowship Application Deadline Dates (NIH 4304)

PROCEDURE NOTICE
(Correction)

The procedure notice published on page four of NIH Guide for Grants and Contracts, No. 6, April 26, 1971, carried an error in the deadline date for the Fall round of research career award applications. It should be amended to read September 1 instead of October 1 as published.