GUIDELINES FOR THE

CONDUCT OF RESEARCH

WITHIN THE

PUBLIC HEALTH SERVICE

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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Introduction

Scientists who conduct research in the Public Health Service generally are responsible for conducting their work consonant with the goals of each individual Agency, Bureau, Institute, Center, and Division.

PHS scientists must be committed to the responsible use of the process known as the scientific method to seek new knowledge. The general principles of the scientific method--formulation and testing of hypotheses, systematic ways of gathering data and conducting studies, analysis and interpretation of data, and oral and written presentation of all of these components to scientific colleagues for discussion and further conclusions--are universal. Although their detailed application may differ in different scientific disciplines in the PHS, and in varying circumstances, it is only by adherence to the highest standards of intellectual honesty in formulating, conducting, and presenting research that science can advance and scientists can fulfill their responsibility to the community at larqe.

These Guidelines state general principles that PHS scientists are expected to follow in their research activities. They address supervision of trainees, data management, publication practices, authorship, peer review, use of privileged information, clinical and epidemiological investigations, and health services research. These Guidelines promote the uniform application of the highest ethical standards to the conduct of all scientific research. It is the responsibility of each

Laboratory or Branch Chief, and successive levels of supervisory individuals (especially Division, Center, Institute, Bureau, and Agency Directors), to ensure that each PHS scientist is cognizant of these Guidelines, and to resolve issues that may arise in their implementation.

These Guidelines supplement existing statutes regarding confidentiality, FDA regulations on the monitoring and conduct of regulated research, and existing PHS policies on the conduct of research concerning Institutional Review Board oversight of human subjects research protocols; animal use; radiation, chemical and other safety issues; and other aspects of the Standards of Conduct for all federal employees.

The guidelines described in this document apply to all PHS intramural research, research training, or research-related activities regardless of sources of funds or authority. This Guidance makes explicit the unwritten canons of good science that have traditionally governed the conduct of research in the intramural research programs of the Public Health Service.

These Guidelines are not intended to address issues of scientific misconduct. No set of guidelines, not even explicit rules, can prevent willful scientific misconduct. The PHS hopes that these Guidelines will contribute to the clarification and the continued application of the scientific method in changing circumstances.

The community will ultimately judge the PHS by its adherence to these intellectual and ethical standards, as well as by its development and application of important new knowledge through scientific creativity.

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Supervision ot Trainees

Research training in science is a complex process, the central aspect of which is an extended period of research carried out under the supervision of an experienced scientific mentor. This supervised research experience represents not merely performance of tasks assigned by the supervisor, but rather a process wherein the trainee takes on an increasingly independent role in the choice of research projects, development of hypotheses and the performance of the work. Indeed, if training is to prepare a young scientist for a successful career as a research investigator, it must be geared toward providing the trainee with the aforementioned skills and experiences. It is particularly critical that the mentor recognize that the trainee is not simply an additional laboratory worker.

Each trainee should have a designated primary scientific mentor. It is the responsibility of this mentor to provide a training environment in which the trainee has the opportunity to acquire both the conceptual and technical skills of the field. In this setting, the trainee should undertake a significant piece of research, chosen usually as the result of discussions between the mentor and the trainee, which has the potential to yield new knowledge of importance in that field. The mentor has the responsibility to supervise the trainee's progress closely and to interact personally with the trainee on a regular basis in such a way as to make the training experience a meaningful one. Styles of research differ, both among fields and among investigators in a given field, so that no specific rules should be made about the number of trainees that is appropriate for a single mentor to supervise. Nonetheless, mentors should limit the number of trainees in their laboratory or other research setting to the number for whom they can provide an appropriate research experience.

There are certain specific aspects of the mentor-trainee relationship that deserve emphasis.

o First, mentors must be particularly diligent in avoiding the involvement of trainees in research activities that do not provide meaningful training experiences but which are designed mainly to further research or development activities in which the mentor has a potential monetary or other compelling interest.

o Second, training must impart to the trainee appropriate standards of scientific conduct. The mentor conveys these standards by instruction and by example.

o Third, mentors have a responsibility to provide

trainees with realistic appraisals of their performance and with advice about career development and opportunities.

Data Management

Research data, including detailed protocols, data from laboratory instruments, questionnaires on study participants, and statistical procedures of reduction and analysis of primary data, are the essential components of scientific progress. Scientific integrity is inseparable from meticulous attention to the acquisition and maintenance of these research data.

It is expected that the results of research will be carefully recorded in a form that will allow continuous and future access for analysis and review. Attention should be given to annotating and indexing notebooks and documenting computerized information to facilitate detailed review of data. All data, even from observations and experiments not directly leading to publication, should be annotated, indexed, and documented. All of these data shall be maintained and protected in accordance with statutory confidentiality restrictions. However, research data should always be immediately available to scientific collaborators and supervisors for review. In collaborative projects, all investigators should know the status of all contributing data and have access to them consistent with confidentiality statutes.

Similarly, research data, including the primary experimental results, should be retained for a sufficient period of time to allow analysis and repetition by others of published findings from those data consistent with confidentiality statutes. Retention time may vary under different circumstances. In some fields, five or seven years are specified as the minimum period of retention. A minimum of five years is required.

All research data, e.g. questionnaires, statistical analyses, and supporting materials, such as unique reagents, belong to the Public Health Service. They should be maintained in the Institute, Center, Bureau, or Division in which they were developed. Departing investigators may take photocopies of their notebooks or other written material for further work subject to mandatory confidentiality restrictions. If the recognized senior or principal investigator departs the institution, it is the responsibility of that investigator and that Agency, Institute, Center, Bureau, or Division to ensure that the data and unique materials are appropriately maintained and will be accessible.

Data management, including the decision to publish, is the responsibility of the principal investigator. After publication, the research data and any unique reagents that form the basis of that communication shall be made

available promptly and completely to all responsible scientists seeking further information (at the cost of the requestor)[1]. Certain restrictions related to privacy may apply to clinical, epidemiological, and health services research data, or proprietary data in the case of regulatory components of the PHS.

The Public Health Service advocates and encourages open scientific communication. By promptly submitting research findings for publication, and presenting findings at scientific conferences and workshops, the researcher invites the sharing of information. After publication, researchers shall share with other researchers, when requested, at no more than incremental costs and within a reasonable time, the data samples, physical collections, and other supporting materials created or gathered in the course of the work.

Sharing and openness is the most traditional and effective way to encourage responsible conduct of research.

In cases where assurances of confidentiality are required or have been given to study participants, every effort must be made by researchers to protect individual identities and not only guard against direct disclosures but also against inadvertent disclosures resulting from release of information which might allow identification through inference. This protection of confidentiality shall extend to the physical protection of records while in the control of researchers, data processors, contractors, and others having authorized access to individually identifiable data.

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Publication Practices

Publication is an integral and essential component of research. Other than presentation at scientific meetings, publication in a scientific journal should normally be the mechanism for the first public disclosure of new findings. An important exception is prior to the publication of epidemiologic investigations when findings must be made known to individuals and/or communities for serious public health or safety reasons. Although appropriately considered the end point of a particular research project, publication is also the beginning of a process in which the scientific community at large can substantiate, correct, and further develop any particular set of results.

Timely publication of new significant results is important for the progress of science, but fragmentary publication of the results of a scientific investigation or multiple publications of the same or similar data are inappropriate. Each publication should make a unique and substantial contribution to its field. As a corollary to this principle, performance appraisals and promotions shall be based more on the importance of the scientific accomplishments than on the number of publications in which those accomplishments were reported.

Each paper should contain sufficient information for the informed reader to assess its validity. The principal method of scientific verification, however, is not review of submitted or published papers, but the ability of others to replicate the results to the extent that it does not threaten the well-being of any human subjects.

Therefore, all information that would be necessary for the scientific peers of authors to repeat the studies should be in each paper or made available from the authors. This principle requires that any unique materials (e.g. monoclonal antibodies, bacterial strains, mutant cell lines), analytical amounts of scarce reagents and unpublished data (e.g. protein or nucleic acid sequences) that are essential for repetition of the published experiments be made available to other qualified scientists. It is not necessary to provide materials (such as proteins) that others can prepare by published procedures, or large quantities of materials (such as polyclonal antisera) that may be in limited supply, although it is desirable to do so.

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Authorship

Authorship refers to the listing of names of participating scientists in all communications, oral and written, of experimental results and their interpretation to scientific colleagues. Authorship is the fulfillment of the responsibility to communicate research results to the scientific community for external evaluation.

Authorship is also the primary mechanism for determining the allocation of credit for scientific advances, and thus the primary basis for assessing a scientist's contributions to developing new knowledge. As such, it potentially conveys great benefit, as well as responsibility. For each individual the privilege of authorship should be based on a significant contribution to the conceptualization, design, execution, and/or interpretation of the research study, as well as a willingness to take responsibility for the defense of the study should the need arise. In contrast, other individuals who participate in part of a study may more appropriately be acknowledged as having contributed certain advice, reagents, analyses, patient material, space, support, etc., but not be listed as authors. It is expected that such distinctions will become increasingly important in the future and should be explicitly considered.

The average number of authors per communication is increasing. In part, this increase is due to the needs of modern research projects for contributions from many individuals, frequently those with different specialized skills. While multi-authorship is not a problem in itself, it raises many issues such as criteria for inclusion as an author, ability of each author to evaluate and defend all aspects of a study, sequence of listing of authors, and separation of various experimental results to increase numbers of communications and authorship citations. To clarify some of these concerns, consideration should be given in interdisciplinary studies to preparing brief statements of the exact contribution of each author to the work described in each communication.

Because of the variation in detailed practices among disciplines, no universal set of standards can be easily formulated. It is expected, however, that each research group and laboratory or branch will freely discuss and resolve questions of authorship before and during the course of a study. Further, each author should review fully material that is to be presented in public forums or submitted (originally or in revision) for publication. Each author should be willing to support the general conclusions of the

study and be willing to defend the study.

The submitting author should be considered the primary author with the additional responsibility of coordinating the completion and submission of the work, satisfying pertinent rules of submission, and coordinating responses of the group to inquiries or challenges. The submitting author should assure that the contributions of all collaborators are appropriately recognized and must be able to certify that each author has reviewed and authorized the submission of the manuscript. The practice of some journals in requiring approval signatures from each author before publication is felt to be a useful step in regard to fulfilling the above.

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Peer Review and Privileged Information

Peer review can be defined as expert critique of either a scientific treatise, such as an article prepared or submitted for publication, a research grant proposal, a clinical research protocol, or an investigator's research program, as in a site visit. Peer review is an essential component of the conduct of science. Decisions on the funding of research proposals and on the publication of experimental results must be based on thorough, fair and objective evaluations by recognized experts. Therefore, although it is often difficult and time-consuming, scientists have an obligation to participate in the peer review process and, in doing so, they make an important contribution to science.

Peer review requires that the reviewer be expert in the subject under review. The reviewer, however, shall avoid any real or perceived conflict of interest that might arise because of a direct competitive, collaborative or other close relationship with one or more of the authors of the material under review. Normally, such a conflict of interest would require a decision not to participate in the review process and to return any material unread.

The review must be objective. It shall be based solely on scientific evaluation of the material under review within the context of published information and should not be influenced by scientific information not publicly available.

All material under review is privileged information. It should not be used to the benefit of the reviewer unless it previously has been made public. It must not be shared with anyone unless necessary to the review process, in which case the names of those with whom the information is shared should be made known to those managing the review process. Material under review shall not be copied and retained or used in any manner by the reviewer unless specifically permitted by the journal or reviewing organization and the author.

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Clinical Research

Clinical research, for the purposes of these Guidelines, is defined as research performed on human subjects or on material or information obtained from human subjects as a part of human experimentation. All of the topics covered in the Guidelines also apply to the conduct of clinical research. Clinical research, however, entails further responsibilities for investigators.

The preparation of a written research protocol ("Clinical Research Protocol") according to existing guidelines prior to commencing studies is almost always required. By virtue of its various sections governing background; patient eligibility and confidentiality; data to be collected; mechanism of data storage, retrieval, statistical analysis and reporting; and identification of the principal and associate investigators, the Clinical Research Protocol provides a highly codified mechanism covering most of the topics dealt with elsewhere in these Guidelines. The Clinical Research Protocol is generally widely circulated for comment, review and approval. It should be scrupulously adhered to in the conduct of the research. The ideas of the investigators who prepared the protocol should be protected by all who review the document.

Clinical investigators are responsible for assuring that the proposed clinical research will be conducted only if the Clinical Center, or other clinical facilities, has the appropriate capability and support structure to ensure that the research can be done safely and efficiently. The principal investigator should be familiar with the functioning of the clinical unit and should allow the investigation to continue only if the unit can provide adequate clinical care.

Investigators who are neither clinicians nor trained in clinical research may perform laboratory research on material derived from humans. To conform to the requirement of working under approved human experimentation guidelines, they should ordinarily be advised by or collaborate with trained clinical investigators.

The supervision of trainees in the conduct of clinical investigation is complex. Often the trainees are in fellowship training programs leading to specialty or subspecialty certifications as well as in research training programs. Thus, they should be educated in general and specific medical management issues as well as in the conduct of research. The process of data gathering, storage, and retention can also be complex in clinical research and sometimes not easily subject to repetition. The principal investigator is

responsible for the quality
and maintenance of the records
and for the training and
oversight of all personnel
involved in data collection.

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Epidemiologic Research

For purposes of this document, epidemiologic research consists of studies involving observations related to the presence or absence of disease in groups of individuals. While all of the responsibilities of investigators and guidelines for scientific procedure described in other sections of these Guidelines (with the exception of some of those mentioned in the section on Clinical Research) pertain to epidemiologic investigation, certain aspects of epidemiologic research deserve special mention.

In contrast to clinical investigation, epidemiologic investigation generally does not involve the investigator's assignment of subjects to groups that are then treated differently. Epidemiologic studies may involve investigation of the effect of an intervention designed to modify the health status of study subjects, but only if that intervention is undertaken independent of any effort to study its effect. Studies linked to the intervention the effect of which is being investigated (e.g., prospective vaccine trials) should be considered clinical research.

Since epidemiologic investigations examine the patterns of disease as they occur independently of any intervention related to the study, the ethical constraints in epidemiology are somewhat distinct from those that apply to clinical research. Normally, the epidemiologist does not assume the same responsibility for a patient's care as does the clinical investigator. In general, existing health care systems and personnel can appropriately be relied on to assume responsibility for the care of individual patients. The epidemiologist, however, has the responsibility to take steps to ensure that the investigation of a disease problem in no way interferes with a patient's clinical care.

While development and review of appropriately detailed study protocols are as important in epidemiology as in any other health science, there are often circumstances under which studies need to be planned and implemented expeditiously, and certain steps in the protocol development and review process must be appropriately shortened. Such circumstances chiefly involve the epidemiologic investigation of acute epidemic or outbreak situations for which the results of the epidemiologic investigation may provide data of crucial importance to the identification and mitigation of a threat to public health. Nevertheless, even in outbreak situations, systematic planning prior to the implementation of an epidemiologic study is of great importance. Within the time constraints imposed by

the situation, the investigator should make every attempt to formalize the study design in a written document and to have that design reviewed by appropriately selected peers and colleagues prior to implementing the research.

In many epidemiologic research investigations it is important to report the findings to participants in the study and various health officials for immediate public health reasons. Although it is the practice of some journals not to publish research findings partially released to the public, the health of the public is preeminent.

Conclusion

These Guidelines are intended to provide a framework for the fair and open conduct of research without inhibiting scientific freedom and creativity. They indicate what is commonly considered appropriate scientific conduct in intramural research, research training, and related activities.

NOTE:

1. See also: Public Health Service Policy Relating to Distribution of Unique Research Resources Produced with PHS Funding. NIH Guide - Vol. 20, No. 5, February 1, 1991