MISCONDUCT IN SCIENTIFIC RESEARCH

OFFICE OF INSPECTOR GENERAL

OFFICE OF ANALYSIS AND INSPECTIONS

MARCH 1989

OFFICE OF INSPECTOR GENERAL

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THIS REPORT

Entitled "Misconduct in Scientific Research," this inspection was conducted to determine the extent to which the National Institutes of Health and its grantee institutions have developed and implemented policies and procedures to prevent, detect, and handle scientific misconduct, as required by the Health Research Extension Act of 1985.

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MISCONDUCT IN SCIENTIFIC RESEARCH

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OAI-88-07-00420

MARCH 1989

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PURPOSE

To determine: (1) the extent to which the National Institutes of Health (NIH) and its grantee institutions have developed and implemented policies and procedures to prevent, detect and handle scientific misconduct cases; and (2) what selected grantee institutions have learned and implemented as a result of their cases of impropriety in scientific research.

BACKGROUND

The most commonly accepted definition of "scientific misconduct" involves plagiarism and fabrication, falsification, and misrepresentation of data. Isolated cases of such practices surfaced from the mid-1970's through the early 1980's. The NIH, the primary funder of biomedical research, received a growing number of reports of alleged misconduct among its grantees. At that time, research institutions were not prepared to deal with cases of deliberate deception because they lacked procedures for handling such allegations. The cases of misconduct which have recently emerged have greatly sensitized the scientific community to the problems and complexities which must be resolved when misconduct occurs in the scientific setting. Several grantee institutions have now developed procedures to handle allegations of misconduct.

Congress has perceived the increased volume of reported cases of misconduct as a threat to the public trust in biomedical research. In an attempt to address the issue, Congress passed a section within the Health Research Extension Act of 1985 (Public Law 99-158) to deal with the problem. The law required those applying for NIH funds to submit with their application an assurance that they have procedures in place for dealing with scientific misconduct. They also must have an administrative process to review reports of misconduct and to report to the Secretary of the Department of Health and Human Services (HHS) investigations which produce substantial evidence of unscientific practices. The Department has not yet finalized regulations on scientific misconduct to implement these requirements.

METHODOLOGY

We conducted this inspection in three phases: (1) we held discussions on selected issues with HHS officials, scientific societies and associations, and other knowledgeable individuals; (2) we conducted a telephone survey of a random sample of NIH grantee institutions; and (3) we visited nine grantee institutions to learn from their experience with scientific misconduct cases.

FINDINGS

1. Within the Department there is no central locus of responsibility or accountability for scientific misconduct.

2. The NIH has been slow in formalizing policies and procedures for dealing with scientific misconduct and handles investigations of allegations on an ad hoc basis resulting in inconsistencies.

3. Only 22 percent of NIH grantee institutions overall have policies and procedures in place to deal with cases of scientific misconduct, as required by law. However, 93 percent of grantee institutions with 100 or more awards do have such policies and procedures.

4. Grantee institutions are awaiting guidance from NIH to develop their policies and procedures for scientific misconduct, although 53 percent overall say the development of procedures is primarily their responsibility.

5. Scientific misconduct procedures that are in place are generally not comprehensive and are limited.

6. Virtually all of the grantee institutions' procedures include steps for investigating allegations. However, most do not provide for notifying NIH at the initiation of an investigation. All of the large grantee institutions considered investigations their responsibility, although only 54 percent of the small grantee institutions shared this view.

7. Grantee institutions stress the complexities of conducting scientific misconduct investigations and want flexible procedures. Half of the grantee institutions with 100 or more awards have used outside expertise.

8. Grantee institutions say that detecting actual misconduct is problematic, and there is heavy reliance on the "whistle blower." They also say it is not possible to guarantee confidentiality and to protect the whistle blower.

9. Thirty-six percent (17 of 47) of the grantee institutions with procedures reported cases of misconduct which required the use of their procedures. Sixteen of the 34 cases (47 percent) investigated by these 17 grantee institutions were substantiated. Over half of these institutions are revising their procedures.

10. A few grantee institutions have developed or are developing guidelines for preventive and ethical scientific practices. Grantee institutions have expressed interest in receiving guidance in this emerging area.

11. Grantee institutions say that the principal investigator has a major responsibility for fostering scientific integrity and that scientific misconduct would be less likely to occur if the principal investigator adequately performs his/her responsibilities.

RECOMMENDATIONS

1. The Secretary should provide for independent oversight, and develop a more formalized and centralized process to deal with scientific misconduct including the following elements: (1) an independent third party to act as a fact gatherer and collect, retain and analyze investigative data; (2) an independent scientific review board to assist in analyzing information concerning scientific misconduct; and (3) an independent decision making authority or ombudsman type function. This is especially important given the congressional concern regarding the lack of independence of investigative units.

2. The Department should expedite completion and publication of a final regulation on the responsibilities of Public Health Service (PHS) awardee and applicant institutions for dealing with and reporting possible misconduct in science, as required by law. This will facilitate the development of procedures by grantee institutions.

3. The Department should require all applicant institutions to submit their scientific misconduct procedures on an annual basis to assure compliance with the law. The PHS should review the procedures on a sample basis and also in all instances where scientific misconduct cases are reported to assure that essential areas are covered.

4. The first line of responsibility for conducting an inquiry and/or investigation into an allegation of misconduct rests with the grantee institution. However, regulations issued by the Department should require that grantee institutions immediately notify the Department whenever they detect or receive an allegation of scientific misconduct, maintain records of all inquiries and investigations and provide the Department with periodic status reports. The regulations should specify time frames for reporting and conducting inquiries and investigations. Although we recognize the grantee institutions are concerned about flexibility, these requirements are, nevertheless, necessary to assure adequate monitoring and oversight by the Department.

5. The Department should keep complete and uniform records concerning investigations undertaken by the grantee institutions and PHS in order to maintain baseline data on the incidence of cases. This information could also be used in refining guidance and direction to grantee institutions in conducting future investigations.

6. The Department should encourage individuals with information about instances of possible scientific misconduct to come forward. Grantee institutions should be informed of the Office of Inspector General (OIG) Hotline, which receives allegations concerning fraud and abuse in the Department's programs.

7. The Department should explore ways to protect the "whistle blower," since detection of possible scientific misconduct relies so heavily on individuals willing to make an allegation. Currently Federal employees who engage in "whistle blowing" are protected by law. Similar protection should be provided to individuals reporting possible scientific misconduct by grantees.

8. The Department should explore alternative methods of detecting possible misconduct. Examples of possible methods are spot audits of scientific data, or special reviews by editors of scientific journals.

9. The Department should develop a table of penalties, such as the model adopted by the Office of Personnel Management, to assure that sanctions are applied consistently and fairly in cases of scientific misconduct.

10. The PHS should assume a leadership role and provide guidance to the grantee institutions in matters related to scientific misconduct.

    - The PHS should sponsor a consensus conference to develop model guidelines for use by grantees in addressing all relevant areas of scientific misconduct.

    - The PHS should continue its efforts in the area of prevention, such as the contract with the Institute of Medicine to develop scientific standards for the conduct of responsible science. The PHS should develop model preventive guidelines and require that institutions adopt these measures as a condition of funding.

AGENCY COMMENTS

The Public Health Service (PHS) indicated that the OIG draft report on Misconduct in Scientific Research was "a useful discussion of some important issues related to allegations of misconduct in PHS extramural programs." The PHS provided general and specific comments on the draft of this report which are included in appendix E. In response to these comments, we made revisions where appropriate in the final report.

INTRODUCTION

PURPOSE

To determine: (1) the extent to which the National Institutes of Health (NIH) and its grantee institutions have developed and implemented policies and procedures to prevent, detect and handle scientific misconduct cases; and (2) what selected grantee institutions have learned and implemented as a result of their scientific misconduct cases.

THE PROBLEM OF SCIENTIFIC MISCONDUCT

Although the precise definition of scientific misconduct is at issue, it is generally understood to involve deceit rather than error. The Public Health Service (PHS) policy defines misconduct as "serious deviation, such as fabrication, falsification, or plagiarism, from accepted practices in carrying out research or in reporting the results of research. . ." Scientific misconduct can have serious consequences and weakens the knowledge base upon which future experiments are performed. It diverts research funds from the work of ethical scientists and undermines public confidence in scientific research. Most alarmingly, if it goes undetected, scientific misconduct can lead to dangerous changes in clinical treatment and medical practices.

Traditionally, the scientific community has relied upon two defenses against misconduct: (1) the integrity of its scientists and (2) the scientific principle which gives credence only to results which can be replicated by other researchers. These defenses have not proved impregnable. Like all fields, scientific research has attracted a very small minority of unethical individuals and replication is not always an effective defense.

Despite the intensifying public focus on the reported scientific misconduct cases during the 1980's, no consensus has emerged on the proper way to deal with the problem. Some of the issues in dispute are the precise definition and prevalence of scientific misconduct, the most effective way to detect and prevent misconduct, the practices to promote responsible conduct of research, and the proper procedures for handling allegations of misconduct.

FEDERAL INVOLVEMENT IN SCIENTIFIC RESEARCH

The NIH, an agency of the PHS in the Department of Health and Human Services (HHS), is charged with fostering the public health through research and research training conducted or funded by its 16 bureaus, institutes and divisions. The NIH is the largest funder of biomedical research in the world. In Fiscal Year 1986, the NIH awarded 23,445 grants totalling over $3.7 billion to 1,303 institutions. Approximately one-third of this money went to indirect costs for housing the grant, including general administration, plant and equipment, quality control, and costs for dealing with scientific misconduct. In Fiscal Year 1987, over $4.4 billion in research grants was awarded.

Each NIH component uses some variant of the same grant application and monitoring process. This process stresses the scientific merit of the proposals and accounting for the expenditure of Federal funds. Grant applications undergo an external scientific peer review that judges scientific merit and technical qualities, and a subsequent review by institute advisory councils that addresses whether the proposed research will benefit public health. While receiving Federal funds, grantees are required to provide progress reports. In addition, NIH grants management and program officials review the programmatic progress and business management of grants.

Issues of research integrity and quality control are not explicitly addressed during the grant approval and management process. They are considered the responsibility of the grantee institution and carried out by the principal investigator. The NIH becomes involved only when a grantee institution has notified NIH that one of its researchers has committed an act of misconduct, or when NIH believes that a grantee institution has failed to fully investigate an allegation of misconduct. Since January of 1982, NIH has received 102 allegations of scientific misconduct and the Department has issued a sanction or taken formal corrective action in 21 cases. The sanctions may include debarments from receiving future funding for a specified period of time.

FEDERAL ACTION ON THE PROBLEM OF SCIENTIFIC MISCONDUCT

In 1981 the Subcommittee on Investigations and Oversight of the House Committee on Science and Technology heard testimony from scientists and philosophers interested in the legal, ethical, and scientific consequences of scientific misconduct. The hearing demonstrated that neither grantee institutions nor NIH had procedures for dealing with allegations of misconduct in federally funded research. The subcommittee found that there had been instances of misconduct but that NIH handled each of them in an ad hoc, case-by-case basis.

In 1985, Congress passed "The Health Research Extension Act" (the Act). The conference report accompanying the final legislation referred to the NIH scientific misconduct procedures in place at that time as "informal" and "ad hoc." It noted that NIH, even in cases of admitted wrongdoing, took over a year to complete reviews and impose sanctions. The report also argued that sanctions should include the recovery of misspent Federal research dollars. The major provisions of the Act require that: (1) the Director of NIH establish procedures to ensure prompt response to information regarding scientific fraud, facilitate the receipt of such information, and expedite appropriate action with respect to misconduct; (2) the Secretary of HHS establish regulations requiring those applying for NIH funds to submit with their applications an assurance that they have procedures for dealing with scientific misconduct; and (3) applicants have an administrative process to review reports of misconduct and report to the Secretary investigations which uncover substantial evidence of unscientific practices.

Subsequently, representatives from the PHS agencies developed a set of interim guidelines, "The Policies and Procedures for Dealing with Possible Misconduct in Science," which were approved in 1986. These interim guidelines set forth awardee obligations as follows: (1) assume primary responsibility for preventing, detecting, and dealing with misconduct; (2)

develop policies and procedures for dealing with possible scientific misconduct; (3) inform PHS of the initiation of any formal investigation of possible malfeasance; and (4) maintain a fact-finding system, which generally consists of an "inquiry" to determine whether an allegation has substance enough to warrant an investigation, and an "investigation" which is a formal evaluation of all relevant facts to determine if misconduct has occurred. However, until PHS publishes final regulations, these requirements are not binding on the grantee institution.

Under these guidelines NIH has the following options: (1) accept the grantee institution's investigation report, if it believes the report is factual, fair to all concerned, and addresses all misconduct issues; (2) conduct its own review if it has reason to believe that the institution's report is incomplete or unreliable; or (3) begin an investigation if it feels that the grantee institution is not satisfactorily pursuing an allegation of misconduct.

The NIH usually conducts its investigations by appointing a panel of scientific peers to review the case. Panel members are primarily drawn from outside of NIH. Usually they have expertise in the subject matter of the research being questioned and should not have real or perceived conflict of interest with the accused.

In April 1988, two congressional committees held hearings on scientific misconduct. Both of these committees were concerned over allegations that significantly more cases of misconduct exist than are reported and investigated. During the hearings committee members questioned the capability of grantee institutions to handle allegations of misconduct and to conduct investigations of alleged improprieties. Members criticized the Department about the lack of resources, lack of timely resolution of cases, treatment of whistle blowers and the lack of appreciation of conflict of interest with respect to selection of panels of scientific peers. A hearing was also held in September of 1988 to further explore these issues as well as to inquire into potential conflict of interest cases in academic research. The committee members indicated that they intend to introduce significant legislation unless the Department corrects the perceived deficiencies.

In September 1988, prior to issuing a final regulation implementing the Health Research Extension Act, the PHS published a notice of proposed rulemaking (NPRM) on the responsibilities of PHS awardee and applicant institutions for dealing with and reporting possible misconduct in science. Simultaneously, PHS published an advanced notice of proposed rulemaking (ANPRM) to aid in the development of future regulations protecting against misconduct in research. Also in September 1988, the PHS published two Grants Administration Manual Issuances, providing the basis of departmental procedures for dealing with instances of alleged misconduct in science.

SCIENTIFIC COMMUNITY ACTIONS ON THE PROBLEM OF SCIENTIFIC MISCONDUCT

In the early 1980's two organizations, the American Association of Universities (AAU) and the Association of American Medical Colleges (AAMC), published guidelines for maintaining integrity in scientific research. While in general these guidelines do not offer specific proce-

dures, they do address the primary areas that institutions need to consider in developing procedures. Currently, the AAU and the AAMC are collecting procedures from various institutions to establish a base of information on the types of procedures in use throughout the country. Recently, a consortium of educational organizations under the direction of the AAU has developed a framework, or model guidelines, for institutional policies and procedures to deal with scientific misconduct.

In the fall of 1987 the American Association for the Advancement of Science (AAAS) and the American Bar Association (ABA) held a National Conference of Lawyers and Scientists. The participants, from universities involved in allegations of misconduct, NIH, and the National Science Foundation, exchanged problems, experiences, and information. Subsequent conferences will address policies and procedures for handling allegations and some of the broader issues involved in scientific misconduct.

Little information exists on the extent to which grantees have policies and procedures, since very few studies have been done in this area. A survey conducted from 1982 to 1984 found that only 23 percent of academic institutions and hospitals had written rules for dealing with allegations of fraud.

METHODOLOGY

This study was conducted in three phases. First, we held discussions on selected issues with HHS officials, representatives of scientific societies and associations, grantee institutions, and other knowledgeable individuals. Our contacts included the Society for Research Administrators, Institute of Medicine, Association of State Colleges and Universities, American Association of Medical Colleges, and the American Association for the Advancement of Sciences. Additionally, we reviewed pertinent literature, including journal articles, books, legislation, regulations and Government manuals and guidelines.

In the second phase we surveyed a random sample of Fiscal Year 1986 NIH grantee institutions by telephone to determine the extent to which NIH grantee institutions have established policies and procedures relating to scientific misconduct. We also requested each grantee institution to send us its scientific misconduct policies and procedures.

The telephone survey was completed through interviews with representatives of the sampled universities or institutions. The initial contacts with the various institutions nationwide requested access to the individual knowledgeable about administration of scientific misconduct procedures for NIH research grants. Telephone interviews at the institutions were held with deans, associate deans and administrators of research and/or grants programs; vice chancellors, associate and vice provosts; professors and principal investigators; and corporate officers.

The sample was divided into three strata: 30 grantee institutions with 100 or more research awards which represented 86 percent of all award money in the sample; 31 grantee institutions with 10 to 99 research awards representing 11 percent of the funding; and 28 grantee institutions with less than 10 research awards which made up less than 2 percent of the funding.

Those with more than 100 research awards were generally large universities with considerable NIH funding in their biomedical research department or medical school. State universities, teaching hospitals, and research foundations comprised most of the institutions receiving 10 through 99 research awards. The institutions with less than 10 research awards consisted mainly of small corporations, hospitals, and regional universities. Geographically, over one-third of the institutions in all three strata were located in the Northeast and the West. For a full discussion of the survey methodology, see appendix A.

The third phase of the study consisted of site visits to nine grantee institutions which had experience with scientific misconduct cases. These grantee institutions were not necessarily a part of the random sample for the telephone survey. Discussions with individuals at the grantee institution included the following topics: (1) definition of misconduct, (2) development and use of procedures, (3) prevention and detection, (4) role of the principal investigator, and (5) lessons learned. Discussions were held with provosts, deans, principal investigators, legal counsel and administrators. At some institutions, we also met with individuals against whom allegations of misconduct had been made, as well as some whistle blowers.

FINDINGS AND RECOMMENDATIONS

ROLE OF NIH

Within the Department there is no central locus of responsibility or accountability for scientific misconduct.

Several NIH components and PHS agencies are currently responsible for handling allegations and investigations of misconduct or other improprieties. Consequently, the responsibilities are diffuse. The designated units within Department are as follows:

- The Office for Extramural Research in NIH has been delegated the responsibility to develop and assess policies and procedures for preventing, detecting, reporting, and handling instances of alleged scientific misconduct. The director of this office is the PHS misconduct policy officer. Although this office oversees and coordinates PHS activities related to misconduct, only two full-time professionals, who had additional responsibilities, were assigned to this area at the time our study was conducted. Since that time two professionals and one secretary have been added to the NIH office that handles allegations of misconduct in science (See Agency Comments).

- The Office for Protection from Research Risks in NIH has the responsibility for human subject protection and animal welfare. This office investigates alleged or apparent violations of Federal regulations governing the protection of human subjects or PHS animal welfare policy in cases involving PHS funded research. These violations are included in the PHS definition of scientific misconduct.

- The Division of Management Survey and Review in NIH manages the PHS ALERT system which collects, controls and disseminates information about institutions or individuals under investigation for possible scientific misconduct or sanctioned for misconduct. The PHS officials use this information to make informed decisions regarding funding, although such information does not automatically result in the withholding of funds. This unit also reviews allegations of grantee fiscal improprieties and has audit responsibilities over grantees.

- The Office of Inspector General (OIG) also has audit responsibilities for grantees, as well as investigative responsibility for those scientific misconduct cases with potential criminal violations. The Inspector General Amendments Act of 1978, P.L. 95-452, as amended, provides that the OIG have the responsibility to supervise, coordinate, and provide policy direction for auditing and investigative activities relating to programs and operations of the Department; and to prevent and detect fraud and abuse in its programs and operations. However, the Secretary has not delegated the overall responsibility for scientific misconduct to the OIG.

Each PHS agency (including the NIH; the Alcohol, Drug Abuse and Mental Health Administration; the Food and Drug Administration; the Centers for Disease Control and the Health and Resources Administration) also has a misconduct policy officer who, among other duties, provides leadership to ensure appropriate agency implementation policies and procedures for the fair and prompt handling of instances of alleged or apparent misconduct.

Allegations of scientific misconduct are currently received by the various offices discussed above, as well as the grants project officers in the many institutes and other components in each of the agencies. Additionally, some allegations are received by the OIG hotline. (The PHS has recently developed a reorganization proposal to deal with allegations of scientific misconduct, which has not yet been approved. This proposal was described in their comments to the draft report, dated January 30, 1989.)

As noted earlier, Congress has held hearings on the issue of scientific misconduct and the Department's ability to deal with allegations and investigations of scientific misconduct. A major focus of those hearings was the diffusion of responsibility for dealing with scientific misconduct as well as the inherent conflict of interest by the placement of this activity within the funding agencies. Some members of Congress have called for an independent and objective screening and review of allegations of scientific misconduct.

The NIH has been slow in formalizing policies and procedures for dealing with scientific misconduct and handles investigations of allegations on an ad hoc basis resulting in inconsistencies.

Until recently, the NIH relied upon interim guidelines, entitled, "Policies and Procedures for Dealing with Possible Misconduct in Science," issued in 1986, for determining how PHS handles cases of scientific misconduct. In accordance with the requirements of the Health Research Extension Act of 1985, the guidelines indicated that several steps would be taken promptly to formalize this process, including: (1) incorporating sections on scientific misconduct into standard guidance documents such as the "Grants Administration Manual;" (2) publishing a notice of proposed rulemaking to implement grantee responsibilities as required by law; and (3) establishing a PHS committee on scientific misconduct to exchange information about investigations and discuss relevant policy proposals.

In September 1988, the PHS published two Grants Administration Manual Issuances, which put into place fully binding departmental policies on scientific misconduct. Additionally, a notice of proposed rulemaking (NPRM) on the responsibilities of PHS awardee and applicant institutions for dealing with and reporting possible misconduct in science was published in the Federal Register. A final rule is expected to be published by the middle of this year. Also, the first meeting of the PHS committee on scientific misconduct was held in December 1987.

The Grants Administration Manual Issuance on misconduct in science closely resembles the interim guidelines and provides general principles rather than an explicit procedure with specific standards and criteria. Although the publication of the Grants Administration Manual Issuance formalized the process, the manual issuance has the same deficiencies as the interim

guidelines. Therefore, the same weaknesses identified by NIH staff with the interim guidelines, described below, will continue to persist.

According to key NIH staff, NIH handles investigations of scientific misconduct on an ad hoc basis. They characterized the process as informal and stated that they did not always follow the interim guidelines, because the guidelines were broad and offered few specifics. Inconsistencies occurred because the interim guidelines did not include standards for prompt and complete reviews, i.e. time frames for conducting an investigation are not specified. Further, the guidelines did not offer explicit criteria for determining, among other things: (1) when PHS should initiate its own investigation or (2) how to select scientific review panels, which review grantee institution's reports of investigations and sometimes conduct NIH investigations.

Some grantee institutions said that NIH is inconsistent and should examine its own procedures. Others said that NIH's handling of investigations is greatly influenced by the media, and that this results in inconsistencies. Still others commented that NIH's investigative process is disorganized and slow, and that NIH's procedures could be more explicit.

Further, criteria to determine appropriate sanctions or debarment periods have not been established. After an allegation has been substantiated, sanctions are imposed on a case-by-case basis. Some grantee institutions commented that sanctions, debarment periods and especially the decision to recoup funds appear to be inconsistent. Additionally, the Conference Report for the Health Research Extension Act of 1985 states that the NIH procedures should include a mechanism for the recovery of Federal funds. Since 1982, PHS has only recovered a total of $382,000 from four institutions.

Recommendation: *The Secretary should provide for independent oversight, and develop a more formalized and centralized process to deal with scientific misconduct including the following elements: (1) an independent third party to act as a fact gatherer and collect, retain and analyze investigative data; (2) an independent scientific review board to assist in analyzing information concerning scientific misconduct; and (3) an independent decision making authority or ombudsman type function. This is especially important given the congressional concern regarding the lack of independence of investigative units.*

Recommendation: *The Department should develop a table of penalties, such as the model adopted by the Office of Personnel Management, to assure that the sanctions are applied consistently and fairly in cases of scientific misconduct.*

ABSENCE OF PROCEDURES

Only 22 percent of NIH grantee institutions overall have policies and procedures in place to deal with cases of scientific misconduct, as required by law. However, 93 percent of grantee institutions with 100 or more awards do have such policies and procedures.

The NIH has delegated the primary responsibility for preventing, detecting and addressing scientific misconduct to its grantee institutions, as required by the Health Research Extension Act of 1985. All applicants will be required to make assurances that they have procedures in place to deal with scientific misconduct, as required by law, when regulations are published.

Only 22 percent of the NIH grantees overall have procedures in place to deal with cases of scientific misconduct. In the group of grantee institutions with 100 or more awards and 86 percent of the funding, 93 percent (28 of 30) have procedures. This still means that two institutions with over 100 awards from NIH have not yet developed procedures. In addition, the majority of NIH grantee institutions are small, having less than 10 awards. In this group only 11 percent (3 of 28) had developed procedures.

Grantee institutions who have had experience with cases of misconduct stress the importance of having policies and procedures in place prior to the occurrence of an allegation. Most of the nine institutions visited had developed procedures in reaction to cases of misconduct at other institutions where no procedures existed. As a consequence, when cases occurred at their institution, they were prepared to deal with them. These institutions also pointed out that having written procedures helps to prevent the appearance of a cover-up or of persecuting an individual.

A few grantee institutions in our telephone survey who had developed procedures remarked that they had not done so until a substantial charge of misconduct had been alleged, at which time painstaking effort was required on the part of faculty members and committees to develop misconduct procedures. This further supports the need for written procedures *before* cases occur.

Grantee institutions are awaiting guidance from NIH to develop their procedures, although 53 percent overall say the development of procedures is primarily their responsibility.

When asked who should have primary responsibility for developing procedures, 53 percent said the grantee institution should have the primary responsibility. However, a number of grantee institutions indicated that they are looking to the NIH for more guidance on developing misconduct procedures and on deciding what should be included in the procedures. Several of the grantee institutions said that the NIH and the institutions should work together in developing a misconduct policy. Also, some institutions commented that because of the heterogeneity of the grantee institutions, the NIH should review applicants' procedures to determine that the appropriate issues were addressed.

Although NIH has developed interim guidelines in response to the Act, final regulations implementing grantee institution responsibilities have not been published. Some say they are waiting for final regulations to be published before developing procedures. Of the grantees with procedures, 23 of 47 had developed their procedures prior to the Act and 20 have developed procedures since then - - after NIH's interim guidelines were issued. Four grantees did not know when their procedures had been developed. Grantee institutions have delayed action in developing procedures, waiting for final rules.

Some of the small grantee institutions indicated that they were unaware that misconduct procedures will need to be in place in order to receive NIH funding. A few of the small institutions were unconcerned about misconduct, stating that this would not happen at their institution because of their small size. Other small grantee institutions are particularly concerned regarding the development of procedures and future requirements. Only 44 percent of the grantee institutions with less than 10 awards, that do not have procedures, said they intend to develop procedures.

Recommendation: *The Department should require all applicant institutions to submit their scientific misconduct procedures on an annual basis to assure compliance with the law. The PHS should review the procedures on a sample basis and also in all instances where scientific misconduct cases are reported to assure that essential areas are covered.*

Recommendation: *The Department should expedite completion and publication of a final regulation on the responsibilities of PHS awardee and applicant institutions for dealing with and reporting possible misconduct in science, as required by law. This will facilitate the development of procedures by grantee institutions.*

NATURE OF PROCEDURES

Scientific misconduct procedures that are in place are generally not comprehensive and are limited.

We compared the grantee institutions' procedures in place to the recommendations of the NIH interim guidelines and other areas identified as important by the Association of American Medical College's "The Maintenance of High Ethical Standards in the Conduct of Research" and the Association of American Universities' "Report of the Association of American Universities Committee on the Integrity of Research." We asked if the procedures covered the following areas: inquiries and investigations of allegations of misconduct; specified time frames for conducting inquiries and investigations; reporting to the NIH; protection of confidentiality for the accused and the individual making the accusation; due process and appeals; retention, storage, and ownership of data; validation of research results; retraction of published articles shown to be fraudulent; and responsibility of coauthors.

Based on this analysis, few grantee institutions covered all the elements noted, and less than half include provisions for the retention, storage and ownership of data; validation of research results; retraction of articles; or responsibility of coauthors. See appendix B for areas incorporated and percentages of grantee institutions whose procedures included those elements.

Well over three-fourths of the grantee institutions with procedures have provisions for confidentiality for the whistle blower and the accused. In many procedures there was a general reference to "the protection of the reputation of those who, in good faith, report misconduct" or an admonition that confidentiality must be maintained at all times during both levels of inquiry. It should be noted that grantee institutions expressed equal concern for the protection of the accused. Although many institutions have measures to protect confidentiality, all agree

that confidentiality cannot be guaranteed. Also, three-fourths of the grantee institutions include provisions for due process and appeals and almost all institutions provide for internal sanctions in cases of wrongdoing, including penalties for those who make false accusations.

Procedures in place at the grantee institutions we visited, also were varied and somewhat limited. However, half the institutions had developed separate policy statements addressing most of the elements listed above. Most commented that they prefer a flexible policy, since in their combined thinking, no two cases are alike. Therefore, grantee institutions claim a framework for a variety of cases is necessary.

Virtually all of the grantee institutions' procedures included steps for investigating allegations. However, most do not provide for notifying NIH at the initiation of an investigation. All of the large grantee institutions considered investigations their responsibility, although only 54 percent of the small institutions shared this view.

Almost all (99%) of the grantees' procedures included steps for investigating allegations. All of the large grantee institutions considered such investigations their responsibility. However, only 54 percent of the small institutions shared this view, and most of these institutions would support a more active NIH role in investigating allegations. Some of the grantee institutions surveyed, felt that small institutions should not handle their own cases, and a few recommended that other entities, such as arbitration panels, address serious cases.

Procedures established by most of the grantee institutions included two levels of response to allegations: an inquiry and a formal investigation. Generally, the department in which the alleged misconduct occurred handles the first step by trying to determine if there is substance to the charge. The number of participants at this point is small in order to ensure confidentiality and to protect the accused and the accuser. Most of the misconduct procedures designated a second level of review which was identified as a formal investigation.

Procedures varied on whether or not they reported to NIH after the first level of inquiry. Over three-fourths of the large grantee institutions, and approximately half of the institutions overall, do not report to the funding agency after the first level of inquiry, which is set forth in current PHS guidelines. Most grantee institutions felt that NIH should not be informed until misconduct was substantiated.

Most of the procedures reviewed did not provide specified time frames for conducting an inquiry or an investigation, although procedures referred to pursuing investigations "expeditiously," "rapidly," or "as soon as possible." If time frames were given, the initial allegation was usually reported, reviewed and decided upon within 10 work days. The investigation phase was sometimes given a time frame of 120 days. However, a representative of a large institution stated that time frames were inappropriate: "in complicated cases the only way to go about it is a dogged, time-consuming effort." Many grantee institutions noted that the complexity of scientific misconduct cases, and the amount of resources (staff, time and money) required to investigate such cases made it difficult to establish time frames.

Recommendation: *The PHS should sponsor a consensus conference to develop model guidelines for use by grantee institutions in addressing all relevant areas of scientific misconduct.*

Recommendation: *The first line of responsibility for conducting an inquiry and/or investigation into an allegation of misconduct rests with the grantee institution. However, regulations issued by the Department should require that grantee institutions immediately notify the Department whenever they detect or receive an allegation of scientific misconduct, maintain records of all inquiries and investigations and provide the Department with periodic status reports. The regulations should specify time frames for reporting and conducting inquiries and investigations. Although we recognize the grantee investigations are concerned about flexibility, these requirements are, nevertheless, necessary to assure adequate monitoring and oversight by the Department.*

PROBLEMS WITH INVESTIGATIONS AND DETECTION

Grantee institutions stress the complexities of conducting scientific misconduct investigations and want flexible procedures. Half of the grantee institutions with 100 or more awards have used outside expertise.

Grantee institutions expressed the need for flexible procedures to encompass the complexities and uniqueness of each individual case. We were told that initially after an allegation is raised, a grantee institution must decide who should provide the substantiation, and what and how much substantiation is required to initiate a formal investigation. This varies from case to case.

When the formal investigation is initiated, if there are enough scientists with appropriate expertise and without conflict of interest available within the institution, the institution will conduct its own internal investigation. The grantee institution may request assistance, if necessary, from others within the institution with scientific expertise, such as nurses and technicians. However, some grantee institutions may need to elicit experts from outside the institution to avoid conflict of interest or to obtain the necessary expertise in a very specialized area. Half of the grantee institutions with 100 or more awards said that outside expertise was used when investigating cases. However, all the institutions emphasized that only scientists were able to conduct the investigations.

We were told that an investigation consumes an extraordinary amount of resources including time, money and labor. Investigators must search for raw data, review the data, review medical records and other documentation, interview knowledgeable parties and must duplicate experiments. Sometimes, the investigation includes reviews of earlier publications as well. These may go back several years in time. Additional time may be spent seeking retractions of fraudulent articles.

If the accused leaves the institution before or during the investigation, this may complicate the case even further. However, 93 percent of the grantee institutions indicated they would continue to pursue an allegation of misconduct if the accused left the institution.

Grantee institutions say that detecting actual misconduct is problematic, and there is heavy reliance on the "whistle blower." They also say it is not possible to guarantee confidentiality and to protect the whistle blower.

Grantee institutions say that detection of scientific misconduct is difficult and they must rely on the "whistle blower." Two-thirds of the grantee institutions said that principal investigators would report peers or subordinates engaged in misconduct, although some noted that reporting might depend on the severity of the situation or the relationship of the parties involved. Some grantee institutions felt that the principal investigator would resolve the problem in the laboratory setting if at all possible and only notify the department head if the dispute could not be settled.

However, some grantee institutions stated that young researchers are afraid to "blow the whistle," not wanting to jeopardize their careers, and that it is particularly difficult for graduate students to report a superior. Although many institutions have measures to protect the whistle blower, all agree that confidentiality cannot be guaranteed. A few grantee institutions suggested that an ombudsman be designated to receive allegations.

Grantee institutions expressed concern regarding their heavy reliance on "whistle blowers" to detect misconduct. Even so, they did not consider other methods, such as scientific data audits by outside reviewers, to be cost-efficient or effective.

Grantee institutions noted that detection may be one of the most vexing issues. Most indicated that the past occurrences of misconduct could take place again and that anyone who is determined to commit scientific misconduct will initially get away with it. However, ultimately the grantee institutions believe it would be detected.

We learned that in cases of substantiated misconduct, astute reviewers detected the misconduct due to statistical naivete and data that was "too clean." In a few cases, misconduct was detected through replication of the experiment.

Recommendation: *The Department should explore ways to protect the "whistle blower," since detection of possible scientific misconduct relies so heavily on individuals willing to make an allegation. Currently Federal employees who engage in "whistle blowing" are protected by law. Similar protection should be provided to individuals reporting possible scientific misconduct by grantees.*

Recommendation: *The Department should explore alternative methods of detecting possible misconduct. Examples of possible methods are spot audits of scientific data, or special reviews by editors of scientific journals.*

Recommendation: *The Department should encourage individuals with information about instances of possible scientific misconduct to come forward. Grantee institutions should be informed of the OIG Hotline, which receives allegations concerning fraud and abuse in the Department's programs.*

ESTIMATE OF THE OCCURRENCE OF CASES

Thirty-six percent (17 of 47) of the grantee institutions with procedures reported cases of misconduct which required the use of their procedures. Sixteen of the 34 cases (47 percent) investigated by these 17 grantee institutions were substantiated. Over half of these grantee institutions are revising their procedures.

Even though detection is problematic, 36 percent (17 of 47) of the grantee institutions with procedures have had cases of misconduct which required the use of these procedures. These 17 grantee institutions reported a total of 34 cases, or an average of 2 cases per institution, which were investigated under their procedures. Over half of these grantee institutions are revising their procedures to provide for more comprehensive, precise and clear direction. Some of the grantee institutions visited are making revisions based on their experiences in addressing actual cases of misconduct.

Currently there is no cumulative information concerning the number of cases of alleged scientific misconduct that have been investigated by NIH or the grantee institutions. Based on the number of cases reported by the grantee institutions in our sample, we estimate that 95 cases (47 substantiated and 48 unsubstantiated) have been addressed by NIH grantees. This figure is similar to the number of cases reported to NIH since 1982. According to NIH, 102 cases have been investigated by the grantee institutions and reported to the agency during that time period.

We cannot gauge the extent of scientific misconduct accurately. Our estimate does not represent an annual incidence of cases, but rather a cumulative occurrence of cases reported, since the data reported was for inconsistent time periods. Also, it should be noted that some grantee institutions were reluctant or hesitant to report this information and a few institutions did not know.

The estimate of 95 cases does not represent an estimate of the actual *prevalence* of scientific misconduct. In fact, the grantee institutions were about evenly split on whether or not more misconduct occurs than is reported.

Recommendation: *The Department should keep complete and uniform records concerning investigations undertaken by the grantee institutions in order to maintain baseline data on the incidence of cases. This information could also be used in refining guidance and direction to grantee institutions in conducting future investigations.*

NEED FOR PREVENTION AND ETHICS

A few grantee institutions have developed or are developing guidelines for preventing scientific misconduct. Grantee institutions have expressed interest in receiving guidance in this emerging area.

Of the grantee institutions surveyed, 21 percent have measures intended to prevent scientific misconduct. The most common examples include orientation programs or seminars focusing on ethics and misconduct issues (usually aimed at new researchers) and training programs for principal investigators.

In general, while grantee institutions stressed the need to raise the consciousness of faculty and students about prevention programs, they spoke in terms of guidelines for scientific practices and ethics rather than preventive measures. Most grantee institutions do not believe that misconduct can be prevented. Rather, they believe that emphasizing responsible scientific practices will deter sloppy science which can lead to misconduct.

Several grantee institutions, moreover, alluded to the resistance of faculty to deal with practices they believed were already a part of research activity, to handle additional paperwork, and to cope with a "police state" mentality. However, most commented that if the scientific community does not take some action, it will be imposed from the outside.

Only a few grantee institutions have developed or are developing actual guidelines for scientific practices to ensure the quality and integrity of research, although this area is receiving increased attention. [See, for example, "Fraud in Biomedical Research: A Time for Congressional Restraint," *New England Journal of Medicine*, June 2, 1988, which commends Harvard Medical School for developing preventive guidelines but calls for even more stringent measures such as requiring the adoption of these standards. Appendix C contains the journal editorial and the Harvard Medical School "Guidelines for Investigators in Scientific Research."] Some grantee institutions have expressed interest in guidance from NIH in this emerging area.

The types of provisions we found in the preventive guidelines developed by a few grantee institutions were quite similar to those developed by Harvard Medical School. These provisions include: (1) closer supervision of research trainees; (2) more careful gathering and storage of primary data; (3) validation of research results; (4) explicit criteria for authorship of a scientific paper; and (5) an emphasis on quality rather than quantity of publications.

Grantee institutions say that the principal investigator has a major responsibility for fostering scientific integrity and that scientific misconduct would be less likely to occur if the principal investigator adequately performs his/her responsibilities.

Several grantee institutions greatly stressed the responsibility of the principal investigator for teaching integrity in research. In addition to the many competing roles of a principal investigator such as identifying research funds, managing grants, overseeing multi-site projects and

treating patients, grantee institutions said that the principal investigator should continually monitor and be constantly involved in the research effort. Grantee institutions commented that if the principal investigator was adequately performing his/her duties, misconduct would be less likely to occur.

The grantee institutions described the following practices that a principal investigator should follow to foster scientific integrity in the laboratory including: serving as a mentor or designating among the senior researchers a mentor for the inexperienced researcher to work with on a daily basis; maintaining open communication; reviewing and signing off on all written material that leaves the lab; reviewing all raw data; screening all research applicants carefully; developing a system of data retention and storage; and conducting formal staff assessments for junior researchers.

The principal investigators who had dealt with a case of scientific misconduct in their laboratory told us they had experienced a change of attitude. Prior to the case, they had been more trusting, but afterwards, they had become much more cautious and no longer assumed the trustworthiness of another scientist. Also, their approach to supervision in the laboratory became more structured and disciplined.

Recommendation: *The PHS should continue its efforts in the area of prevention, such as the contract with the Institute of Medicine to develop scientific standards for the conduct of responsible science. The PHS should develop model preventive guidelines and require that grantee institutions adopt these measures as a condition of funding. The role of the principal investigator should be addressed in the preventive measures.*

AGENCY COMMENTS AND OIG RESPONSE

The Public Health Service (PHS) indicated that the OIG draft report on Misconduct in Scientific Research was "a useful discussion of some important issues related to allegations of misconduct in PHS extramural programs." The PHS provided general and specific comments on the draft of this report which are included in appendix E. In response to these comments, we made revisions where appropriate in the final report. The comments PHS made with regard to the OIG recommendations are discussed below.

1. OIG Recommendation

The Secretary should provide for independent oversight, and develop a more formalized and centralized process to deal with scientific misconduct including the following elements: (1) an independent third party to act as a fact gatherer and collect, retain and analyze investigative data; (2) an independent scientific review board to assist in analyzing information concerning scientific misconduct; and (3) an independent decision making authority or ombudsman type function. This is especially important given the congressional concern regarding the lack of independence of investigative units.

PHS Comment and OIG Response

The PHS agrees that greater central management is needed in the Department to deal with scientific misconduct and therefore has developed a reorganization proposal involving the NIH as well as the Office of the Assistant Secretary for Health (OASH). The proposal calls for establishing a new Office of Scientific Integrity within NIH with the operational responsibility for conducting investigations. Another office would be established in the Office of the Assistant Secretary for Health to oversee operations of the research agencies and to review and propose policies.

The new Office of Scientific Integrity, reporting to the Director of NIH would have the ongoing operational responsibilities of monitoring investigations initiated by awardee institutions as well as conducting independent investigations. The office needs to assure that the scientific panels convened to conduct independent investigations do not have real or perceived conflict of interest with the accused. The individuals selected should be knowledgeable about the scientific area of inquiry but should not be involved with the research in question and should have no ongoing close professional, academic or financial relationship with the accused.

Although including the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) extramural research in the scope of responsibility of the office within the NIH will help to centralize this function, this arrangement may have logistical problems.

The PHS indicates that the office also plans to foster scientific integrity by developing prevention and education programs to be conducted by the extramural research offices throughout

NIH and ADAMHA. We encourage the PHS in this effort. However, the PHS must assure that adequate resources are allocated to this office to deal with the range of issues regarding scientific misconduct and to provide a "prompt and appropriate" response to allegations as required by the Health Research Extension Act of 1985.

The office to be established at the OASH level, which would be outside of the funding component, would oversee operations of the research agencies and would adjudicate cases investigated by NIH or ADAMHA and impose sanctions if warranted. The PHS is also considering the establishment of an outside advisory group to review and evaluate PHS policy and procedures governing scientific integrity. We believe this would provide an additional perspective to the process. The advisory group should involve a variety of participants, including representatives from the scientific community as well as public members.

We look forward to reviewing the complete reorganization proposal and functional statement and monitoring its implementation.

2. *OIG Recommendation*

The Department should expedite completion and publication of a final regulation on the responsibilities of PHS awardee and applicant institutions for dealing with and reporting possible misconduct in science, as required by law. This will facilitate the development of procedures by grantee institutions.

PHS Comment and OIG Response

The PHS concurred that the publication of a proposed rule was urgently needed and long overdue. As of September 1988, two Grants Administration Manual Issuances were published. Additionally, a notice of proposed rulemaking (NPRM) on "Responsibilities of PHS Awardee and Applicant Institutions for dealing with and Reporting Possible Misconduct In Science" was published in the Federal Register in September 1988. Currently, the PHS is in the process of preparing a final rule to be published.

Final regulations implementing these requirements will be published some time this year. Since Congress has raised questions about the adequacy and effectiveness of the current self-regulatory system in dealing with allegations of scientific misconduct, we believe that more explicit and stricter regulations are needed. We are pleased that PHS has already strengthened some provisions of the NPRM based on our recommendations. We believe that there is still need for improvement, as discussed in the recommendations that follow.

3. *OIG Recommendation*

The Department should require all applicant institutions to submit their scientific misconduct procedures on an annual basis to assure compliance with the law. The PHS

should review the procedures on a sample basis and also in all instances where scientific misconduct cases are reported to assure that essential areas are covered.

PHS Comment and OIG Response

In our draft report we had recommended that policies and procedures be submitted with each grant application. We agree with the PHS that annual submissions would be sufficient for monitoring purposes and have revised our recommendation accordingly.

4. OIG Recommendation

The first line of responsibility for conducting an inquiry and/or investigation into an allegation of misconduct rests with the grantee institution. However, regulations issued by the Department should require that grantee institutions immediately notify the Department whenever they detect or receive an allegation of scientific misconduct, maintain records of all inquiries and investigations for a specified time period and provide the Department with periodic status reports. The regulations should specify time frames for reporting and conducting inquiries and investigations. Although we recognize the grantee institutions are concerned about flexibility, these requirements are, nevertheless, necessary to assure adequate monitoring and oversight by the Department.

PHS Comments and OIG Response

The PHS indicated that immediate notification of all allegations of scientific misconduct to the Department appears too broad to be practical. We disagree.

Under the proposed rules, the awardee institution must complete an inquiry of an allegation or other evidence of misconduct within 60 days. The funding agency is only notified of allegations if an institution determines that an investigation is warranted. The rules do not require the reporting of all allegations to the funding component.

We believe all allegations, which reach a certain level within the academic institution such as the dean, the department head or other official designated by the institution, should be reported regardless of whether an investigation is pursued. This would assure adequate monitoring and tracking of cases by the Department. The PHS should review, on a sample basis, written reports of the inquiries of those cases that are not investigated. Additionally, knowing the number of substantiated cases as well as the total number of allegations would provide some perspective to the problem. More importantly, reporting allegations at an early stage of development should be considered in the best interest of the grantee institution. Early notification will prevent charges of cover-up against the grantee institution since there is an inherent appearance of impropriety when a grantee institution investigates itself.

5. OIG Recommendation

The Department should keep complete and uniform records concerning investigations undertaken by the grantees and/or PHS in order to maintain baseline data on the incidence of cases. This information could also be used in refining guidance and direction to grantee institutions in conducting future investigations.

PHS Comment and OIG Response

The PHS concurs that complete and uniform records are highly desirable for the reasons outlined in the report. The PHS has also established a data base, in addition to the PHS-wide ALERT system, to track open cases and to archive key information about cases that have already been closed. As part of our oversight responsibility we will determine whether the PHS is documenting and maintaining adequate records concerning investigations.

6. OIG Recommendation

The Department should encourage individuals with information about instances of possible scientific misconduct to come forward. Grantee institutions should be informed of the OIG Hotline, which receives allegations concerning fraud and abuse in the Department's programs.

PHS Comments and OIG Response

The PHS concurs with our recommendation and indicates that notices regarding the reporting of misconduct will be published in the NIH Guide for Grants and Contracts on an annual basis as well as the notice of a grant award.

7. OIG Recommendation

The Department should explore ways to protect the "whistle blower," since detection of possible scientific misconduct relies so heavily on individuals willing to make an allegation. Currently, Federal employees who engage in "whistle blowing " are protected by law. Similar protection should be provided to individuals reporting possible scientific misconduct by grantees.

PHS Comment and OIG Response

The PHS concurs that improved protection for "whistle blowers" is essential to the integrity of the process and is in the process of examining additional means of providing proper protection. Perhaps the PHS should prohibit awardee institutions from taking retaliation against an employee that has made an allegation in good faith at the risk of losing their funding. Another protection for the accuser could be exemption from liability or requiring the institution to

defend the whistle blower if any legal proceedings are initiated. We agree with the PHS that appropriate protection for the whistle blower will require legislation. We understand legislation may be introduced in this area.

8. OIG Recommendation

The Department should explore alternative methods of detecting possible misconduct. Examples of possible methods are spot audits of scientific data or special reviews by editors of scientific journals.

PHS Comments and OIG Response

The PHS concurs in principle regarding this topic, although they do not believe that data audits are feasible. Also, the PHS is not clear as to what is meant by special reviews by editors of scientific journals. We have suggested this because we believe that journal editors who have access to key scientific papers could perform a random audit of research papers submitted for publication. This has also been suggested by the deputy editor of the Journal of the American Medical Association (JAMA). The purpose of the audit would be to determine whether or not basic information exists such as whether or not records and patients really exist.

As noted by PHS, while it is not appropriate for the Federal Government to specify that journal editors conduct special reviews, we believe that it is proper to encourage them to do so and to support other appropriate proposals to deter scientific misconduct suggested by editors such as archiving data. As stated by the deputy editor of JAMA, journal editors are independent of the research institutions and are interested in assuring the integrity of what they publish. Therefore, an audit supervised by journal editors would be impartial and fair. Such an approach would not require setting up a large bureaucracy.

9. OIG Recommendation

The Department should develop a table of penalties, such as the model adopted by the Office of Personnel Management, to assure that sanctions are applied consistently and fairly in cases of scientific misconduct.

PHS Comments and OIG Response

The PHS concurs with the thrust of this recommendation, but doubts that they can develop a formula or a table. We believe that a table of penalties, which would include acceptable standards of conduct and sanctions that may be imposed for failure to meet those standards is essential in assuring consistency and fairness.

10. OIG Recommendation

The PHS should assume a leadership role and provide guidance to the grantees in matters related to scientific misconduct.

- The PHS should sponsor a consensus conference to develop model guidelines for use by grantees in addressing all relevant areas of scientific misconduct.

- The PHS should continue its efforts in the area of prevention, such as the contract with the Institute of Medicine to develop scientific standards for the conduct of responsible science. The PHS should develop preventive guidelines and require that institutions adopt these measures as a condition of funding.

PHS Comments and OIG Response

The PHS concurs with this recommendation. We encourage PHS to sponsor the conference to develop model guidelines in the near future, since regulations requiring institutions to develop policies and procedures will be effective soon. As PHS stated, such model guidelines would help to assure more consistency in procedures, policy and protections. Additionally, smaller institutions, as noted by PHS and supported by our findings, are looking for additional guidance in this area.

The PHS agrees that it should have a role in supporting education regarding ethical issues of science and should continue its efforts in this area. However it notes that the imposition of such guidelines may not be desirable or enforceable. Recently, the Institute of Medicine issued their report of the study to develop scientific standards for the conduct of responsible science. Similar to our recommendation, the report recommends that the NIH require all institutions receiving NIH grants to have written policies and procedures in place for promoting quality and integrity in research practices.

APPENDIX A

Telephone Survey Methodology

Telephone Survey Methodology

The survey used a stratified random sampling method. A list of all 1986 research grantees was obtained from the NIH. The list included the total number and amount of research awards for each grantee. By eliminating all foreign institutions, the population was limited to 1,214 institutions. This population was then divided into three strata, those with 100 or more awards per institution, those with 10 through 99 awards per institution and those with fewer than 10 awards. The following table summarizes the results of this stratification.

SELECTED INFORMATION ON NIH GRANTEE INSTITUTIONS BY STRATUM

Strata	No. of Instit.	Tot. No. Awards	Total Amounts	Amt. Per Instit.	Amt. Per Award
100+	74	15,243	$2,599,810,599	$35,132,575	$170,558
10-99	186	6,003	890,293,363	4,768,523	148,308
<10	954	1,985	232,690,637	243,911	117,225
	1,214	23,231	$3,722,794,559	$ 3,066,552	$160,251

Systematic random sampling was used to select approximately 30 institutions from each strata. The following table summarizes the results of the sampling process.

SELECTED INFORMATION ON SAMPLED NIH GRANTEE INSTITUTIONS BY STRATUM

Strata	No. of Instit.	Tot. No. Awards	Total Amounts	Amt. Per Instit.	Amt. Per Award
100+	30	7,097	$1,311,966,670	$43,732,222	$184,862
10-99	31	1,005	155,964,189	5,031,103	155,188
<10	30*	66	8,991,209	299,707	136,230
				**	**
	91	8,168	$1,476,922,068	$ 3,695,259	$142,082

* Only 28 of the 30 institutions could be reached by telephone.

** Weighted average based upon weight derived from the population of institutions.

The sample consists of 40 percent of the institutions with 100 or more awards, 16.1 percent of the institutions with 10 through 99 awards, and 3.1 percent of the institutions with 9 or fewer awards. The sample slightly overestimates the average award amounts but is still within sampling variations. Because the survey used a sample, weighted averages and totals were used for projecting to the universe of the institutions. In the following table, the weights are the proportion that each stratum is of the universe of institutions.

Strata	Number in Universe	Number in Sample	Weight
I	74	30	0.061
II	186	31	0.153
III	954	28*	0.786
Total	1,214	89	

* Only 28 of the 30 institutions could be reached by telephone.

APPENDIX B

Areas Incorporated in Procedures/Policies

Areas Incorporated in Procedures/Policies
Telephone Survey Of Grantees

	100+ Awards	10 to 99 Awards	<10 Awards	Weighted Average
Investigations into allegations of misconduct	27 (96%)	16 (100%)	3 (100%)	99%
Time frames for inquiries and investigations	13 (46%)	10 (63%)	0	35%
Do not alert NIH at initiation of investigation	23 (82%)	4 (33%)	1 (33%)	47%
Alerting NIH at anytime	23 (82%)	11 (69%)	3 (100%)	84%
Protection of confidentiality	23 (82%)	16 (100%)	2 (67%)	83%
Due Process and appeals	21 (75%)	14 (88%)	2 (67%)	76%
Retention, storage and ownership of data	7 (25%)	7 (44%)	1 (33%)	35%
Validation of research	9 (32%)	7 (44%)	1 (33%)	37%
Retraction of published articles shown to be fraudulent	14 (50%)	6 (38%)	1 (33%)	39%
Responsibility of coauthorship	11 (39%)	6 (38%)	0	24%

This is based on the number of grantees that reported having policies and procedures in place to deal with scientific misconduct: 28 (93%) with 100+ awards; 16 (52%) with 10 to 99 awards; and 3 (11%) with awards.

APPENDIX C

The Emerging Area of Preventive Measures:
"Fraud In Biomedical Research: A Time For Congressional Restraint,"
and
"Guidelines For Investigators In Scientific Research"

matic. When they are confirmed, such observations will need to be related to recent findings on the role of certain metabolites of procainamide, such as procainamide hydroxylamine[10] and the nitroso derivative, which can bind to histones.[11]

Continuing study of these syndromes should deepen our understanding not only of these clinical syndromes but also of systemic lupus erythematosus. Physicians should be on the lookout for relevant drug and environmental associations and bring them to the attention of those concerned with understanding these syndromes.

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FRAUD IN BIOMEDICAL RESEARCH

A Time for Congressional Restraint

IN April the U.S. Congress held two sets of hearings to investigate the extent of fraud in biomedical research and the response of the scientific community to it. Clearly, some members of Congress believe that there is a good deal of fraud and, more important, that the scientific community's response to it has been inadequate. There have been suggestions that the biomedical-research enterprise requires some sort of policing by the government, since we have seemed unwilling or unable to police ourselves. Legislators have even suggested that a separate oversight agency be established for that purpose and that researchers thought guilty of misconduct be subject to criminal indictment.

What would be the results of an attempt by the federal government to monitor the integrity of the biomedical-research enterprise in this way? First, by its nature such an attempt would almost certainly be clumsy and bureaucratic. Researchers already burdened by having to prepare seemingly endless grant applications and reports would probably acquire still more paper obligations — in this case designed to demonstrate their honesty. Worse, if the hearings themselves are an indication of the government's understanding of the way research is done, the government's attempt might be badly misinformed. The hearings often seemed to equate error with fraud, and the same indignation was shown toward both. Error due to carelessness is culpable, as Engler et al. have pointed out,[1] but honest error is not. The latter is at least as much a part of scientific research as truth. Even with the best effort, no scientist can be certain of not having made an error. Thus, efforts by the government to make biomedical research free not only of fraud but of error as well would create a climate that would almost certainly dissuade young people from becoming biomedical researchers, at a time when our pool of new talent is already dwindling.

Federal oversight might be worth the risks if it could ensure fraud-free science, but it cannot. First, the government does not have a strong record in its oversight efforts; witness the Pentagon's monitoring of defense contractors. Second, misconduct is inevitable in all fields of endeavor. There may be less of it in scientific research than in other fields. The National Institutes of Health (NIH), which support the work of approximately 50,000 scientists, receive a yearly average of only 15 to 20 reports of alleged misconduct in its extramural programs[2]; we have no way of knowing, of course, how many instances of fraud go unsuspected.

Many defenders of the integrity of research have pointed out that science is self-correcting by virtue of its traditions of peer review and openness and its requirement of verifiability. Furthermore, the penalty for fraud is loss of reputation and effective banishment from the scientific community — consequences that few would risk. Nevertheless, we have probably been too complacent in relying on these safeguards; we have seen too many recent instances in which they have failed to prevent or detect egregious dishonesty, and too many dilatory investigations of serious charges.

The research community therefore cannot afford to dismiss the concern that has given rise to the recent hearings. Congress is responding to a widespread view that the research community has not taken the episodes of dishonesty in its midst seriously enough, that we have been "stonewalling" the problem. There is some truth to this charge. When the first highly publicized episodes of fraud emerged in the late 1970s and early 1980s, we were reluctant to give them due attention; we wanted to believe that each was an isolated aberration that would not recur. In addition, research institutions did not have established procedures for

dealing with allegations of fraud, so each episode was handled on an ad hoc basis, often by people so close to the situation that there was an inherent conflict of interest.

Since then, the research community has learned a good deal about dealing with fraud. Soon after the Darsee case in 1981, a number of organizations and institutions, including the NIH and the Association of American Medical Colleges, developed procedures for responding to allegations of fraud. These procedures incorporate due concern for both the accused and the "whistle-blower," and in some cases provide for participation in the investigation by experts outside the institution in question to facilitate objectivity. Early this year the International Committee of Medical Journal Editors issued guidelines for editors to follow in dealing with this problem.[3] With procedures in place, institutions that earlier floundered in handling cases of fraud have more recently resolved them effectively and in an orderly way. However, these later cases have perhaps been resolved too privately. The public's demand for accountability in the spending of tax dollars on biomedical research is, after all, legitimate; the research community must not only police itself, but be seen to do so.

Guidelines issued to date have mainly concerned the *response* to fraud. In March of this year, Harvard Medical School issued a set of guidelines dealing with its *prevention*. These call for closer supervision of research trainees, more careful gathering and storage of primary data, the establishment by departments of explicit and meaningful criteria for authorship of a scientific paper, and a limitation on the number of publications reviewed for faculty appointment or promotion. The introduction to the guidelines emphasizes that they are just that, not rules, hence they are not binding. Herein lies one of their weaknesses. To accomplish the purpose, institutions will have to develop rules, not simply guidelines, and these rules will have to be somewhat more detailed.

One of the reasonably explicit recommendations of the Harvard guidelines is that the number of publications reviewed for faculty appointment or promotion be limited. They suggest, for example, that no more than 5 papers be reviewed for appointment to the position of assistant professor, 7 for associate professor, and 10 for professor. If such a recommendation is widely adopted — by study sections at the NIH as well as by the medical schools — it will be a sharp departure from the present system of relying largely on the size of the bibliography in evaluating candidates for promotion or funding.[4] This reliance produces an intense pressure on investigators to publish as frequently as possible, and almost certainly leads to sloppiness and perhaps to more serious misconduct. It also produces a bias in the system favoring relatively simple studies that can be completed rapidly over longer, difficult ones that may be more important. In essence, we have been giving investigators a contradictory message: on the one hand, they are expected to do good, careful work; on the other, they are to do it in a hurry. Implementing the recommendation of the Harvard guidelines would be an important step toward rectifying this situation. For this proposal to be effective in fostering quality over quantity, publications above the stipulated number should receive no attention. To emphasize substance over number even further, citations of references in proposals for academic appointment and grant applications might be required to include brief summaries of the content of each article, together with explanations of its contribution to the field.

The Harvard guidelines, although they are only a first step, represent an important effort to control the temptation to cut corners in biomedical research. The Institute of Medicine of the National Academy of Sciences, under the sponsorship of the NIH, is also studying ways in which the system could be reformed to discourage misconduct in biomedical research.

Even the most strictly monitored system can never eliminate occasional episodes of fraud, but the research community itself can do much to reduce their incidence and facilitate their detection.[5-9] Government can have its most valuable role here by ensuring that research institutions receiving government support have appropriate programs established for accomplishing these purposes. Congress has already taken an important step in this direction by requiring (P.L. 99-158) that any organization applying for research funding must provide assurances that it has established a process for responding to allegations of fraud and that it will report to the secretary of the Department of Health and Human Services when an investigation is begun.[2] It must be understood, however, that the job itself cannot be done from outside the research community without jeopardizing the freedom that is required for research to flourish.[10] The biomedical-research community is willing and able to police itself and is taking steps to do so more effectively. Let us hope that Congress will give this process time to work.

MARCIA ANGELL, M.D.
ARNOLD S. RELMAN, M.D.

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Guidelines for Investigators in Scientific Research

I. Introduction

These guidelines describe practices generally accepted by members of the Faculty of Medicine and already in effect in their laboratories. The primary intent of codifying them is to bring them to the attention of those beginning their careers in scientific research. These recommendations are not intended as rules, but rather as guidelines from which each group of investigators can formulate its own set of specific procedures to ensure the quality and integrity of its research.

II. Supervision of Research Trainees

Careful supervision of new investigators by their preceptors is in the best interest of the institution, the preceptor, the trainee, and the scientific community. The complexity of scientific methods, the necessity for caution in interpreting possible ambiguous data, and the need for advanced statistical analysis, all require an active role for the preceptor in the guidance of new investigators. This is particularly true in the not uncommon circumstance of a trainee who arrives in a research unit without experience in laboratory science.

Recommendations:

1. The responsibility for supervision of each junior investigator should be specifically assigned to some faculty member in each research unit.
2. The ratio of trainees to preceptors should be small enough that close interaction is possible for scientific interchange as well as oversight of the research at all stages.
3. The preceptor should supervise the design of experiments and the processes of acquiring, recording, examining, interpreting, and storing data. (A preceptor who limits his/her role to the editing of manuscripts does not provide adequate supervision.)
4. Collegial discussions among all preceptors and trainees constituting a research unit should be held regularly both to contribute to the scientific efforts of the members of the group and to provide informal peer review.
5. The preceptor should provide each new investigator (whether student, postdoctoral fellow, or junior faculty) with applicable governmental and institutional requirements for conduct of studies involving healthy volunteers or patients, animals, radioactive or other hazardous substances, and recombinant DNA.

III. Data Gathering, Storage, Retention

A common denominator in most cases of alleged scientific misconduct has been the absence of a complete set of verifiable data. The retention of accurately recorded and retrievable results is of utmost importance for the progress of scientific inquiry. A scientist must have access to his/her original results in order to respond to questions including, but not limited to, those that may arise without any implication of impropriety. Moreover, errors may be mistaken for misconduct when the primary experimental results are unavailable. In addition, when statistical analysis is required in the interpretation of data, it should be used in the design of studies as well as in the evaluation of results.

Recommendations:

1. Custody of all original primary laboratory data must be retained by the unit in which they are generated. An investigator may make copies of the primary data for his/her own use.
2. Original experimental results should be recorded, when possible, in bound books with numbered pages. An index should be maintained to facilitate access to data.
3. Machine print-outs should be affixed to or referenced from the laboratory notebook.
4. Primary data should remain in the laboratory at all times and should be preserved as long as there is any reasonable need to refer to them. The chief of each research unit must decide whether to preserve such primary data for a given number of years or for the life of the unit. In no instance, however, should primary data be destroyed while investigators, colleagues, or readers of published results may raise questions answerable only by reference to such data.

IV. Authorship

A gradual diffusion of responsibility for multi-authored or collaborative studies has led in recent years to the publication of papers for which no single author was prepared to take full responsibility. Two critical safeguards in the publication of accurate, scientific reports are the active participation of each co-author in verifying that part of a manuscript that falls within his/her specialty area and the designation of one author who is responsible for the validity of the entire manuscript.

Recommendations:

1. Criteria for authorship of a manuscript should be determined and announced by each department of research unit. The Committee considers the only reasonable criterion to be that the co-author has made a significant intellectual or practical contribution. The concept of "honorary authorship" is deplorable.
2. The first author should assure the head of each research unit or department chairperson that s/he has reviewed all the primary data on which the report is based and provide a brief description of each co-author. (In multi-institutional collaborations, the senior investigator in each institution should prepare such statements.)
3. Appended to the final draft of the manuscript should be a signed statement from each co-author indicating that s/he has reviewed and approved the manuscript to the extent possible, given individual expertise.

V. Publication Practices

The Committee has observed certain practices that make it difficult for reviewer and reader to follow a complete experimental sequence: the rapid publication of data without adequate tests of reproducibility or assessment of significance, the publication of fragments of a study, and the submission of multiple similar abstracts or manuscripts differing only slightly in content. In such circumstances, if any of the work is questioned, it is difficult to determine whether the research was done inaccurately, the methods were described imperfectly, the statistical analyses were flawed, or inappropriate conclusions were drawn. Investigators should review each proposed manuscript with these principles in mind.

Recommendations:

1. The number of publications to be reviewed at times of faculty appointment or promotion should be limited in order to encourage and reward bibliographies containing fewer but more substantive publications rather than those including many insubstantial, fragmented reports. (It has been suggested, for example, that no more than five papers be reviewed for appointment as Assistant Professor, no more than seven for Associate Professor, and no more than 10 for Professor.)
2. Simultaneous submission of multiple similar abstracts or manuscripts to journals is improper.

VI. Laboratory Guidelines

Because each research unit addresses different scientific problems with different methods, each unit should develop its own specific guidelines to identify practices that seem most likely to enhance the quality of research conducted by its members. These guidelines should be provided to the new investigator upon starting work

APPENDIX D

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APPENDIX E

AGENCY COMMENTS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date JAN 30 1989

From Assistant Secretary for Health

Subject PHS Comments on OIG Draft Report "Misconduct in Scientific Research," OAI-88-07-00420

To Inspector General, OS

Attached are the PHS comments on the subject OIG draft program inspection report.

Robert E. Windom, M.D.

Attachment

COMMENTS OF THE PUBLIC HEALTH SERVICE ON THE OFFICE OF INSPECTOR GENERAL DRAFT REPORT "MISCONDUCT IN SCIENTIFIC RESEARCH" OAI-88-07-00420, SEPTEMBER 1988

General Comments

In its report, the OIG attempts to determine (1) the extent to which the National Institutes of Health (NIH) and its grantee institutions have developed and implemented policies and procedures to prevent, detect, and handle scientific misconduct cases; and (2) what selected grantee institutions have learned and implemented as a result of their investigations of alleged scientific misconduct. In general, the Public Health Service (PHS) views this draft report as a useful discussion of some important issues related to allegations of misconduct in PHS extramural programs. We believe, however, that many of the recommendations merit further careful analysis and discussion because of their potential impact on the relationship between the university community and the Federal Government. The need for open communication cannot be overemphasized, especially in this sensitive and highly visible area. This is especially true for the recommendation to establish an independent oversight body for scientific misconduct investigations. While the feasibility of establishing such an office has not been established, it is imperative that such an office not be divorced from the scientific community, as the expertise and experience of scientists are vital to the development of responsive and responsible policies and procedures in the area of scientific misconduct.

The implications of the study's findings have not been fully assessed in the text of the report. In developing its final recommendations, OIG should compare the ramifications of strengthening the current NIH program, versus those of diminishing NIH's responsibilities and establishing a central locus elsewhere in the Department. The current draft does not examine the various strategies that might be adopted to strengthen the overall role of the Department in dealing with scientific misconduct issues. Such an in-depth analysis would make recommendations emerge more clearly.

In the area of "findings," some of the statements are not actually factual findings but are judgmental interpretations that have reference to an unstated standard. We question whether these statements add anything meaningful to the report. We also note that some of the recommendations have been overtaken by events; for example, the Notice of Proposed Rulemaking on grantee responsibilities and the Advance Notice of Proposed Rulemaking were published on September 19. This recommendation should be revised accordingly.

Some aspects of the methodology were not explicit. For example, we do have some concerns about the validity of the telephone survey methodology. The report does not provide any information regarding positions and titles of those who participated in the 89 telephone interviews. This is particularly important since it appears that some of the respondents approached the survey as individuals rather than as representatives of their institution. Neither the background of the interviewers was described nor what the interview schedule was. In addition, the gamut of experience of the respondent could very well influence the nature of individual responses. Was there more than one respondent from each institution? Which institutions had more than one allegation or case from which to draw? The reliability of the statistics provided in the OIG study depend on the consistency between interviews.

Additionally, the information gleaned from the telephone surveys and the site visits is not clearly distinguished. Since one of the two main objectives of the OIG study was to determine what selected grantee institutions have learned from their investigations of alleged misconduct and whether their experiences have caused them to modify their institutional guidelines, it might be useful to present information obtained from the nine site visits in a separate section and clearly identify it as such. Furthermore, it would be easier for the reader to distinguish data obtained from the nine site visits from that gathered in the 89 phone interviews if each finding that is currently prefaced with "some grantees" or "a number of grantees" or "a few grantees" is substituted with statistics (e.g., 4/9, 3/30, etc.).

We are also concerned about the emphasis on numbers of grantees not having procedures, particularly in view of the sampling nature of the survey and the absence at that time of specific regulatory requirements. PHS shares OIG's concern that the 1986 guidelines are not being implemented by a majority of the institutions receiving NIH grants. However, the key finding that 93 percent of NIH grantee institutions holding 100 or more awards do have such policies and procedures should not be underemphasized. The survey results tend to support our experience that the research-intensive institutions are increasingly well prepared to deal with allegations of misconduct.

It appears that the authors of the report may have misinterpreted some of the information provided about NIH procedures. The variability cited in the handling of cases does not necessarily result in inconsistencies; rather, it represents an effort to fine-tune procedures based on accumulated experience and individual circumstances.

OIG Recommendation

The Secretary should provide for independent oversight and develop a more formalized and centralized process to deal with scientific misconduct including the following elements: (1) an independent third party to act as a fact gatherer and collect, retain and analyze investigative data; (2) an independent scientific review board to assist in analyzing information concerning scientific misconduct; and (3) an independent decision making authority or ombudsman type function. This is especially important given the congressional concern regarding the lack of independence of investigative units.

PHS Comment

We agree that greater central management is needed to deal with scientific misconduct. PHS has developed a reorganization proposal which would make changes both at NIH and in the Office of the Assistant Secretary for Health. This has been presented to the Under Secretary but not yet approved.

At NIH we would establish a new Office of Scientific Integrity reporting to the Director of NIH. This office would have operational responsibility for conducting independent investigations when needed and monitoring investigations undertaken by awardee institutions. Its scope would include the Alcohol, Drug Abuse, and Mental Health Administration's (ADAMHA) extramural research activities as well as NIH's. On the positive side, the office would foster

scientific integrity by developing prevention and education programs to be conducted by the extramural research offices throughout NIH and ADAMHA. The office would also develop and propose policies and procedures for approval by the Assistant Secretary for Health (ASH). The office would have an initial staffing of six full-time employees.

At the ASH level, an office would be established to oversee operations of the research agencies and review policy proposals from NIH before they are submitted to ASH for approval. In addition, the office could independently propose policies for ASH approval. Finally this office would adjudicate cases investigated by NIH or ADAMHA and impose sanctions if warranted. This would assure appropriate independence of the adjudicative process. The staffing level for this office has not been determined. We are also considering the establishment of an outside advisory group to review and evaluate PHS policy and procedures governing scientific integrity.

OIG Recommendation

The Department should expedite completion and publication of a regulation addressing scientific misconduct, as required by law. This will facilitate the development of procedures by grantees. However, the Department's reliance on the PHS interim guidelines in developing regulations may be unwarranted in light of the current concerns about scientific misconduct.

PHS Comment

We concur that the publication of a proposed rule was urgently needed and long overdue. The interim guidelines, which were published in 1986, were to be in effect only until policies could be put into place. This occurred recently, on September 1, 1988, with the publication of two Grants Administration Manual Issuances. Hence, fully binding policies now are in effect and communicated via the Notice of Grant Award. We are optimistic that a firm regulatory base will encourage and guide grantees in their efforts to deal with allegations of misconduct. Moreover, the comment about the Department's reliance on PHS's interim guidelines is inaccurate in view of the pending Advance Notice of Proposed Rulemaking's invitation for comment on a broad range of policy and procedural options. These comments were due by December 19, and final rules regarding procedures should occur soon after that.

OIG Recommendation

The Department should require grantees to attach scientific misconduct procedures to the grant application to assure compliance with the law. The PHS should review the procedures on a sample basis and also in all instances where scientific misconduct cases are reported to assure that essential areas are covered.

PHS Comment

We concur that grantee institutions should be required to submit copies of their misconduct procedures. However, we recommend that this be modified to request submissions from all applicant institutions to the funding agencies on

a yearly basis. It is not realistic to request that this information be sent with each application: it would be at odds with the Paperwork Reduction Act and would generate duplication of effort at grantee institutions since it is often the case that more than one application is submitted by the same grantee institution. In addition, attachment of this information to each application would unnecessarily complicate application processing and expenses at the NIH Division of Research Grants, which annually receives approximately 35,000 applications.

OIG Recommendation

The first line of responsibility for conducting an inquiry and/or investigation into an allegation of misconduct rests with the grantee. However, regulations issued by the Department should require that grantees immediately notify the Department whenever they detect or receive an allegation of scientific misconduct, maintain records of all inquiries and investigations and provide the Department with periodic status reports. The regulations should specify time frames for reporting and conducting inquiries and investigations. Although we recognize the grantees are concerned about flexibility, these requirements are nevertheless necessary to assure adequate monitoring and oversight by the Department.

PHS Comment

We concur that all allegations should be reported to the Department if they are found by the institution to warrant a formal investigation. However, the Summary Recommendation statement that ". . . regulations issued by the Department should require that grantees immediately notify the Department whenever they detect or receive an allegation of scientific misconduct . . ." appears to be too broad to be practical. The institutions are likely to object strongly to such a requirement prior to their having any evidence of substance to the allegation. Furthermore, a requirement for such early reporting probably would not be feasible from the point of view of the Federal Government, as it would probably lead to Federal involvement prematurely in local disputes or personal conflicts.

We also agree that time frames for reporting and for conducting inquiries and investigations are needed. The issue of timing is dealt with in the Notice of Proposed Rulemaking. It is important to emphasize the need for flexibility in timing, because the nature and complexity of investigations sometimes necessitate a longer investigational period. Grantees should, however, provide regular status reports to the funding agency if an inquiry or an investigation takes longer than the specified period.

Certainly, individuals should have easy access to the PHS personnel responsible for dealing with misconduct issues. In addition, institutions should report immediately any allegations of scientific misconduct that could have potentially particularly serious ramifications, such as the health or well being of human or animal subjects.

In any case, we question whether the early reporting requirement as set forth in this recommendation is consonant with the legislative history of P.L. 99-158.

OIG Recommendation

The Department should keep complete and uniform records concerning investigations undertaken by the grantees and PHS in order to maintain baseline data on the incidence of cases. This information could also be used in refining guidance and direction to grantees in conducting future investigations.

PHS Comment

We concur that complete and uniform records are highly desirable for the reasons outlined in the OIG's report and as a basic safeguard for equitable handling of investigations. In addition to the PHS-wide ALERT system for tracking individuals who are either ineligible to receive PHS funds or for whom funding decisions are subject to special review, both NIH and ADAMHA have established data bases that are designed both to track open cases and to archive key information about cases that already have been closed. The tracking system for open cases includes time schedules for processing as well as the status of individual cases under investigation. The trend in developing procedures and records has been toward increased standardization and completeness of information collected. We welcome OIG's advice on improvements in this area.

OIG Recommendation

The Department should encourage individuals with information about instances of possible scientific misconduct to come forward. Grantees should be informed of the OIG Hotline, which receives allegations concerning fraud and abuse in the Department's programs.

PHS Comment

We concur with the recommendation to encourage individuals to come forward with allegations of misconduct; this already is being done. The funding agency should be notified regarding possible misuse of funds, and the OIG should be notified in the case of possible criminal violation. For the last 5 years, notices of a grant award include information about the OIG Hotline; however, this information does not necessarily reach all individuals associated with a research project. We agree that more needs to be done to educate researchers, students, and administrators in this regard. We will publish notices regarding the reporting of misconduct on at least an annual basis in the NIH Guide for Grants and Contracts, which reaches over 30,000 recipients.

OIG Recommendation

The Department should explore ways to protect the "whistleblower," since detection of possible scientific misconduct relies so heavily on individuals willing to make an allegation. Currently Federal employees who engage in "whistleblowing" are protected by law. Similar protection should be provided to individuals reporting possible scientific misconduct by grantees.

PHS Comment

We concur that improved protection for "whistleblowers" is essential to the integrity of the process. PHS is aware of the need to protect the "whistleblower." Some protection currently is provided to "whistleblowers," by the acceptance of anonymous allegations. PHS currently is in the process of examining additional means of providing proper protection. This is occurring by communication with the research community, including direct discussions with "whistleblowers." An important aspect of this effort is the need to encourage and maintain responsibility in whistleblowing efforts and to discourage the use of the misconduct reporting system for the resolution of personal or professional disputes. Appropriate protection for the "whistleblower" will require legislation.

OIG Recommendation

The Department should explore alternative methods of detecting possible misconduct. Examples of possible methods are spot audits of ~~scien~~tific data or special reviews by editors of scientific journals.

PHS Comment

We concur in principle regarding this complex topic. We would support exploration of reasonable methods to detect misconduct. Indeed, existing trials of investigational drugs and other interventions already have audit procedures built into their design, and several instances of misconduct have been detected in this way. However, we are skeptical about the utility of large-scale audits, given the difficulty of interpreting large volumes of original data. Recommendations such as this, which would dramatically affect the relationship between the university community and the Federal Government, should receive further public comment and discussion. While we do not believe such data audits are feasible, any serious consideration to perform such audits should not occur without input from the grantee community.

In addition, it is not clear what is intended by "special reviews by editors of scientific journals." It is unlikely that editors would be willing to serve as agents of the Department. There is, however, considerable evidence that journal editors are aware that greater vigilance is needed. Scientific misconduct was the topic of a recent meeting sponsored by the Editorial Policy Committee of the Council of Biology Editors, Inc. While it would not be appropriate for the Federal Government to specify that journal editors conduct special reviews, the Federal Government should work with the editors to encourage their reviewers to become more vigilant and involved in reviewing manuscripts for discrepancies.

OIG Recommendation

The Department should develop a table of penalties, such as the model adopted by the Office of Personnel Management, ~~to~~ assure that sanctions are applied consistently and fairly in cases of scientific misconduct.

PHS Comment

We concur with the thrust of this recommendation. The PHS interim policies as developed and implemented are intended to provide a balance between consistency and the need for flexibility. While we doubt that these considerations can be reduced to a formula or table, the continued accretion of experience will no doubt improve the process. At this stage, we have grouped the sanctions into levels of severity, and further experience may permit us to develop an appropriate model.

OIG Recommendation

The PHS should assume a leadership role and provide guidance to the grantees in matters related to scientific misconduct.

-- The PHS should sponsor a consensus conference to develop model guidelines for use by grantees in addressing all relevant areas of scientific misconduct.

-- The PHS should continue its efforts in the area of prevention, such as the contract with the Institute of Medicine to develop scientific standards for the conduct of responsible science. The PHS should develop model preventive guidelines and require that institutions adopt these measures as a condition of funding.

PHS Comment

We concur. PHS has exercised a leadership role in this area and will continue to do so. It is worth noting that the grantee community has welcomed and sought leadership from PHS, as indicated by invitations to present at national association and professional society meetings, extensive formal and informal consultation, and inquiries about the status of regulations. With regard to the specific recommendations:

-- We believe that both PHS and the private sector have provided ample opportunity for public discussion of model guidelines. Clearly, there are areas in which consensus has not been achieved, e.g., the timing and threshold for reporting allegations of misconduct and the proper balance between due process and expeditious resolution of cases. In addition, the process initiated with the publication of the Advance Notice of Proposed Rulemaking continues the opportunity for full discussion of these issues. On the other hand, viewed in historical perspective, there is an impressive degree of consensus about institutional responsibilities.

We support the recommendation for sponsorship of a conference at the appropriate time. This would be particularly helpful to smaller institutions, which would appear to welcome additional guidance in this area. Such model guidelines would help to ensure more consistency in procedures, policy, and protections.

-- The PHS believes that it should have a role in supporting education regarding ethical issues of science and should continue its efforts in this regard, in cooperation with the private sector, in identifying and promoting the responsible conduct of research. The PHS will continue its discussions with outside groups who are experienced in dealing with effective educational procedures. It is unlikely, however, that preventive guidelines could adequately cover every situation. Nor is it clear that the imposition of guidelines is desirable or enforceable.

It should be noted that the Department permits considerable variations in financial accountability procedures, provided the procedures allow for sound management and audit trails in grant transactions. Given the complex nature of scientific accountability, it seems reasonable to allow comparable flexibility in that area, provided basic fiduciary obligations are met.

It is important to recognize that discussions already are ongoing under a variety of sponsorships (e.g., American Association of Universities, American Association for the Advancement of Science, Institute of Medicine) and in response to our own Advance Notice of Proposed Rulemaking and Notice of Proposed Rulemaking announcements that were published recently. A "framework" document to provide guidelines for institutions is being developed, which involves input from a large number of different agencies. The National Conference of Lawyers and Scientists is continuing a dialogue on this proposed framework. All these mechanisms provide effective interactions between Federal and non-Federal personnel. One goal of this interaction is the development of model preventive guidelines and appropriate procedures for dealing with misconduct.

Technical Comments

Page 1, Purpose

It should be stated in the report that at the time of the study grantees were not yet required by regulation to have procedures in place but, nevertheless, the Office of Inspector General wanted to determine to what extent such procedures have been developed.

Page 1

While we recognize that this report focuses on NIH, many of the requirements also apply to other agencies of PHS. We believe it would be more accurate to add a statement to this effect at the beginning of the report.

Page 1, The Problem of Scientific Misconduct

In the last paragraph, the report refers to ". . . the increasing number of reported scientific misconduct cases during the 1980's. . . ." We have no evidence of such an increase. Furthermore, the report should be clarified to state that these represent a minuscule fraction of investigators supported by NIH.

Page 2, Federal Involvement In Scientific Research

Paragraph 2 should be revised to reflect (1) that issues of research integrity and quality control are addressed during the grant approval and management process, e.g., in clinical trials, plans for quality control and monitoring are considered during review and post award, and (2) PHS agencies become involved if allegations are reported directly to the agency and during monitoring of the status of inquiries and investigations before a finding of misconduct is confirmed. The statement in this paragraph regarding sanctions or formal corrective actions should be clarified to state whether this refers only to actions by the Secretary or also to actions by the agencies.

Page 2, Paragraph 2, Third Sentence

The sentence states that "Grant applications undergo an internal scientific review. . . ." Grant applications undergo an external review by peers of that scientist who have been determined not to have a conflict of interest with the principal investigator or grantee institution. In addition to an assessment of the scientific merit and technical qualities of the research proposal, the reviewers consider the background, training, and track record of the investigator(s). In addition to the peer review and subsequent review by the institute advisory council, the application receives review by NIH grants management and scientific program personnel to determine whether appropriate consideration has been given with respect to human and animal subjects as well as fiscal considerations and overlap with other research support. NIH programmatic personnel, who are trained scientists, and grants management specialists review all noncompeting renewal as well as competing applications. The programmatic personnel apply their own scientific background and experience toward making the best funding decisions with respect to the science. They also monitor scientific progress, read the scientific literature, attend scientific meetings when funds permit, and generally are alert to detect misconduct or other irregularities.

While it is true that NIH normally gets involved in an allegation of misconduct only after the completion of the initial inquiry or after receipt of communication from the "whistleblower," NIH will continue to monitor cases at an earlier stage when circumstances require it, for example if NIH learns that a grantee institution is less than fully prepared to deal with an allegation of research misconduct.

Page 2, Federal Action on the Problem of Scientific Conduct

The report states that NIH has been perceived as having moved slowly in handling allegations and in functioning on an ad hoc basis. Yet, both NIH personnel and the institutions agree that individual cases differ considerably, and their experience so far has occurred within a relatively limited number of cases. Moreover, in order to provide at least the elements of due process, such as review and rebuttal of findings from all parties to an investigation, the PHS agencies have emphasized accuracy and fairness in handling allegations. Certainly, it is important to examine what patterns can be learned from

individual cases, what procedures work best, and what sanctions should be applied. However, it is difficult, and probably inappropriate, at this stage to try to constrain a diverse group of cases into a constricted or limited approach.

Indirect costs are narrowly defined and might or might not be of direct assistance in monitoring and investigating cases of alleged research misconduct.

Page 3, Paragraph 4

Since NIH does not always conduct its investigations by appointing a panel of scientific peers, we suggest that the first sentence be changed to read "The NIH usually conducts its investigations. . . ."

Pages 3 and 4

The following paragraph, which refers to the Institute of Medicine study, was omitted from the final draft.

> "Since the passage of this legislation, the Department has: issued "The Policies and Procedures for Dealing with Possible Misconduct in Science" (discussed above); established the "PHS Committee on Misconduct in Science" to exchange information about investigations and discuss relevant policy proposals; been developing the regulations called for in the bill; been developing criteria/guidelines on appropriate debarment periods for misconduct in science; and contracted with the Institute of Medicine to identify ways for NIH to encourage the scientific community to engage in reasonable and responsible conduct focusing on preventive measures."

This paragraph describes actions that the Department has implemented since passage of the Health Research Extension Act. We believe it should be included in this report to provide an accurate picture of current Federal efforts.

Page 4, Last Paragraph

There are clear indications in this report that the situation reported by Penelope J. Greene, et al, in "Policies for Responding to Allegations of Fraud in Research," Harvard University, Division of Health Policy Research and Education, is vastly different today, and there is general agreement that much has changed.

Page 6, Bullet 1

At the time of the OIG interviews, there were two full-time professionals assigned to the office which deals with misconduct. This is in addition to the Director of the Office of Extramural Research, who serves as the PHS Misconduct Policy Officer. To provide the reader with the current status of NIH staffing in the misconduct area, we recommend that you indicate the assignment of additional professional staff to the misconduct area. Since the time of the OIG interviews, two professionals have been added to the NIH office that

handles allegations of misconduct in science, the Institutional Liaison Office. This increases the core staff of that office to five full-time equivalent positions, including the following: Chief, Institutional Liaison Office; Health Scientist Administrator; Examiner; Program Analyst; and secretary. The main responsibility of the Chief and the entire responsibility of the Health Scientist Administrator and of the Examiner are with scientific misconduct investigations, while the responsibilities of the Program Analyst and of the secretary are divided between misconduct investigations and publication of the NIH Guide for Grants and Contracts.

Page 8, Paragraph 2

This paragraph should acknowledge that investigations of misconduct are handled on an individual basis, as the circumstances of each case vary. However, to the extent that similar allegations or problems have been dealt with, NIH does use past experience in guiding future actions. PHS guidelines (NIH Guide to Grants and Contracts, July 1986) provide specific guidance as to what steps staff are to undertake when allegations are received.

Page 9, Absence of Procedures

Since the estimates in the report are based on a sample survey and derived weighted estimates, this should be made explicit in the report. Since the number of grantee institutions contacted is relatively small, it would be useful to provide the numbers which correspond to the stated percentages, thereby giving the reader a better sense of the context of the estimates.