

## To All Members of the University Research Community

In the past several years, and at a pace which is accelerating, the conduct of research at American universities has been subject to increased scrutiny, evaluation, and regulation by public agencies. This attention has already led to substantial changes in the way research is conducted at Penn, and, in all likelihood, will lead to further changes in the next several years. In reflecting on this situation during this past summer, I became convinced that it was important to inform the research community at Penn of both recent and impending changes in research policies. Most of these are in response to specific agency mandate, although some are generated in response to more general trends. The articles that follow summarize these changes, as viewed by those offices of the University that have the major responsibilities for insuring that research at Penn is carried out in accord with pertinent governmental regulations and guidelines. An open meeting to discuss issues raised in these articles will be held in the Dunlop Auditorium, Stemmler Hall, on Monday, October 19, 1992 from 10 a.m. until noon.

*Barry S. Cooperman, Vice Provost for Research*

## New Issues in the Conduct of Research: Increased Scrutiny by Funding and Regulatory Agencies

Imagine you are a scientist in the Medical School, and are offered a position on the Scientific Advisory Board of a small biotechnology company, and, perhaps, given some shares of stock as partial compensation for your time. If the company later makes use of your research work in a commercial endeavor, and you have failed to disclose the relationship to the University, you may be in violation of the proposed new National Science Foundation (NSF) guidelines for conflict of interest disclosure. This might have a serious negative impact not only on your research program, but on the University's as well.

Or perhaps you are an investigator at the Veterinary School injecting a saline solution in uninfected horses. You walk back to your office and realize you are still carrying a syringe, so you drop it in the trash. At a transfer station, a site where University trash is taken for consolidation prior to disposal, an employee steps on the trash bag containing the syringe and needle, and the needle punctures the side of his foot. The operator of the transfer station contacts the Pennsylvania Department of Environmental Resources (DER), which determines, based on written material in the trash, that it came from your office. DER could assess a civil penalty against the University, your lab, and you personally. Moreover, the Office of the Attorney General's Environmental Crimes Division might seek criminal sanction. The transfer station employee could sue the University and you. All of these consequences could result, notwithstanding that the procedural error involved non-infectious horse blood.

These are merely two examples of how failure to follow the growing body of regulatory requirements could interfere with or even bring to a halt a flourishing research program. The open meeting on October 19 will provide information on recent changes in policies and procedures which may have an impact on the costs and conduct of research programs.

This special *Almanac* insert presents an overview of the many new issues affecting the conduct of research, including new regulations and oversight policies with which research investigators must now comply. The University offices at right are responsible for various aspects of assisting research investigators with compliance and providing the institutional oversight mandated by government agencies.

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106 College Hall/6381  
898-7236

Office of Research Administration  
300 Mellon Building/3246  
898-7293

Office of the General Counsel  
110 College Hall/6303  
898-7660

Center for Technology Transfer  
Suite 300, 3700 Market/3147  
898-9585

Office of Environmental Health and Safety  
1408 Blockley Hall/6021  
898-4453

Office of Radiation Safety  
1412 Blockley Hall/6021  
898-7187

Office of University Laboratory Animal Resources  
100 Blockley Hall/ 6021  
898-6466

Regulatory Affairs Section of Research Administration  
300 Mellon Building/3246  
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## New Issues in the Conduct of Research: Increased Scrutiny by Funding and Regulatory Agencies

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### Indirect Costs

A recent article in *Science*, "Cracks in the Ivory Tower," a discussion of the many pressures on our research universities, stated: "The number one topic on the agenda is money." The article went on to discuss the budget problems of higher education including the reality that federally-funded university research, for years protected from the budget wars in Washington, is facing little or no growth in the coming year. In FY92, the University received a total of \$247,264,046 in sponsored research/training annualized awards, with the distribution by sources indicated in the chart below.

Current prospects are that NSF's budget will be flat, while the National Institutes of Health (NIH) will receive less than a 2% increase, at a time when inflation is running above 3%. At the same time, the Office of Management and Budget (OMB), working with the White House Office of Science and Technology Policy (OSTP), is preparing further revisions to OMB Circular A-21 which may profoundly alter the way in which the government reimburses universities for the costs of research, both direct and indirect. And to complicate matters further, federal agencies are being pressured by Congress to demonstrate better accountability for the way in which research funds are allocated and expended, resulting in more contentious negotiations over award amounts, arbitrary reductions in awards and increased audit activity. The impact of these events is being felt at Penn in a variety of ways.

In 1991, Penn was one of 13 universities to be audited by the federal Department of Health and Human Services (DHHS) as a result of Congressman Dingle's investigation of indirect cost improprieties at Stanford. The audit was focused on central administration costs included in our indirect cost rate. Costs of alumni relations activities had inadvertently been included in our indirect cost proposal, resulting in a disallowance of less

than \$200,000 for the year in question. The government applied this to a five-year period resulting in reimbursement of \$930,642 from the over \$250,000,000 received in indirect costs during the same period.

Subsequent to the settlement of the indirect cost audit, Penn was successful in negotiating new indirect cost rates with DHHS for three years. Although changes to OMB Circular A-21 (see below) capped administrative cost components of the indirect cost rate, the University negotiated rates of 62.5% for FY93 & 94, and 63.5% for FY95. These rates will allow the University to adequately maintain its research infrastructure for the next three years.

In October 1991, OMB Circular A-21 was revised to include a limitation on the amount of administrative costs which could be included in the indirect cost rate. Fortunately for the University, its most recent indirect cost calculation for administrative costs was under the 26% ceiling. The revised circular also disallows several types of expenditures as charges to federal funds, including housing for university officers, certain dues, alcohol, entertainment, etc. The impact of these changes on the University should be negligible.

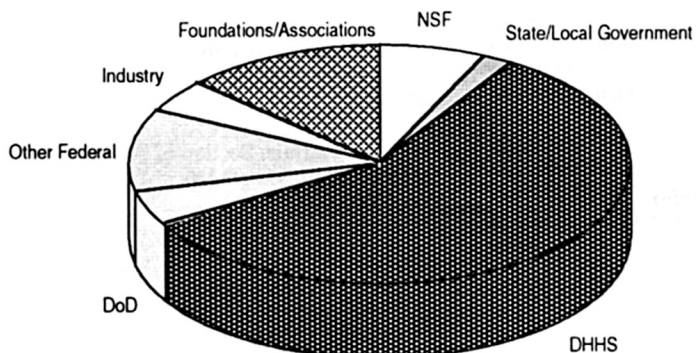
An OMB/OSTP Task Force has been working on further revisions to OMB Circular A-21. It is anticipated they will publish a revision for comment this month. Among the issues which may be addressed are: (a) reviewing the manner of charging graduate research assistant tuition; (b) achieving consistency in how different Federal Agencies interpret OMB Circular A-21; (c) charging different rates for administrative costs and facilities costs; (d) imposing rate limitations, thresholds and fixed allowances; and (e) achieving more systematic and consistent determinations of library costs.

As these federal audits have been occurring, other groups have been considering the ever contentious indirect cost issue. A joint study by the Association of American Universities and the Council on Governmental Relations, in which Penn participated, attempted to identify the total costs of research and who paid them. Some observations from the study include:

1. Indirect costs are not easily understood because those costs are recorded differently from university to university.
2. Comparisons based on rates do not reflect accurately differences in costs.
3. Universities share significantly in the costs of research.
4. Universities bear the major share of their indirect costs and, therefore, have a significant incentive to control or reduce those costs.
5. Supporting costs of research are identified in more than forty areas. These costs are neither frivolous, nor optional. Changes to the indirect cost system should not be made by denying the existence of these costs.

The impact of any changes in OMB Circular A-21 to Penn are of course unknown, but it is unlikely they

**Sponsored Research/Training  
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Sources of Funding**



would provide for any increase in indirect cost recovery, although there is the possibility for administrative savings through simpler requirements. Any reductions in our ability to recover the legitimate costs of sponsored research will only further exacerbate our already precarious budgetary situation.

Increased audit activity of individual awards has resulted in closer scrutiny of how federal funds are expended. A recent audit by NSF, triggered by a Congressional inquiry, raised questions about how universities

charge graduate student tuition to grants, publication costs, pre-award costs, administrative costs charged directly and the allocation of telephone costs. University administrators were also questioned about personnel activity report systems, service centers, prior approval systems for budgetary revisions, and travel policies. The findings of this audit are not final, but it is representative of the greater degree of accountability to which all universities are being held.

## Conflict of Interest

The rapid growth of university research and its commercial application has increased the concerns of funding agencies about potential conflicts of interest. This was highlighted in a recent U.S. General Accounting Office report, *Controlling Inappropriate Access to Federally Funded Research Results*, which opened with the following statement: "The importance of university research to technological innovation increased dramatically during the 1980's, creating new linkages among the academic community, industry, and the federal government. Universities expanded programs to collaborate with businesses and transfer technologies that can benefit the U.S. economy. In fiscal year 1990, businesses spent \$1.1 billion, while the federal government spent \$9.6 billion, in sponsoring research at universities. However, closer ties between universities and businesses raise concern about possible conflicts of interest or other relationships that might give a business inappropriate access to, and therefore an unfair advantage in commercializing, the results of federally funded research." The report recommends that the Secretary of Health and Human Services and the Director of NSF require that their grantees have procedures in place to effectively manage potential conflicts of interest. Such procedures should, at a minimum, require disclosure of specified types of outside interests to appropriate university representatives by: (a) investigators and other key personnel as part of the grant award process and annually thereafter for the duration of the grant; and (b) technology licensing personnel and others involved in making licensing decisions for technologies developed in whole or in part with NIH or NSF funding. Additional recommendations are that NIH and NSF review their funding recipients' policies and procedures to ensure that they adequately address conflicts of interest issues, and that NIH and NSF develop policies that address the extent to which U.S. and foreign industrial liaison program members can be given advance access to research the agencies have funded.

In response to pressures from Congress, NSF published in the *Federal Register* (July 16, 1992, 31540-31541) proposed changes to award conditions and proposal contents which would require limited and targeted disclosure of investigator financial interests, and resolution of any conflicts of interest revealed. While NSF does not believe that conflicts of interest are frequent in the work it funds, it does not have any data by which to prove the point. The new guidelines would help develop such data. In addition the guidelines would require that grantee institutions maintain "an appropriate written and enforced policy on conflicts of interest."

## Changes at NIH

Recent changes at NIH have led to both explicit and implicit changes which may have an impact upon the preparation of research proposals. Overall, there has been an increased awareness of the importance of applied research. Although the importance of basic research is still emphasized, there is an increased interest in facilitating the application of fundamental research to human disease. One effort is to stimulate the interaction of scientists in basic science departments with those in clinical departments. Other mechanisms are under consideration to further emphasize the importance of applied research to the NIH mission. This concept was emphasized in the recently formulated NIH Strategic Plan.

The supervision of NIH funding has increased. Additional restrictions have been placed on human studies and on animal studies. Supervision is carried out at the university level by more rigorous review and supervision. Amendments to the Animal Welfare Act have changed the requirements for animal housing and research. Additional restrictions regarding the use and disposal of radioactive materials have increased. These new regulations are discussed later in this article.

The NIH grant application has been revised to 25 pages of scientific description as opposed to the previous 20 pages. One goal of this extended application is to eliminate the Appendix section and to provide a mechanism

Among other requirements, institutional conflict of interest policies would have to provide for: (a) financial disclosures by faculty and professional staff involved in NSF funded work of any business in which the individual is a principal, relevant consulting arrangements, significant financial ties of the faculty member or his/her immediate family or close business associates with firms which might be affected by the results of the project; (b) designation by the institution of persons to review disclosures and resolve actual or potential problems; (c) establishment of enforcement mechanisms; and (d) arrangements for informing sponsors of problems and their resolution.

Each NSF proposal would require indication that investigators have disclosed any significant financial ties with parties whose financial interests could be directly and significantly affected by the work to be funded. Of particular concern are: (a) any significant financial ties with a company engaged in producing or marketing a product that the researcher is evaluating or developing; (b) work of relevance to an entrepreneurial venture in which the investigator has significant financial ties; and (c) overlap with work the investigator does as a consultant. Although information provided to NSF *will not* be used in merit review, it would be considered in determining whether an award should be made. This would be accomplished by submitting information on any potential conflicts and their proposed resolution in a separate, sealed attachment to a proposal to be opened only after completion of merit review and recommendation for award.

The Public Health Service, parent of the NIH, has not published its revised policy, but it is likely to require establishment of an institutional committee to "solicit, review and annually update financial disclosure statements from each investigator who is participating or is planning to participate in PHS-funded research." Complex record systems would have to be maintained on an award-by-award basis, and procedures established for resolving any allegations of undisclosed or misrepresented financial interests including appropriate sanctions. Among the financial interests to be disclosed are stock and other holdings, consulting income, and other commercial or employment relationships. Failure to comply could result in suspension or termination of an award, debarment of an institution or an investigator or, for submission of false information, criminal prosecution.

for increasing tables and figures within the body of the application. The intent is not to increase the length of the document. The new NIH grant format requires considerably more detail in two areas: sources of funding and collaborators/consultants. Ongoing grants need to be discussed in more detail and potential overlap of funding carefully delineated. A more specific description of the role of each collaborator and consultant is now required. This may include, for example, the specific experiments to be performed or the specific reagents to be provided by the consultant. A two-page biographical sketch of each consultant or collaborator involved in the research grant is required.

It is likely that the NIH will take an increasing role in the oversight of biomedical research. This may involve more extensive interaction of each investigator with NIH officials or with the establishment of university oversight programs. In addition, NIH will continue to initiate programs to stimulate research in areas which are felt to be of high priority. For example, current areas of focus continue to include women's health issues, especially breast cancer research, aging and cancer biology.

report continues next page

# Revision of the University Patent Policy

The current version of the University Patent Policy was first approved by the Trustees in January, 1966. (The complete text of the Patent Policy begins on page 32 of the 1990 *Research Investigator's Handbook*). The procedures for implementing the policy were last revised in April, 1981. From then until now there have been significant changes in the ways that universities relate to commercial concerns. Moreover, case law, numerous changes in United States Patent Law, as well as a series of public laws governing the rights and responsibilities of universities with respect to inventions made with federal sponsorship have had a profound impact on the enterprise of university technology transfer. To address these changes, the Office of the Provost, the Office of the Executive Vice President and the Center for Technology Transfer have proposed significant revisions to the Patent Policy. Among the changes, the proposed revised policy would alter the formula for sharing royalty income and the provisions for handling equity in companies received in lieu of license fees.

The following text is based on the contents of the draft revised policy which is currently scheduled for review by several committees, including the Provost's Council on Research and Academic Planning and Budget. This draft will also be submitted to the Faculty Senate.

### The Revised Policy

The draft revised policy affirms University ownership of all inventions resulting from work carried out in the course of employment at the University, or from work carried out on University time or at University expense, or with University resources. There are, however, several major changes from our current policy. During the last 25 years, the responsibility of the University to government sponsoring agencies, foundations and corporate sponsors has significantly increased. As a result, the revised policy attempts to identify with greater specificity inventions that are subject to University ownership. The revised policy will address the rights and responsibilities of each member of the University community, emeritus professors, visiting professors, adjunct professors, graduate students and undergraduate students, with a single, uniform statement. In addition, the policy may call for employees to sign a Participation Agreement, acknowledging the University's rights in inventions.

The revised policy also will address the procedures for implementation of the policy, including royalty distribution, the manner in which the intellectual property officer and the Center for Technology Transfer manage inventions, publication of commercially sponsored research, and the relationship of the policy to outside activity of the faculty and University employees.

### Distribution of Income from Inventions

The distribution of royalties under the revised policy would be significantly revised and simplified. A possible income distribution scheme is shown in Table 1. It is important to emphasize that the figures shown are subject to change in the final draft of the policy. However, this table does represent a wide consensus that income should be distributed to the inventor(s), to the laboratory(ies), department(s), and School(s) of the inventor(s), and to the Research Foundation, as well as to the Intellectual Property Fund to help offset the cost of managing the University's intellectual property rights.

Table 1

	Net Royalty Income	Net Equity Income
Inventor(s):	25.0% (Note 1)	N/A (Note 2)
Intellectual Property Fund (See Note 3)	5.0%	5.0%
Balance =		
Academic Income	70.0%	95.0%
<b>Distribution of Academic Income</b>		
Inventor's Laboratory (See Note 4)	22.5% (to Cap of \$500,000)	
Department of Inventor (See Note 5)	22.5% (to Cap of \$500,000)	
School of Inventor (See Note 6)	27.5% (55.0% after Cap)	
Research Foundation (See Note 7)	27.5% (45.0% after Cap)	

The following Notes are referred to in the table on this page:

- Note 1:** The 25% share set aside for the inventors will be divided among all inventors.
- Note 2:** Inventors will receive their shares of equity directly from the licensee and shall receive no further personal share from those equity shares issued directly to the University.
- Note 3:** The share received by the Intellectual Property Fund shall be used solely to support the cost of procuring, protecting and maintaining intellectual property rights. It may not be used to support the annual operating expenses of the Center for Technology Transfer.
- Note 4:** The share designated for the laboratory of the inventor(s) must be used for research purposes only through a budget approved by the Dean(s) of the relevant School(s). The cap of \$500,000 is the total amount to be made available for the laboratories of all involved inventors and it is administered on the basis of total income collected from all licenses for a given patent or set of related patents.
- Note 5:** The share designated for the department(s) of the inventor(s) must be used for research purposes only through a budget approved by the Dean(s) of the relevant School(s). The cap of \$500,000 is the total amount to be made available for the departments of all involved inventors, and it is administered on the basis of total income collected from all licenses for a given patent or set of related patents.
- Note 6:** The share received by the School(s) of the inventor(s) may be used at the discretion of the Dean of that School, provided that such use is restricted to research purposes.
- Note 7:** The Research Foundation share is for use at large under Research Foundation rules. The Research Foundation will release periodic reports describing the source and use of funds.

The major differences between the income distribution in Table 1 and that described in our current policy are:

1. The proposed structure calls for "flat rate" distribution of royalties, whereas the current policy distributes a share of royalties to the inventor(s) on a declining basis, i.e., as the amount of royalties received by the University increases, the portion shared with the inventor decreases. The basis of the current policy was to provide a greater incentive at the "early" end of a royalty stream because the majority of projects yield relatively modest returns. There was also concern that a large percentage of royalties distributed to an inventor in the case of a remarkable success would be disproportionate to the needs of the University community as a whole, thus the inventor's share diminished to ten percent (10%). Over time, the University's experience has demonstrated that most inventions are made by more than one inventor. Furthermore, several patents on a related technology are typically licensed as a package. The growing complexity of both University license agreements and the use of University patents by University corporate licensees has made it very difficult to delineate when multiple inventions should be treated separately under the University's current declining scale. Most universities have moved to a flat rate approach.
  2. The inventor's laboratory, department and school will have defined shares in the proposed policy, whereas in the current policy the inventor's laboratory is entitled to a defined share of only the first \$100,000 in royalties received. The balance of funds is then dedicated to the Research Foundation. The current policy calls for the Research Foundation to repatriate royalties, when practical, to the source of the invention, i.e., the inventor's laboratory, department and school. There is, however, no specific entitlement. The proposed policy specifically defines how royalties will be distributed.
  3. The proposed new policy addresses the management and distribution of equity accepted by the inventor and the University in lieu of up-front license fees, a provision made necessary by the changes in university-industry relationships over the last decade.
- Extensive information was gathered from other major research universities and used in this draft formulation.

# Environmental Health and Safety

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The goals of the University's environmental health and safety programs are to protect faculty, staff, students and the environment from harmful exposures to biohazardous materials and chemicals, as well as to protect experimental materials. *The University Biological Safety Manual* provides guidance on the biological safety program, and the Chemical Hygiene Plan describes the University's chemical safety program. Copies of *The University Biological Safety Manual* and the Chemical Hygiene Plan are available from the Office of Environmental Health and Safety (OEHS).

## Biological Safety

In biosafety the major regulatory changes are in the Pennsylvania Infectious Waste regulations, and the Occupational Safety and Health Administration's (OSHA's) Blood Borne Pathogen Standard.

On August 8, 1992, Pennsylvania made changes in its infectious waste regulations. The significant regulatory changes are: 1) the addition of fluids (liquid volumes 20 cc or greater) to the wastes that must be segregated at the point of generation, i.e., the lab or clinic; and 2) the removal of the general requirement to consider all pasteur pipettes infectious waste. The changes, along with proposed courses of action, were detailed in *Almanac OF RECORD* September 15, 1992. Copies of the article are available from OEHS. There are other changes which present administrative challenges, but it is hoped that researchers will be largely unaffected by these changes.

A new federal regulation, OSHA's Blood Borne Pathogen Standard (BBP), requires extensive effort on the part of investigators and their staff. This standard, which became fully effective on July 6, 1992, requires that all laboratories and work areas where there is a potential for exposure to human blood and blood products, as well as other human body fluids and tissue culture, must develop and have available an Exposure Control Plan (ECP). In order to provide the most complete protection possible, each lab or clinical area should develop and make available its own ECP, see *Almanac OF RECORD* May 26, 1992, for information on the ECP. To facilitate this goal the ECP is available on disk from OEHS (A 3 1/2 inch blank disk is required.) The University's Exposure Control Plan is available at OEHS and on PennInfo (See Policies and Procedures, Environmental Health and Safety). Laboratories conducting research with the hepatitis B virus (HBV) or human immunodeficiency virus (HIV) have additional training and work practice requirements. Additionally, the BBP standard requires that all personnel with potential exposure to blood borne pathogens be offered vaccinations against the hepatitis B virus. Faculty and staff who wish to receive the vaccine, should contact Occupational Health and Services at the Hospital of the University of Pennsylvania (622-2354).

## Chemical Safety

Another regulation which has a direct impact on faculty and researchers is OSHA's rule on Occupational Exposure to Hazardous Chemical in Laboratories, also known as "The Lab Standard." The Lab Standard is performance-oriented and does not prescribe specific instructions regarding activities with particular chemicals. OSHA does, however, require that laboratories develop Chemical Hygiene Plans (CHP). The CHP is similar to the Exposure Control Plan for Blood Borne Pathogens; copies of the University's CHP are available from OEHS, or on PennInfo.

## Training Requirements

The BBP and the CHP require annual training. OEHS conducts training monthly. Times and locations are posted in the *Almanac* and on PennInfo. OEHS will conduct training for departments upon request.

## Chemical Waste Program

Chemical waste regulations under the Resource Conservation and Recovery Act (RCRA) established a system to handle hazardous waste from "cradle to grave". Since a chemical may be hazardous by characteristics, i.e., ignitable, corrosive, reactive, toxic, etc., as well as by virtue of its status under government regulations, University policy prohibits drain disposal of chemical wastes. By prohibiting the use of sinks for waste disposal, the University relieves researchers of the responsibility of determining what wastes may be disposed of down the drain. OEHS will collect chemicals at the laboratory. If there is any uncertainty about the proper disposal of any chemical OEHS should be contacted.

Amendments to the chemical waste laws (RCRA) mandate that the

University institute a waste minimization program. OEHS will consult with individual laboratory groups to identify possible methods of waste reduction. The amendments do not require unacceptable changes to research protocols but rather that reductions be made where practical.

## Laboratory Survey Program

In order to support researchers and departments in biological and chemical safety and to identify training needs, OEHS has undertaken a laboratory survey program. OEHS works with departments to schedule visits and will also visit labs on request.

## Grant Approval

Penn is required by the National Institutes of Health to provide an approval process for research with toxic and carcinogenic chemicals and biohazardous agents. If the grant transmittal form indicates the use of these agents, OEHS must be called or receive a copy of the grant. While OEHS will make every effort to provide an expeditious review and approval, there are occasions which warrant review by the Institutional Biosafety Committee (IBC) or possibly government agencies. The IBC is composed of faculty, two extramural members (one representing the Philadelphia Health Department) and the director of the OEHS. The IBC is required by the NIH for all grant recipient institutions conducting recombinant DNA research. At the University, the IBC, a subcommittee of the Environmental Health and Safety Committee, is charged with reviewing and providing policy advice to the Vice Provost for Research on safety and health matters including work involving recombinant DNA, human pathogens, oncogenic virus and other infectious agents. The IBC, at the request of the OEHS, will also review grants to advise what pertinent safety measures are necessary for the safe conduct of research.

## Summary

Granting agencies such as the National Institutes of Health and National Science Foundation, and foundations such as the Howard Hughes Medical Institutes require that grantees comply with environmental health and safety requirements. The University must also certify annually to NIH, through its "Assurance Statement," that it has a comprehensive safety and health program.

In recent years there has been a vast expansion of environmental laws and regulations. University research is now expected to be in strict compliance with all of these regulations. New laws and regulations hold individuals responsible for some types of violations, and federal and state agencies may, in some circumstances, initiate criminal proceedings against individuals who violate these regulations. Substantial penalties may be imposed for minor unintentional violations such as record keeping violations, regardless of the absence of harm to persons or the environment.

OEHS provides information and consultation on the requirements of environmental health and safety regulations. Changes in regulations and the University's response to comply with them are published in *ALMANAC* and distributed during training sessions. OEHS provides health and safety training on a scheduled basis and will provide specific training to departments on request.

# Radiation Safety

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Radioactive materials play a unique and vital role in the University's clinical and research programs. Insuring that radioactive materials are used safely is the responsibility of the Radiation Safety Committee and its operational arm, the Radiation Safety Office (RSO). Last year the University received over 10,000 shipments of radioactive materials that were used by over 400 principal investigators in research and clinical procedures. The use of this material produced over 30,000 pounds of dry radioactive waste that was shipped for disposal.

Currently eight different Federal and State agencies regulate the transportation, use, and disposal of radioactive material. The United States Nuclear Regulatory Commission (NRC) and the Pennsylvania Department of Environmental Resources (DER) are the agencies that have the primary

oversight for the use of radioactive material at the University. These two agencies issue the licenses under which all use of radioactive material is authorized. Serious violations of the conditions of these licenses by any member of the University community jeopardizes all use of radioactive material on campus. The NRC inspects the University's facilities annually, and no serious violations have been identified by the last three inspections.

Earlier this summer, the Pennsylvania DER revised its regulations governing the medical use of radioactive material. The University is in the process of amending its license to adjust to these changes. The NRC also has new regulations that become effective in 1994 that will, in addition to other matters, require changes in how radioactive packages are received.

The one change in regulations that will have the greatest immediate effect on the University concerns radioactive waste disposal. This change follows from federal legislation that was passed over ten years ago and may leave the University with no place to dispose of radioactive waste after January 1, 1993. The federal Low-Level Radioactive Waste Policy Act, passed in 1980 and amended in 1985, requires that individual states or groups of states (compacts) establish their own low-level radioactive waste disposal sites and that the existing national sites be closed to outside states/compacts on January 1, 1993. A provision of the act required the states to take possession of the waste if they did not have a disposal site by January 1, 1996. A recent (June 19, 1992) Supreme Court decision has upheld the principles of the legislation with the exception of a clause that required the states to take title to the waste on January 1, 1996. Although there was an eight-year lead time built into the legislation, the national sites will close to states outside their compacts at the end of 1992 without a single state having started construction on a new waste disposal site.

Pennsylvania is a member of the Appalachian Compact and has plans to open a disposal facility. The most optimistic predictions indicate, however, that the site will not be ready until mid 1996. There is a possibility that the Appalachian Compact may reach an agreement with a compact/state that has an operational disposal site which would accept radioactive waste from generators in Pennsylvania. The RSO is closely monitoring these

negotiations. One issue is clear, however; disposal costs would exceed 200% of current costs.

In order to allow for the uninterrupted use of radioactive materials by researchers, and to permit the orderly flow of radioactive waste from research facilities, the following steps are being taken:

1. An increase in the University's centralized waste storage capacity. The RSO estimates the University will require approximately 1000 sq. feet of new storage space per year to store the waste it currently ships off campus. We presently have space to store approximately six months accumulation of waste.
2. Implementation of procedures to reduce the volume of the waste the University is currently generating. Compactors and shredders are being tested.
3. A modification of the existing procedures that will permit the disposal by storage for ten half-lives for selected radioisotopes with half-lives of up to 120 days. Current regulations limit this procedure to radioisotopes with half-lives of up to 65 days.
4. Encouraging investigators to utilize more fully the existing NRC sewer disposal allocation and requesting an increase in this allocation from the NRC.
5. Requiring investigators to segregate wastes by radionuclide and other characteristics that will permit processing into waste streams that remain open for use. Currently these waste streams are sewer disposal, storage for decay, and decontamination.
6. Providing assistance to investigators to help them minimize the waste generated from experimental procedures.

The steps taken to deal with the shutdown of the existing waste disposal sites are the same ones that will be used to contain the costs of waste disposal after the Pennsylvania facility is available for use. It is our intention to pursue and refine these procedures in order to provide University investigators with a cost effective and safe radioactive waste stream.

## Animal Care and Use

Over the past several years changes in federal requirements and guidelines have significantly changed laboratory animal care and use policies. The Public Health Service Policy for the Care and Use of Animals used in Biomedical Research (Policy) and the Guide for the Care and Use of Research Animals (Guide) underwent major revisions in 1985. All investigators should be familiar with the animal care requirements in these documents which apply to their research. These were followed in 1989 with a revision to the Animal Welfare Act, a federal law which is implemented by the United States Department of Agriculture (USDA) primarily through regular unannounced visits to animal facilities.

Periodic amendments to the Animal Welfare Act often change the requirements imposed by the federal government and affect how animals are housed, cared for, and used at research universities. Through 1991, USDA inspectors primarily looked at animal facilities, cages, and care and husbandry provided in the animal facility. Amendments in 1985 led to changes in regulations that were enforced in 1991 by the United States Department of Agriculture. As a result, the University has completely renovated all housing areas for dogs and will soon provide exercise in specially made pens for all research dogs. Regulations have also changed for nonhuman primates and now require positive environmental enrichment for all primates. Environmental enrichment and social interaction should result in happier, healthier animals, which in turn should provide better research models for investigators working with these animals.

The USDA in early 1991 and early 1992 announced a change in how they review animal care and use at research institutions. USDA veterinarians who regularly make unannounced visits to our facilities have in the past followed engineering standards and checked the University's compliance with cage size, animal care and other specifically required arrangements for animals. In 1991, the USDA announced that their inspectors will add "performance standards" to their inspection visits, and will be more concerned with actual experimentation and research efforts going on at the university. This will include visits to research laboratories, discussions with research investigators, observation of work with animals and careful

scrutiny of animal research protocols. Research investigators and faculty can expect to see and hear regularly from USDA field inspectors, and will be expected to discuss their work with USDA officials so that a complete understanding of the scientific efforts underway can be shared. Particular attention will be given to the reason for using animals and how the species being used was selected. Use of anesthesia will be reviewed and the technical skill and experience of those conducting the animal work will be observed and considered. While these USDA visits are unannounced, it is entirely appropriate that the Attending Veterinarian should be included in these facility tours and discussions with research investigators. Faculty who have any questions or concerns about the activity of USDA veterinarians in their laboratories or facilities on campus, are encouraged to contact their ULAR Attending Veterinarian and/or the ULAR Director and have ULAR participation in these visits.

The IACUC records have already become a major part of the USDA visit, and animal protocol records and IACUC record keeping must be timely and accurate. It is important that IACUC/investigator interactions be clear and well documented. Changes and modifications must be recorded and documented, and all work with animals must be clearly and completely described.

Attending veterinarians can be a valuable ally in assuring that investigators are aware of the latest and best comparative medical information and that animal health and welfare is being provided in the best possible way. ULAR faculty members and postdoctoral resident veterinarians are available for routine or emergency veterinary medical care and collaborate with investigators on animal protocol development and review on a regular basis.

At the present time, the USDA inspecting veterinarians do not include rats and mice in their inspection visits. It has been announced that strong consideration is being given at this time to include rats and mice under the purview of the USDA. Changes are expected in the USDA regulations sometime in the next two-to-three years to include all animals including small rodents under discussion by and with USDA inspecting veterinarians.

Animal care regulations continue to be closely scrutinized and changes

may be expected frequently over the coming years. Litigation is currently underway between the Humane Society of the United States and the United States Department of Agriculture, and the result will very likely be further changes in either the Animal Welfare Act and/or the USDA Regulations. These will be carefully monitored by the Office of University Laboratory Animal Resources, and ULAR Attending Veterinarians in each school will keep School Animal Care Committees updated and informed.

### Public Health Service (PHS) and NIH Requirements

The Public Health Service Policy on Humane Care and Use of Laboratory Animals (Policy) and the Guide for the Care and Use of Laboratory Animals (Guide) should be on the desk of each Penn faculty and staff member who uses animals in their work. (Copies can be obtained from the ULAR office or directly from the Government Printing Office). Written assurance of our compliance with these policies is provided to the Office for the Protection from Research Risks (OPRR) on an annual basis. This assurance is reviewed annually and it must be fully acceptable for submission of research grant proposals. PHS requires that each institution have an active Institutional Animal Care and Use Committee (IACUC) which has direct reporting responsibility to the government on animal care and use.

### Animal Care Costs

The cost of providing direct animal care was heavily subsidized by the University and Schools prior to 1991. It has been a goal of each school to fully recover all direct animal care costs by charging a daily fee for the housing and care provided for animals used in research and teaching. This has required close observation of animal care and use programs at the University and several faculty committees have been formed to provide this oversight and review. While the cost of animal care to the research investigator has increased somewhat over the past five years, direct animal care costs have decreased with closer attention to efficiency and good management, and clinical care and husbandry have improved significantly. In FY92, all costs of direct animal care were fully recovered from per diem fees for the first time, and all direct animal care budgets were in balance. The sources of income to ULAR in FY92 are shown below.

No further increases in animal care costs beyond inflation are projected for the coming years. A major cost accounting effort is taking place at the present time, and with the advice of outside expert consultants, fee structures for animal care and husbandry will be further examined and modified as required.

### AAALAC Accreditation

The highest standard of humane care for animals is participation in the American Association for the Accreditation of Laboratory Animal Care (AAALAC) Program. Penn's long-range goal has been to meet the highest standards for animal care and use and strive for accreditation by this independent accrediting body. The AAALAC Accreditation team will be on campus November 12 and 13 site visiting the School of Medicine. The University is hopeful full accreditation by AAALAC will follow. The University expects to seek accreditation for all other schools at the Univer-

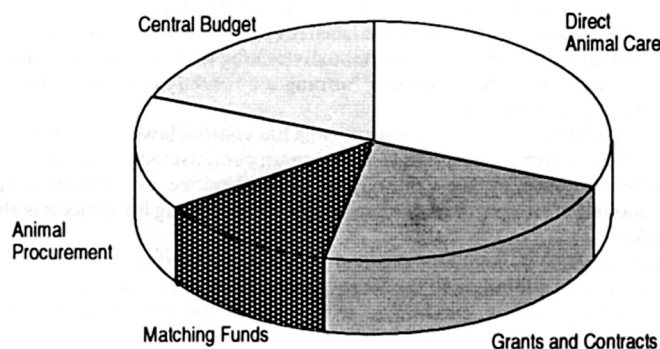
sity in the next several years. AAALAC accreditation is peer recognition of all aspects of animal care and use at the institution and is testimony to the institution's commitment to the highest standards of humane care for animals being used in research and teaching programs.

### Animal Care Education and Training

Under the newly formed Office of University Laboratory Animal Resources, a Postdoctoral Residency Training Program for veterinarians wishing to specialize in laboratory animal medicine was proposed and received federal support and funding in 1988. This program has brought six postdoctoral residents in Laboratory Animal Medicine to the University and has expanded to include participation and support from industrial institutions in the tri-state area. Specialty trained veterinarians now provide daily observation and care for all teaching and research animals at the University and also collaborate with research faculty in the design and conduct of research being conducted. Two new postdoctoral resident veterinarians each year join this program and are actively seeking scientific research laboratories with which they can affiliate and collaborate. Laboratory directors and senior faculty are encouraged to contact the Office of University Laboratory Animal Resources to discuss integration of these veterinary scientists into their research programs.

Laboratory Animal Medicine faculty coordinate and oversee the animal care and use seminar required by the Institutional Animal Care and Use Committee (IACUC), and are prepared to assist faculty and investigators in research planning for animal related projects. In addition, training sessions are offered and routinely provided for research staff who wish direct hands-on experience with the various animal species. These complement the clinical support provided. Faculty and research investigators are encouraged to take advantage of these training and support opportunities for themselves, their residents, and technical staffs.

**Laboratory Animal Medicine and Care Efforts  
FY 1992**



## Regulatory Information

### Protocols Involving Human Subjects in Research

The University of Pennsylvania is committed to safeguarding the rights and welfare of all human beings who participate as subjects in research conducted at this institution. Internal and cooperative endeavors otherwise supported or subject to regulation by any Federal Department or agency, state or local authority, private sponsor and/or the investigator's School are covered by the same policies and procedures set forth in the University's Multiple Project Assurance (M1025) negotiated and approved by the Public Health Service (PHS) of the Department of Health and Human Services (DHHS) through the Office for Protection from Research Risks (OPRR). This document of "Assurance" outlines specifically what the institution will implement in its program to comply with the laws cited at CFR Title 45, Part 46 of the *Code of Federal Regulations* for the conduct of all biomedical and behavioral research involving humans as subjects proposed by faculty, staff and students of the University.

In order to assist investigators in their pursuit of scientific knowledge and

to assure compliance with applicable rules, the University has established under the National Research Act of 1974, Institutional Review Boards (IRBs) known as the Committee on Studies Involving Human Beings. The charge of these IRBs is to review research protocols as necessary to insure that: 1) Risks to subjects are minimized and are reasonable in relation to potential benefits of the investigation; 2) Selection of subjects is equitable; 3) Informed consent is obtained by adequate and appropriate means unless otherwise waived by the Committee in writing; 4) Ongoing research activity is reviewed at least annually unless the Committee determines that a specific project requires a more frequent re-review; and 5) Additional safeguards have been provided for research involving fetuses, in vitro fertilization, minors, pregnant women, prisoners, mentally retarded, mentally disabled, handicapped and particular populations with catastrophic diseases. The Committee's role in commenting on the research design of a protocol has not been clearly delineated. The Committee does, in certain regulated areas and particularly for internally funded studies which are not submitted for peer review, attempt to evaluate the scientific merit of protocols forwarded

to them. When members of the IRB have relevant expertise, constructive suggestions are communicated in writing to the investigator.

Protocol review by the Committee (IRB) is conducted through one of three methods (exempted, expedited and full) and is dependent on criteria specified in accordance with regulation. The appropriate review process categories can be found in the *Guidelines for the Preparation of Protocols for Review* in the Office of Research Administration. Assistance in making a determination can be obtained by telephoning 988-2614.

Extensive changes to federal regulation as they pertain to research involving human subjects occurred in 1983 and were incorporated into the program at this University. Several additional statutes have been implemented during the past two or three years, and a few deserve brief mention.

1. The Common Rule was promulgated by sixteen Federal departments and agencies to accept (with one minor exception by the Department of Education) HHS-approved Multiple Project Assurances of Compliance (MPA). However, the regulations no longer explicitly list "a grace period" of sixty days for receipt of certification for approved studies from IRBs at MPA institutions. The NIH and PHS agencies will extend the policy of the "grace period" for competing applications and proposals via administrative announcement but not for non-competing continuation applications or others reviewed via a "fast track" process.

2. Policies have been implemented for the inclusion of women and minority populations in research protocols.

3. The U.S. Food and Drug Administration has defined the use of experimental products (drugs and devices) regarding emergency use, single patient use and those utilized under a treatment IND (investigational new drug exemption). Additional regulations have been proposed to provide a faster method of releasing new medications and to delegate the review of certain types of clinical trials to local IRBs. Regulations have been enacted requiring IRBs to review all advertisements for subject recruitment into research studies and to report "adverse effects" encountered in the conduct of clinical trials.

4. Cooperative Project Research Programs (CPRP) have new reporting requirements in accordance with the latest revision to institutional assurances and will require full IRB approval annually as long as the activity continues. The University is in the process of forming a third duly constituted IRB to handle this latest provision.

5. The Commonwealth of Pennsylvania has enacted laws regarding blind testing for research participants. Under certain circumstances, such research must be reviewed by the Commonwealth Committee in addition to the institutional IRB. A provision for pre- and post-counseling for subjects is also included.

6. University policy mandates that fully documented protocols for IRB review must be submitted to the Regulatory Affairs Office no later than the time the proposal for funding is forwarded to the Office of Research Administration for processing.

### Protocols Involving Vertebrate Animals in Research

Title 9, subchapter A of the Code of Federal Regulations, published in the *NIH Guide for Grants and Contracts* and in Chapters 1-43 of the DHHS Grants Administration Manual, requires the establishment of an Institutional Animal Care and Use Committee (IACUC), that is charged with the review of research, testing and teaching involving vertebrate animals. The responsibility of the IACUC is to insure that: 1) procedures with animals will avoid or minimize discomfort, distress and pain to the animals, consistent with sound research design; 2) procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator; 3) animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly sacrificed at the end of the procedure or, if appropriate, during the procedure; 4) the living conditions of animals will be appropriate for their species and contribute to their health and comfort, and further that the housing, feeding and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling and use of the species being maintained or studied; 5) medical care for animals will be available and provided as necessary by a qualified veterinarian; 6) personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures; and 7) methods of euthanasia will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia unless a deviation is justified for

scientific reasons in writing by the investigator. In addition to reviewing protocols, the IACUC is also empowered to suspend an activity when there is substantial evidence that the research is not being carried out in accordance with applicable provisions of the University's Assurance or government regulation.

A specific protocol is approved in principle for a five year period by the IACUC; during that time it must be reviewed annually, to take into account changes in protocol that may be necessary. At the end of five years, the protocol must be redocumented and submitted for full committee review. It is recommended that all protocols be reviewed and signed by the attending veterinarian of the investigator's School prior to IACUC review but this process is not mandatory.

There is a mechanism for an expedited review of certain protocols. Information regarding expedited review may be found in the *University Guidelines for the Preparation of Protocols for Review* or obtained in the Office of Research Administration.

Several changes have been proposed or implemented by regulatory agencies that will affect investigators who use vertebrate animals:

1. In late August President Bush signed the Animal Enterprise Protection Act of 1992 into law. The new law provides and maintains a careful balance between the rights of special interest groups to legitimately protect animal welfare and the right of animal facilities to have adequate protection from illegal activities. It also sets penalties for terrorist activities against biomedical research facilities, farms and other enterprises.

2. Changes are being considered by the USDA to include mice, rats, and birds in the Code of Federal Regulation.

3. The "grace period" of sixty days for receipt of certifications for approved studies by the IACUC at MPA institutions will be available on a more limited basis. The NIH and PHS agencies will extend the policy of the "grace period" for competing applications and proposals via administrative announcement but not for non-competing continuation applications.

4. IACUC will require the signature of the attending veterinarian of the investigator's school on all tabled and disapproved protocols prior to resubmission to the IACUC for review.

5. The University's policy will require that fully documented protocols to the IACUC for review must be submitted to the Regulatory Affairs Office at least by the time the proposal for funding is forwarded to the Office of Research Administration for processing.

### Conclusion

Protocols involving either human beings or vertebrate animals as subjects must be prepared carefully and completely. They become part of the official records maintained by the institution and are subject to inspection, review and copying by various granting and government agencies. It is possible that some protocols in certain circumstances will be subject to public scrutiny under the Freedom of Information Act (FOIA) or the judicial system.

Researchers should consult the *Guidelines for Preparation of Protocols for Review*, two publications disseminated from the Regulatory Affairs Office (one for research involving human subjects and the other pertaining to vertebrate animals), when preparing protocols for review by the Institutional Review Boards or the Institutional Animal Care and Use Committee. These publications summarize the institutional policies, processes and procedures for the conduct of research, training, testing and teaching at the University of Pennsylvania.

For requirements pertaining to record keeping, each investigator must retain a copy of any protocol, signed consent forms (if applicable) and all correspondence pertinent to a specific study. Retention of these materials must be for at least three years after the termination date of the protocol or such longer period of time if specified by the sponsoring agency and/or required by law.

Each protocol approved by the IRBs or IACUC is assigned a specific number by Regulatory Affairs. This unique number appears on all correspondence, and is meant to assist investigators in tracking protocol activity, annual reapproval requirements, animal purchasing and identifies studies which involve the same work and procedures that are submitted to several sponsoring agencies.

Both the IRBs and the IACUC use the same determinations when reviewing a specific protocol at their respective meetings. Outcome and definitions can be found in the "University Guidelines for Preparation of Protocols for Review." However, no research may commence until full approval has been received in writing by the principal investigator.