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Ensuring due process in the IACUC and animal welfare setting: considerations in developing noncompliance policies and procedures for institutional animal care and use committees and institutional officials

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ABSTRACT: Every institution that is involved in research with animals is expected to have in place policies and procedures for the management of allegations of noncompliance with the Animal Welfare Act and the U.S. Public Health Service Policy on the Humane Care and Use of Laboratory Animals. We present here a model set of recommendations for institutional animal care and use committees and institutional officials to ensure appropriate consideration of allegations of noncompliance with federal Animal Welfare Act regulations that carry a significant risk or specific threat to animal welfare. This guidance has 3 overarching aims: *1*) protecting the welfare of research animals; *2*) according fair treatment and due process to an individual accused of noncompliance; and *3*) ensuring compliance with federal regulations. Through this guidance, the present work seeks to advance the cause of scientific integrity, animal welfare, and the public trust while recognizing and supporting the critical importance of animal research for the betterment of the health of both humans and animals.—Hansen, B. C., Gografe, S., Pritt, S., Jen, K.-L. C., McWhirter, C. A., Barman, S. M., Comuzzie, A., Greene, M., McNulty, J. A., Michele, D. E., Moaddab, N., Nelson, R. J., Norris, K., Uray, K. D., Banks, R., Westlund, K. N., Yates, B. J., Silverman, J., Hansen, K. D., Redman, B. Ensuring due process in the IACUC and animal welfare setting: considerations in developing noncompliance policies and procedures for institutional animal care and use committees and institutional officials. FASEB J. 31, 4216–4225 (2017). www.fasebj.org

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ABBREVIATIONS: AV, attending veterinarian; AWA, Animal Welfare Act; AWR, AWA regulation; DoD, U.S. Department of Defense; FOIA, Freedom of Information; IACUC, Institutional Animal Care and Use Committee; IO, institutional official; NIH, U.S. National Institutes of Health; NSF, U.S. National Science Foundation; OLAW, Office of Laboratory Animal Welfare; PHS, U.S. Public Health Service; PI, principal investigator; USDA, U.S. Department of Agriculture

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BACKGROUND

The Institutional Animal Care and Use Committee (IACUC), the attending veterinarian (AV), and the institutional official (IO)—together with principal investigators (PIs) and all research personnel—have the collective institutional responsibility for assuring the welfare of animal subjects used in teaching, research, and testing. The U.S. Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (1) states that the IACUC must review concerns that involve the care and use of animals at the institution; in accordance with the *Guide for the Care and Use of Laboratory Animals* (2), develop methods for reporting and investigating animal welfare; and per the Animal Welfare Act (AWA) and the AWA regulations (AWRs) (3), the IACUC must review, and, if warranted, investigate such concerns that result from complaints or reports of noncompliance received from laboratory or research facility personnel, employees, or the public.* Both the U.S. Department of Agriculture (USDA), which administers and enforces the AWA and AWRs, and the National Institutes of Health (NIH; Bethesda, MD, USA) Office of Laboratory Animal Welfare (OLAW), which administers and coordinates the PHS Policy, rely on institutions to develop and implement policies and procedures for the review and investigation of animal welfare concerns (4). Sound research policies and practices, viewed impartially by experts in the field, must be promoted and supported to assure excellence in research that involves animal subjects while simultaneously avoiding an increase in self-imposed regulatory burden (5, 6).

Here, we provide guidance for developing institutional policies and procedures to assist institutions in the development of fair and reasonable investigation procedures while ensuring appropriate consideration of allegations of noncompliance with federal statutes that carry a significant risk or specific threat to animal welfare. The present model of best practices reflects, in part, other institutional policies, such as those that concern the handling of allegations of misconduct in research, per PHS Policies on Research Misconduct† (7), that have been implemented by institutions to provide thorough and fair protections, both for research subjects and for those who are accused of research misconduct. Many of the procedures described in this work have evolved from those developed by the Office of Research Integrity for examining other forms of alleged misconduct in research. Various research misconduct policies have already been promulgated by multiple academic institutions for the investigation of allegations of research and/or scientific misconduct. Noncompliance in which animal welfare is a concern is not generally evaluated under an institution's research misconduct policies; therefore, all institutions should also have in place a publicly available set of policies that are specific to animal welfare concerns and that clearly explain confidentiality protections in place for the reporting and investigation of animal welfare concerns.

The ideas and recommendations herein can be adapted to fit the needs of each setting.

Core concepts of due process and fundamental fairness for dealing with allegations of noncompliance are described, and guidance to those who are responsible for addressing such allegations is provided.‡ These core concepts of due process—meaning what is due to the respondent in a fundamentally fair proceeding—include the following:

- The right to be informed of the allegations of noncompliance
- The right to receive and review all evidence put forward in support of the allegations, to challenge the evidence and to provide alternative interpretations of it, and to put forward evidence in defense against the allegations
- The right to have the allegations of the complainant and the responses of the respondent heard and decided by [an] impartial and fair decision maker/s, and based solely on evidence included in the proceedings
- The right to assistance from counsel or another adviser, if so desired
- The right to an appeal to correct prejudicial errors in the process, in the application of relevant regulations or guidelines, and/or in sanctions inappropriately levied

Even in a sound animal care and use program, people may voice concerns regarding actions or inactions that involve animals. Those accused of noncompliance regarding the use of animals in research or adverse events that impact animal welfare—referred to herein as the respondents—may include scientists, veterinarians, animal caretakers, or research laboratory staff, and could even include the IACUC itself or the institution. Some perceptions of noncompliance may involve misunderstandings or insufficient knowledge, so care should be taken before labeling an activity as misconduct or noncompliance. Using fundamentally fair procedures to investigate and resolve concerns will help to distinguish true and serious noncompliance from misunderstandings or matters of reasonable and valid disagreement while ensuring the protection of animal subjects.

OLAW and the USDA expect that when a complainant makes an allegation of noncompliance, the IACUC and the IO will take action to ensure the continued welfare of the research animals, but will also act responsibly and fairly toward the respondent, which is as imperative for ensuring institutional integrity as the institution's commitment to animals involved in research. Acting fairly and responsibly toward the respondent is part of the broader goal of assuring that all parties to allegations of noncompliance will experience honest and appropriate deliberative processes and outcomes; however, without clearly defined institutional policies and procedures, concerns may arise as to whether respondents will be accorded fair treatment.

This guidance for the management of allegations of noncompliance or animal welfare concerns is presented in the same spirit as previous model policies that addressed allegations of academic and research misconduct (8, 9)—that is, it is offered freely for use by others as a public and evolving document. These policies and procedures have benefitted from the institutional and personal experiences of individuals with diverse backgrounds and professions,

and will continue to evolve as institutions consider these concepts and develop their own policies.

CONSIDERATIONS IN DEVELOPING POLICIES AND PROCEDURES FOR INVESTIGATION AND RESOLUTION OF CHARGES OF NONCOMPLIANCE WITH ANIMAL RESEARCH REGULATIONS

Core principles

Legal authority

The AWA constitutes the legal authority for assuring the welfare of animals used in research. AWRs state that the IACUC must review, and, if warranted, investigate concerns that arise from the use of animals. The IACUC's investigation of noncompliance allegations must comply with all legal requirements for such investigations on the basis of the regulations and polices below and on the institution's governance framework. As noted above, the PHS Policy (1) states that one function of the IACUC is to review concerns that involve the care and use of animals at the institution. OLAW provides some guidance on the evaluation of such concerns in the IACUC guidebook (10), as well as in relevant notices (*e.g.*, NOD-OD-05-034) (11). In addition, the IACUC handbook (12) offers suggestions. The PHS policy covers extramural or intramural activities that are funded by the NIH, the U.S. Food and Drug Administration, the Center for Disease Control and Prevention, and the Department of Health and Human Services, and also covers—*via* a memorandum of understanding—activities that are funded by the U.S. National Science Foundation (NSF). Other agencies and institutions, such as the U.S. Department of Veterans Affairs and some U.S. Department of Defense (DoD) facilities, have individual OLAW assurances agreeing to adhere to the policy.

Suspension

Both the AWRs and PHS Policy authorize the IACUC to suspend an activity for cause—for example, to halt or prevent an imminent threat to animal welfare or continuing harm to an animal. This authority should not be construed to mean that the IACUC must suspend a noncompliant activity, as in some cases, a noncompliant activity may be readily addressed with an amendment to a protocol. An activity can only be suspended by a majority of a quorum of the IACUC during a convened meeting; a quorum is one more than half of the total committee (a majority of the members of the IACUC). Activity refers to any action that involves animals, such as research, research training, experimentation, teaching, biologic testing, holding, or quarantine. In the context of suspension, activity usually refers to protocol-related work. The IO must review the reasons for the suspension and take appropriate corrective actions, especially if needed to assure the mitigation of a significant threat to animal welfare (AWR §2.31(d) (8); IV.b.7) (3). Of note, other corrective measures may be taken for minor violations.

Reporting requirements

Guidance that concerns the reporting requirements for noncompliance is detailed by OLAW (*http://grants.nih.gov/grants/olaw/reporting_noncompliance.htm*). Noncompliance with PHS Policy or serious deviations from the *Guide* may involve actions that affect animal welfare, but could also involve such an issue as an improperly constituted IACUC—for example, not having all required members appointed—or programmatic failure. If an activity that involves animals falls under the institutional OLAW assurance and is suspended by the IACUC, the suspension must be reported to OLAW and the USDA (if it involves a regulated species), and to any federal funding agency, if applicable. Guidance on what does or does not constitute a reportable event is provided by OLAW in Notice Number NOT-OD-05-034 (11). Whereas some examples are quite clear and represent a substantial deviation from the accepted norms related to animal welfare, others are not, and the IACUC is advised to consult with the IO regarding the reporting of noncompliance and, if needed, reports through the IO to OLAW. A review of the examples provided by OLAW indicates that to be reportable, the noncompliance should be significant—for example, involving jeopardy to the health or well-being of the animals—or should be a continuing and uncorrected problem despite IACUC requests for correction. The IACUC has the right to vote on whether to request that the IO report an incident that likely had no impact on animal well-being, and may determine that the observation did not rise to the level of reporting to OLAW. Suspensions—if this action has been taken as a result of serious risk of or harm to animal welfare—must be reported to both OLAW and the USDA. Some institutions interpret OLAW guidance to require the reporting of all noncompliance to OLAW, even if not impacting animal welfare, but this is neither required, nor advised. Noncompliance with AWA/AWRs or the PHS *Guide* that involves a threat or actual harm to the welfare of animals in PHS or NSF-funded studies must be reported to OLAW. OLAW, being a federal office, is subject to potential Freedom of Information requests (FOIA). Thus, individuals are normally not named except for the IO. Public institutions must follow their state regulations concerning sunshine or other laws, most of which are not required of private institutions.

Fair consideration

The IACUC is responsible for fair and unbiased consideration of allegations of noncompliance and, only if warranted, a full investigation. A formal investigation is not required by either the AWRs or the PHS Policy. Most instances of noncompliance can be addressed by bringing the concerns to the attention of the respondent. In cases in which the respondent agrees with the concerns, it is often prudent for the respondent to propose corrective actions to the IACUC. If the IACUC concurs with the proposed corrective action plan, a protracted administrative process and formal investigation may not be needed.

Clear and detailed process for investigation

The IACUC should have a clear, detailed, and transparent written process for managing such investigations of noncompliance when warranted. The policy and procedures should be posted and be accessible to all researchers and institutional personnel. A copy of the policy and procedures should be included in the notice given to any respondent when initiating an investigation or preliminary fact finding that may lead to an investigation.

Confidentiality of information

The procedures should give authority to certain individuals to obtain and secure all information that is necessary to properly assess the allegations of significant noncompliance. This information and documents generated during the review and investigation should be kept confidential and released only to IACUC members, the IO, the respondent, and others on an as-needed basis or as otherwise provided in the state's public records laws.

Self-reporting mechanism

Every IACUC should develop and support a mechanism for researchers to self-report and self-correct—subject to IACUC oversight—noncompliance in a research laboratory or laboratory animal resource center.

Role of the PI or a director of an animal resource center

The PI of an IACUC-approved protocol is ultimately responsible for all work that is conducted in the research study and should make the approved protocols available to all research staff. The director of the laboratory animal resource center oversees the husbandry and care of all research animals. One should be the primary respondent during a compliance evaluation, even if the alleged noncompliance was an action of an individual under the PI's or director's supervision.

Fair notice and due process

Fundamental procedural fairness should be provided to any person who faces deprivation of property or liberty (construed to include laboratory or academic rights and reputation), all procedures should provide the fundamental tenets of due process as set forth in the U.S. Constitution Amendment 5: no person should be held to answer an allegation without due process of law. Policies should address the requirement for fair notice (what is prohibited or required: complaint time and place), process fairness, and availability of appropriate procedures, including the ability to review any evidence. Both procedural and substantive due process should be provided. Procedural due process concerns the fairness of the investigation and the decision-making process, and addresses, for example, the full disclosure of evidence, including such evidence as may suggest innocence. Substantive due process refers to constraints on the institution. This includes clarity of expectations and requirements as well as prohibitions and sanctions, as represented by the court-adopted vagueness doctrine, which derives from due process concerns and includes the importance of clarity and specificity. In summary, the standards used to judge noncompliance should be clear, fair, and rationally related to the institution's interests in assuring a sound animal research program.

Role of the IO

The IO has a duty and responsibility to the institution to facilitate research, provide appropriate resources, and ensure compliance with all pertinent laws and regulations. The IO should have the explicit authority and responsibility to order a rehearing or independent review whenever the IO's review finds a lack of sufficient evidence to support the finding of noncompliance, lack of a fundamentally fair process, unwarranted interference with or delays imposed on research, or otherwise inappropriate IACUC conduct. The IO should also consider any possible conflicts of interest or appearance thereof, reprisals, delays imposed on funded research, or other unwarranted actions that may have occurred before, during, or after IACUC review. The IO is responsible for meeting the reporting requirements of OLAW as detailed above.

Fundamentals in conducting an investigation

Timeliness

The IACUC's investigation must be conducted in a thorough and timely manner (12). The IACUC should establish timeframes for actions to follow in all cases of noncompliance review or provide individuals who are involved with specific deadlines for response to facilitate the review.

Notification

The respondent should be notified in writing when a concern related to his or her animal research program is received. Although not required, the respondent's immediate supervisor—for example, the departmental chair—may be notified at a point to be decided by institutional policy. In cases in which allegations have come from a whistleblower under the respondent's supervision, it is also important to provide reminders about nonretaliation requirements. As noted above, most PIs attempt to manage a research program that complies with all relevant regulatory requirements and desire to address noncompliance when discovered. Thus, relaying a concern to a respondent is often all that is required to motivate the required changes in his or her animal use program.

Coordination

A primary coordinator should be appointed for each review and investigation, and a backup person should be identified. There is no regulatory guidance on who the coordinator should be. This can be a member of the IACUC, administrative support staff to the IACUC, or other institutional staff. The coordinator should follow a clearly defined written process on how to conduct a review, including whom to contact for relevant information, when to contact them, and how materials are to be shared with the respondent and presented to the IACUC.

Interim actions where there may be significant continuing risk of harm to animals or harm to involved personnel

Assessment of continuing risk of harm

The IACUC should appoint an individual point person or contact person—and an appropriate emergency backup—who is capable of immediately assessing whether a significant continuing risk of harm to animals exists and who can make decisions about any immediate necessary actions—for example, contacting the AV or monitoring or prohibiting a specific procedure pending IACUC review of noncompliance allegations—and is permitted to make prompt direct observations of animals and their environment.

Interim action where continuing risk of harm is determined

The IACUC's investigation should permit prompt interim action to ensure animal welfare in instances where there is a significant risk of harm to the animals. Specifically, immediate action to terminate the risk of harm and provide for any necessary remedial care of the animal is obligatory (12). (Continued prohibition or suspension of an activity, generally believed to refer to a protocol, requires full committee review as previously noted.) Per the AWA and AWRs, the AV or his or her designee shall provide adequate veterinary care to any animals that may be under the IACUC's review.

It is also important that the IACUC take appropriate interim actions to protect the rights of the both the complainant and respondent so that neither is prejudiced in future proceedings.

Persons involved in the IACUC's investigation of noncompliance must be unbiased and impartial

No conflicts of interest

Members of the IACUC and/or any investigation or fact-finding committee that may be appointed by the IACUC chair who have actual or perceived conflicts of interest or who are themselves implicated by or involved with the allegations should recuse themselves from all such proceedings and discussions, including recusal from any votes taken. The institutional policy should indicate what, if any, grounds for recusal may be applicable under various scenarios. For example, a member of the IACUC who makes an allegation should be recused, as should be a collaborator of the complainant or respondent. In addition, any experts that may be consulted should be confirmed by the IACUC to be without conflicts of interest or biases that may reasonably affect their evaluations and presentations.

Opportunity for respondent to object

The respondent should have the opportunity to review and to object in writing to any individual's involvement in either the evaluation or resolution if the respondent has a clear and justifiable reason to believe that said individual or subject matter expert has a conflict of interest or bias. The IACUC and/or the IO should evaluate these objections and attempt to address such objections by proposing an appropriate alternative. The goal should be for the IACUC to assure that any needed expertise is represented by unbiased experts who will assess the allegations in a fair manner.

Information gathering

Documenting the basis for the allegation

A written record should be made of the complaint and the specifics of the alleged noncompliance, including the date, time, and location, and a complete description of the event(s) as provided by the complainant. The written record should include any relevant background that concerns the incident—for example, did this occur during the person's normal job duties, or was this not related to job duties? Furthermore, the complainant's name, position, and relationship to the institution, as well as contact information for any other individuals who were involved should be obtained, as appropriate, to facilitate additional review. The IACUC may offer options for anonymity, but should inform the complainant that complete or sustained anonymity may be impossible given due process considerations and the practical aspects of investigations—for example, when the relevant research environment is small enough that someone may readily guess the identity of the complainant. Details regarding allegations should be documented in writing as soon as possible to ensure an accurate capture of the event and to enable review by other individuals. The complainant should provide—and information-gathering personnel should obtain—all evidence deemed relevant to the investigation (*e.g.*, animal health records, protocol, research records, video surveillance of the facility, and other substantive documents).

Interviews of personnel

Those who are interviewed should include complainants, if known; respondents—that is, any persons against whom allegations are directed; other persons who are reasonably likely to have specific knowledge that concerns the alleged noncompliance or who may be directly affected by the result of the review or investigation; and pertinent program officials, such as the AV.

Option of a fact-finding committee

The policy may provide that the IACUC or IACUC chair designate a fact-finding committee as appropriate. The course of action may depend on the degree to which a reported condition currently jeopardizes the health or welfare of subject animals, and, if the risk is high, the evaluation should be carried out immediately. The AV should be involved with this evaluation, unless there seems to be a perceived or actual conflict of interest, and should propose corrective actions, as noted above. The fact-finding committee may either be standing or *ad hoc*. Standing committees may be useful for large institutions with larger volumes of noncompliance issues. Additional specialized expertise may be needed in certain instances. Emergency meetings may be necessary to ensure the prompt consideration of concerns that have the likelihood of further jeopardizing animal welfare. (IACUCs that are subject to open meeting laws should pay close attention to any applicable requirements.) Likewise, IACUCs should be aware of the impact of time delays on the continuation and/or start of funded research projects.

IACUC evaluation of allegations

Initial review of evidence and determination of accuracy of the record

The IACUC must determine the accuracy of the allegations on the basis of an evaluation of the initial evidence obtained. In some cases, this initial review may determine that the complaint was the result of error, misunderstanding, or misrepresentation by the complainant. In other cases, a brief examination may identify easily rectified problems or find the absence of noncompliance.

Context and thorough evaluation of findings

More broadly, the IACUC should bear in mind that experiments that involve animal subjects are often complex, and it can be difficult to describe every manipulation of animals in a protocol submitted to the IACUC. Moreover, there is a regulatory requirement for the IACUC to approve significant changes to animal activities, but it may not always be clear when a deviation from a protocol rises to the level of a significant change (12). Hence, not all possible details may be included in an IACUC-approved protocol, and, when needed or requested, this information may be added by amendment. In addition, experimental outcomes can be unexpected, such that studies can produce unanticipated changes in animal health. In such cases, although there is not protocol noncompliance, it is prudent for the PI to collaborate with the AV and staff to devise changes in the protocol. Hence, many concerns that are related to animal welfare can be addressed by the submission and review of an amendment to assure that the activities and approved protocol are fully in concert. The amendment might request the deletion of a nonessential activity or may provide a more detailed description and detail of an activity. It might address a potential threat that was never anticipated before experiments were initiated. It might also seek the assurance of improved communications between the various persons who are involved in animal care and research. To avoid the excessive need for amendments, maximum flexibility should be built into the initially submitted and approved protocol. The IACUC Handbook recommends that "when faced with a possible protocol noncompliance, the IACUC's first step should be to determine if a revision to the protocol would make the activity compliant without compromising animal welfare" (12).

The IACUC should also note during their evaluation the degree to which it concludes that differences of professional opinion

or expertise underlie the allegation. It should be noted that the AWA specifically states that nothing in Section 2.31 shall be deemed to permit the IACUC to prescribe methods or set standards for the design, performance, or conduct of actual research or experimentation by a research facility. For example, a researcher may halt a protocol to allow time for interim data analysis or may do less than the IACUC-approved activities during the research upon evaluation by the researcher of the progress of the study and emerging needs. These judgments need not be considered noncompliance with the protocol. The possibility of honest or inadvertent error whenever evaluating allegations and complaints, as well as differences in professional opinions, should be considered. This evaluation should clarify the problem and lead to a proposed way of mitigating or resolving the problem.

Basis for findings

The evidentiary standard or burden of proof that most commonly applies to the IACUC and the animal care setting is the substantial evidence standard. Specifically, the complainant or the IACUC is required to provide enough evidence that a reasonable person would accept to reach a particular conclusion. Reasonable differences of opinion or misunderstanding by the IACUC of research practice in the respondent's field of study should not be the basis for an IACUC finding of misconduct or noncompliance. The activity must represent a substantial deviation from accepted norms (12).

Any protocol noncompliances that are relevant to the AWA and PHS Policy imply those that directly affect animals. Noncompliance issues that are unrelated to significant risk to animal welfare should be handled by protocol amendments or review for other needed clarifications, additions, or corrections, but some programs interpret noncompliance more expansively. State of mind—knowing, reckless, intentional—is an important consideration in determining whether noncompliance or protocol violations constitute misconduct, and appropriate sanctions.

Complainant or whistleblower protection

Protection against retaliation

The policy must provide protection for retaliation against complainants who bring forward good-faith, reasonable-belief charges of noncompliance or animal welfare concerns. The process for reporting concerns should include a description of a mechanism that provides for anonymous reporting and for compliance with applicable whistleblower laws and policies, including nondiscrimination against the concerned and reporting party, and protection from reprisals or retaliation against employees who participate in the reporting or investigation of allegations of wrongdoing on the basis of good faith and reasonable belief. In some institutions, a third party may be used to whom concerns can be directed in an anonymous way, and that party may handle additional interactions between the committee and the complainant. In general, anonymous reporting is disfavored and should be considered unusual. Many institutions have general compliance hotlines or the equivalent to provide for anonymous reporting. Sometimes such hotlines are administratively removed from the IACUC. The IACUC should work with such providers to ensure that options for reporting research misconduct and animal welfare concerns are available and that if any complaints about animals are raised, they should be directed to a point person within the IACUC. It is important that the complainant not be involved in the review or in any subsequent actions on the basis of accusations other than to provide information. The complainant, by virtue of the complaint, does not become an interested party in the determinations of the IACUC. Progress of the review or any additional information from the IACUC or institution may be made available to the complainant as warranted.

Protection for respondents

Due process

The IACUC must inform the respondent of the charges against him or her and allow an opportunity both to respond to the evidence put forward in support of the charge(s) and/or to put forward other evidence in defense against the charges. All evidence that is gathered should be provided to the respondent (PI usually) with the opportunity to review and comment on or to provide additional documentation. Outside experts should be consulted by the IACUC if it lacks expertise in the area of concern.

The respondent should have the opportunity to review the evidence and records with sufficient time to do so, and, after such review, be provided an opportunity to discuss the records with any fact-finding committee and the IACUC. The respondent, or such persons as may be involved, must have the opportunity to provide additional evidence or expert views and the right to have such information and viewpoints fully considered in the evaluation by the IACUC.

Standards for sanctions

Major sanctions against a respondent's research, such as temporary or permanent suspension of one study, of all studies of a research laboratory, or of a person who is involved in animal care and use, should rarely be taken unless the evidence demonstrates that the respondent knowingly and intentionally performed actions that jeopardized the welfare of animals. The past history of serious noncompliance (or lack thereof) that jeopardizes animal welfare should also be considered during deliberations. In most cases, measures to prevent similar or like infractions, additional training, and education, as well as increased oversight by the IACUC are appropriate IACUC recommendations.

IACUC findings, conclusions, and recommended actions that result from an IACUC investigation

Documentation of findings

Final decisions on noncompliance must be supported by evidence obtained *via* investigation and set out in a reasoned, timely, written report provided to the respondent. Any inconclusive or questionable aspects of the investigation should be removed from the report.

Mitigating factors should always be part of the IACUC's deliberations. For example, in its deliberations, the IACUC should consider evidence of self-identification and self-correction of noncompliance by a PI or facility director as evidence of the respondent's intentions.

The report should include a summary of the concern or allegation, the condition of animals and their environment, results of interviews, and results of a review of animal records and documents, together with any additional supporting documentation, such as correspondence, reports, and research records. It should also include detailed conclusions regarding the requirements of the AWRs, the PHS Policy, the *Guide*, and institutional policies and procedures and recommended actions. In all such proceedings, there should be a commitment to dignity and respect for all persons and a dedication to excellence in research and animal care.

Possible outcomes

The IACUC may conclude that: *1*) there is no evidence to support the concern or complaint of animal welfare breaches or serious risks thereof, *2*) certain aspects of the animal care and use program should be further reviewed, and *3*) the complaint is/was valid; however, no additional action is needed after the correction of the inadvertent error or issue, or, alternatively, that actions to prevent recurrence, including possible modification of the protocol, or suspension of activities are needed and specified.

Corrective actions

Recommended corrective actions should correspond with the severity of the adverse incident and the responsiveness and cooperation of the respondent. The goal should be compliance with the AWA and PHS Policy and appropriate animal care and use in research.

Suspension Although the AWRs and PHS Policy authorize the IACUC to suspend a previously approved activity, there is no requirement to do so, and the regulations are silent on any other sanctions (1, 3); therefore, it is recommended that IACUCs explore and adapt corrective actions other than suspension, and that suspension should be reserved for the most egregious acts, including willful and significant noncompliance with federal animal welfare–related regulations or the failure of the respondent to cooperate in a manner that negatively affects animal welfare or that is at significant risk of doing so.

Other corrective actions Examples of mechanisms and methods of corrective action before resorting to suspensions include, but are not limited to, the following, which do not require a vote at a fully convened meeting: counseling, mandatory training, changes in administrative or management processes to prevent recurrence, appropriate amendment to the animal use protocol, regular reports of the respondent to the IACUC, discussions (counseling) with the IO or other institutional management, official letters of reprimand, and direct veterinary or IACUC oversight or monitoring of animal procedures and/or record-keeping. Corrective actions that require time-dependent responses should clearly indicate the deadline dates for any response. These actions should be tailored to specific situations, as it can be difficult to utilize a one-size-fits-all approach when dealing with a variety of concerns.

The only corrective action for which a vote must be taken at a fully convened meeting with a majority vote of the quorum present is that of suspension of specific activities or what may amount to revocation of a person's animal use privileges. All other corrective actions can be set by a subcommittee of the IACUC or other designated IACUC group (and subsequent IACUC approval if needed by institutional policy). In addition, the results of its review may lead the IACUC to recommend other actions, such as changes in policies or procedures to prevent possible future noncompliance.

Referral to other processes

The IACUC may, as a result of its review, find evidence that violations of non–animal-related institutional policies and procedures, local, state, or federal statutes, regulations, or laws may have occurred—for example, scientific misconduct, misuse of monies, fraud, or theft. In such cases, those violations may be referred to the appropriate IO or committee.

Record keeping requirements: OLAW, FOIA, and Sunshine Laws

Records for noncompliance claims that subsequently substantiate serious or continuing noncompliance with the PHS Policy or the *Guide* should be kept in full, and should be secured and identified with a code or other method of masking identities in all records, minutes, and reports. During an inquiry or fact-finding period, the records—defined as a work in progress—are almost invariably not available under open records acts. As with the related reports to OLAW, such records should be kept for a minimum of 3 years or for the duration of a protocol plus 3 years. Those that are found to be unsubstantiated or that carry neither serious nor continuing threats to the welfare of animals should be expunged. If a report has been made to OLAW and the USDA/Animal and Plant Health Inspection Service (APHIS) and subsequently has been found to be unsubstantiated, a formal retraction by the IO to both should be followed by expunging the records of the institution and its IACUC, as well as any other agencies that have received a report.

Federal FOIA law requires that the OLAW, if asked, release such information as is in OLAW's possession or in the control of the federal government. Note that FOIA has some exemptions that may apply in some instances. States also have laws that may be referred to as sunshine laws or open records laws that direct disclosures, but states differ widely from each other. Certain information, such as names, addresses, telephone numbers, and other identifiers may be redacted in accordance with any applicable laws. Many institutions have detailed recommendations and procedures for handling such requests and these should be consulted as they differ between federal, state, and other nongovernmental institutions. Unless a statutory or court-created exception makes a record confidential, each public records request will likely require a fact-specific analysis under state law, noting that there is generally a strong presumption of openness. In summary, record-keeping and release provisions that are related to reports of noncompliance should be carefully crafted in keeping with all applicable laws.

Notification of outcome

IO

The IACUC must notify the IO of its conclusions, provide evidence that supports such conclusions, and recommend to the IO any additional notifications if indicated by the conclusions, including reporting of findings to OLAW, USDA, or other bodies as applicable.

Respondent

Notification of the proposed outcome of the IACUC review of alleged noncompliance should be in the form of an IACUC report to the respondent and, if required by institutional policy, to the respondent's immediate supervisor. This report shall include a copy of the evidentiary record, including access to data and any other evidence that supports the allegations, the investigative report, and recommendations to the adjudicating IO that include any proposed corrective actions. It is often useful for the respondent to propose a corrective plan to the IACUC when noncompliance is brought to the respondent's attention to assure that both the IACUC and the respondent are in agreement about corrective actions.

After notification of the IACUC's proposed findings and any recommended actions, the respondent should be asked to respond in writing—after a reasonable amount of time to review the outcome report—to indicate agreement with the IACUC's decisions and a plan to meet any corrective actions requested, a proposed alternative plan, or an intent to file an appeal.

When corrective actions have been met, the IACUC should provide documentation to the respondent and, if needed, to the respondent's supervisor, that the case is now closed.

Appeal to IO or other appeal committee

An appeal process is neither described nor required by the AWRs, the PHS Policy, or any related guidance documents provided by the regulatory agencies, such as OLAW (*e.g.*, NOT-OD-05-034). These policies deal strictly with noncompliance with the federal regulations that concern animal welfare, and do not deal with the protections of researchers from undue allegations. An institutional appeal process, however, is clearly an expectation of the NIH Office of Research Integrity in accordance with the Federal Research Misconduct Policy (13), which applies to research misconduct cases and should be in place for considerations of animal welfare–related allegations of wrongful conduct.

The right to appeal is a fundamental principle of fairness. Appellate review should examine whether the inquiry or investigation was conducted without bias and with respect for due process to the respondent, whether the process followed the rules, whether the regulations were correctly applied, whether the findings were accurate, and whether there were errors of interpretation or inappropriate corrective actions. An appeal procedure functions as a process for error correction and for clarifying and interpreting regulations. The right to a fair and unbiased appeal is a well-established American tradition. The appeal process should allow the respondent to have the finding of noncompliance reviewed and modified or reversed as appropriate. The appeal process should be defined in advance and included in an institutional policy that has been reviewed and agreed upon by all relevant parties—that is, IACUC members, IO, scientists, institutional counsel, and animal care personnel. The appeal policy should specify the composition of the appeal panel, provide for an independent and unbiased review, and set out the specific procedures to be followed.

Guidance on reporting to OLAW

As noted in Legal and Regulatory Requirements, if the IACUC finds that there has been a serious deviation from the *Guide* that may affect animal welfare or a significant noncompliance with PHS Policy, that finding is referred to the IO for reporting to the OLAW. Minor incidents that carry no likely impact on animal well-being may, upon the judgment and decision of the IACUC, not be reported or may be discussed with OLAW for additional guidance. This decision falls within PHS Policy that "empowers the IACUC and the institution to self-evaluate within a cooperative framework of OLAW's guidance and support." The IACUC and IO reporting policy should also contain a process for withdrawal and/or correction of any inaccuracies in the final report that are found after submission to OLAW.

CONCLUSIONS

- While fulfilling requirements of their animal care and use program, institutions have an obligation to their researchers and staff to have clear, written policies and procedures for considering allegations of noncompliance with the AWA or other key policies and regulations that govern the care and use of animals in research.
- Evaluation of allegations of noncompliance with the animal welfare–related regulations should provide for fundamental procedural fairness and assurance that the key concepts of due process are followed, including respect for the respondent's right to be informed of the allegations, to be provided with all evidence in support of the allegations, to challenge the evidence put forward, to provide alternative evidence or experts in defense against the allegations, to receive a reasoned, honest, and appropriate decision, and to appeal that decision on the basis of unfair procedures, incorrect findings, and/or incorrect application of corrective actions.
- IACUC members who are involved in considerations of noncompliance must be impartial and have an open mind concerning any allegation of wrongful conduct with animals. Conflicts of interest—potential, perceived, or actual—should be eliminated or mitigated/managed.
- As appropriate, complainant or whistleblower protections should be included in the written policies that govern the evaluation of reports of noncompliance.
- A defined appeal process should be available to address errors in the procedures followed or in the resultant conclusions.

ENDNOTES

*The AWA is as found in the United States Code, Title 7—Agriculture—Chapter 54—Transportation Sale, and Handling of Certain Animals, Sections 2131–2159 (*https://www.gpo.gov/fdsys/browse/collectionUScode.action?collectionCode=USCODE*). The AWRs are as found in the Code of Federal Regulations, Title 9—Animals and Animal Products—Chapter 1—Animal and Plant Health Inspection Service, Department of Agriculture—Subchapter A—Animal Welfare—Parts 1–4 (*https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR*). The AWA and AWRs have been reprinted together for ease of access in the "Blue Book" (3). The AWA, passed by Congress originally in 1966, was the first federal legislation to protect the welfare of laboratory animals and is the only federal law in the United States that regulates the treatment of animals in research and exhibition. It does not apply to birds, rats of the genus *Rattus*, or mice of the genus *Mus*, nor any cold-blooded animals. Where federal funds through the NIH or NSF are involved, OLAW provides oversight and an assurance process to assist institutions in meeting these obligations, while leaving specific policies and procedures to the research institutions. While DoD programs may have an assurance on file with OLAW (as do most research institutions in the United States), there is not currently a specific memorandum of understanding that places all oversight of DoD-funded research—at least outside of DoD facilities—under OLAW's authority as there is with NSF-funded research. Institutional assurances must currently state that the terms cover all PHS- and NSF-funded research conducted under the authority of the institution. DoD-funded projects are handled under a separate contractual agreement, and any noncompliance would be managed through DoD rather than directly through OLAW.

†As background, the federal government began to develop policies for handling research misconduct cases in the early 1970s, and in 1985 passed the Health Research Extension Act and its subsequent Final Rule, published in the Federal Register on August 8, 1989, as Responsibilities

of Awardee and Applicant Institutions for Dealing with and Reporting Possible Misconduct in Science (42 CFR Part 50, Subpart A.). Model institutional policies and procedures for handling such processes were published during the late 1980s and early 1990s (8, 9). In 1989, the U.S. Department of Health and Human Services Office of Scientific Integrity took over responsibility for overseeing policies and procedures for handling concerns about research integrity in federally funded projects, later reorganized to the current Office of Research Integrity with its Research Integrity Adjudications Panel of the Departmental Appeals Board. The Federal Commission on Research Integrity reported to the Health and Human Services and to Congress in a 1995 document, Integrity and Misconduct in Research (13). This document presented the Commission's recommendations considered to balance the interests of the federal government, research institutions, scientists, and the public, an obligation also assumed herein concerning the consideration of noncompliance in matters of animal welfare. Redman (14) has reviewed the Commission's findings and noted that the Commission's report was not adopted and that progress has been minimal in addressing the recommendations. Although the 1995 document, according to the Office of Scientific integrity, covers research that involves humans and animals, it was not specific to animal research; the procedures it detailed were designed to ensure the proper protection of both research subjects—humans or animals—and those accused of breaches of research integrity. Nevertheless, there continue to be concerns, recently heightened, about the ethics of science and irreproducibility of research, with specific recent attention to animal-based research.

[‡]After the PHS clarified several years ago that the federal definition of research misconduct extends only to fabrication, falsification, and plagiarism, institutions have had to determine what procedures would be used to address other claims of noncompliance with research rules and norms, including claims of noncompliance that involve the use of animal subjects in research and the welfare of such animals (AWA). AWRs and PHS Policy are silent on processes and procedures, and the *Guide* states that the IACUC is responsible for the "establishment of a mechanism for receipt and review of concerns involving the care and use of animals," but leaves the specifics generally to the institutions. The IACUC *Guide* dedicates one chapter to the evaluation of concerns with animal care and use, and recommends that the committee review be carried out in a systematic manner or procedure to verify concerns (15). It also contains guidance on potential conflicts of interest by IACUC members. Verified concerns should relate to the AWRs, the PHS Policy, or institutional policies, and there should be guidelines for effecting corrective measures when necessary. The *Guide* also states that, "depending upon the severity of the noncompliance or deviation from accepted practices, these range from counseling and mandatory remedial training to specific monitoring of animal use, temporary revocation of animal use privileges, or termination of employment." Some institutions may apply the procedures outlined in the PHS research misconduct model policy and procedures for fabrication, falsification, and plagiarism claims, which are designed to ensure a thorough, competent, objective, and fair response to animal welfare–related noncompliance allegations. Others may use processes that are specific to their IACUC operations, although it has been difficult to locate policy and procedural documents that outline processes that IACUCs and IOs follow in this regard, and the absence of clear standards for conduct and advanced notice of the penalties for misconduct themselves implicate due process and fairness concerns. It should be noted that since the publication of the *Guide*, federal, state, and institutional requirements for conflict of interest disclosure and management have significantly expanded and may occasionally impact the ability of some IACUC members to participate in IACUC reviews of potential noncompliance.

[¶]Due process is a concept that goes back at least as far as the Magna Carta of 1215, and the 5th (1791) and the 14th (1868) Amendments to the Constitution require fundamental procedural fairness for those who face the deprivation of life, liberty, or property, or in the present case of noncompliance, those who face the potential of closure of a laboratory and the loss of employment, pay, or resources. The 14th amendment states "nor shall any State deprive any person of life, liberty, or property, without due process of law; nor deny to any person within its jurisdiction the equal protection of the laws." Due process requires, at a minimum: *1*) notice, *2*) an opportunity to be heard, and *3*) an impartial tribunal. The idea has been incorporated that certain liberties are so important that they cannot be infringed without a compelling reason, no matter how much process is given. In the present instance, the due process policy of IACUCs and IOs addresses fairness and the availability of procedures provided by the institution, including what the institution may forbid or require, and procedural protections, such as notice and a hearing before termination of entitlements. Whereas details may be debated and differ across institutions, overall goals should not differ substantively. The key principles are procedural due process, substantive due process, and fair notice. The U.S. Supreme Court (Johnson *vs*. United States, 2015) reiterated and restated a vagueness doctrine, which when extended to and applied to the IACUC noncompliance situation and states that a regulation "so vague that it fails to give ordinary people (PIs) fair notice of the conduct it punishes, or so standard-less that it invites arbitrary enforcement" imperils due process rights. Furthermore, fairness requires that the IACUC disclose to the PI evidence that may suggest that the PI is innocent of the allegation of noncompliance, and, in addition, that fair notice and the opportunity to be heard are requirements of due process. FJ

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