The American Physiological Society: Instructions for Preparing Your Manuscript

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These instructions pertain to all of the American Journal of Physiology sections, as well as the Journal of Applied Physiology, the Journal of Neurophysiology, and Physiological Genomics. Please note that Advances in Physiology Education, Physiology (invited only), and Physiological Reviews (invited only) have specific instructions that you should review if you are submitting to them.

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Use applications capable of creating high-resolution PDF files. Figures should be generated at the size they are to appear in the journal (printed 1:1). 
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Use of Animals or People in Photographs
- Photographs of animals or people may be published when scientifically necessary to illustrate a setup or convey the findings of the paper. For a photograph of a person, a signed letter of consent is required from the person or their legal agent or guardian. 
- When a diagram is preferable to illustrate a setup, if it is not possible to obtain a drawing, the author should describe the setup in the methods section of the paper.
- Photographs to convey findings may be published when the data are conveyed in the image as in developmental biology or genetic modifications where such photographs are standard practice.
- With respect to other areas, the decision whether to publish a photograph will be based upon the editor’s determination whether the photograph is scientifically necessary.
- The journals should avoid publishing photographs that might be perceived as raising animal welfare concerns. For example, it is preferable to show only the relevant portion of the animal, and photographs should not show blood or people handling the animals except close-ups where only gloved hands are seen.

Tables
Whenever possible, authors are encouraged to submit figures rather than tables. Statistical summary tables should be submitted when possible, rather than tables with many lines of individual values. Lengthy tables of data that cannot be presented in a suitable manner, according to APS standards for print publication, may be extracted and set as a supplement to the online article. These supplements remain an integral part of the article for the reader, as referring text to these tables will remain in the article, and links directly to the supplements will be embedded and prominently indicated at all points of entry to the online article (see Data Supplements, below).
Submitted tables should adhere to the following guidelines:
- Tables must not duplicate material in text or figures.
- Tables should be numbered consecutively with Arabic numerals and prepared with the size of the journal page in mind: 3.5 in. wide, single column; 7 in. wide, double column.
- Each table should have a brief title; explanatory notes should be in the legend, not in the title.
- Nonsignificant decimal places in tabular data should be omitted.
- Short or abbreviated column heads should be used and explained if necessary in the legend.
- Statistical measures of variations, SD, SE, etc., must be identified. (Example: “Values are means ± SE.”)
- Table footnotes should be listed in order of their appearance and identified by standard symbols: *, †, ‡, § for four or fewer; for five or more, consecutive superior lowercase letters should be used.

Mathematical Equations and Modeling
Mathematical aspects of articles normally should be addressed to the many readers of the Journal who are not mathematicians. The presentation should include the mathematical strategy, the assumptions on which the mathematics are based, and a summary of the meaning of the final mathematical statement and its limitations.

Equations
Mathematical equations should be simplified as much as possible and carefully checked.

Use the slant line (/) for simple fractions \((a + b)/(x + y)\) in the text rather than the built-up fraction
\[\frac{a + b}{x + y}\]
which should only be used if the equation is offset from the text as in this example.
Use subscripts or superscripts wherever feasible and appropriate, to simplify the equations.
Please use notation that is consistent with the standard nomenclature in applied mathematics. As an aid to the reader, please state the convention that you are following, especially if it is uncommon.
Symbols should be defined as they first appear in the text, and a Glossary may be included (and helpful) in articles with many different symbols, specifying the units (dimensions) as well as each definition. The Glossary will usually precede the Methods section.
APS style allows punctuation in displayed equations.

Mathematical Models
Presentation of the model(s) must be sufficiently clear to allow physiologists with limited experience in modeling to follow the model development, limitations, and physiological relevance. Assumptions concerning the importance of physiological processes included in the model should be clearly stated.
If the model equation(s) require solution, the method of solution should be described in sufficient detail to permit readers to duplicate the solution in their own laboratories. Algorithms from commercial software libraries should be so identified. Details of the solution strategy may be summarized in an Appendix (for an example, see http://jap.physiology.org/cgi/reprint/96/1/65.pdf).
For simulations, sources or estimation methods for all parameter values should be presented and the numerical values given in the text or a table. A sensitivity analysis must be performed for important parameters (covering ranges of values relevant to the manuscript) to determine how the model predictions are affected by numerical parameter values.
If the model is used to estimate parameter values, measures of the uncertainties associated with the estimated parameter values should be presented.
For models intended for use in a predictive setting, validation of the model with a data set not used for model parameter estimation (i.e., cross-validation) is recommended. Sensitivity analysis or parameter uncertainty determination is an important component of modern modeling practice that allows assessment of the validity of a model.
Results obtained with the model(s) should be compared with appropriate physiological data, either from literature or from new experiments. Simulation results may be examined for prediction of changes or trends in physiological variables similar to those reported for in vitro or in vivo studies. The discussion should include information on the physiological significance of the model study, limitations of the model, and suggestions for new modeling and/or experimental studies.

Data Supplements
Video files, extensive tables of data, and other supplemental material that cannot be feasibly published in the printed journal may be submitted for inclusion in the online journal (without charge to the author). Such material must be submitted for peer review along with the finished manuscript and must meet the approval of the journal Editor.
Questions regarding data supplements may be directed to the Online Production Editor (mgentry@the-aps.org). For microarray data deposits, see above (MIAME Standard for Microarray Data).

Video
Authors are responsible for compiling their own digital video. Files should be in MPEG or Quicktime format and should be no more than 10 megs in size. Authors may be requested to resubmit their videos with shorter running time, smaller frame size, or lower resolution in order to conform to the recommended file size. Authors should include a written caption with each video file, explaining what is happening in the video. Contact the Online Production Editor (mgentry@the-aps.org) for further assistance or questions.

Long Data Tables
Long data tables should be submitted in Microsoft Excel or in Microsoft Word table format. Each table should include a title explaining what the table shows. Tables published online may look different from how they were originally submitted due to the limits of the HTML format.
Ethical Policies and Procedures

**Authorship.** The Editors of the journals of the American Physiological Society (APS) expect each author to have made an important scientific contribution to the study and to be thoroughly familiar with the original data. The Editors also expect each author to have read the complete manuscript and to take responsibility for the content and completeness of the manuscript and to understand that if the paper, or part of the paper, is found to be faulty or fraudulent, that he/she shares responsibility with his/her coauthors. The Mandatory Submission Form should be signed by each author. In cases in which obtaining a signature from each author would delay publication, the corresponding author’s signature is sufficient provided that the corresponding author understands that he or she signs on behalf of the other authors who have not signed the form. An author’s name can be removed only at his/her request, but all coauthors must sign a change of authorship agreement for any change in authorship (additions, removals, or change of order) to be made.

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**Prior Publication.** Material published by the author before submission in the following categories is considered prior publication: 1) articles published in any publication, even online-only, non-peer reviewed publications, such as Nature Precedings or the physics arXiv (see exception to this item for the Journal of Neurophysiology, at http://www.the-aps.org/publications/journal/apsetic.htm#jn_submission); 2) articles, book chapters, and long abstracts containing original data in figures and tables, especially in proceedings publications; 3) widely circulated, copyrighted, or archival reports, such as the technical reports of IBM, the preliminary reports of MIT, the institute reports of the US Army, or the internal reports of NASA.

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Authors with concerns about possible prior publication that does not fall clearly into one of these categories should contact the Director of Publications and forward the material for examination.

**Experiments Involving Animals or Humans.** Authors using humans, animals, fetal tissue, embryos, or embryonic cells in their experiments should refer to APS’s policies on those subjects. Links to these policies can be found at http://www.the-aps.org/publications/Authorinfo.

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If the infraction is less severe, the Editor, upon the advice of the Publications Chair, sends the author a letter of reprimand and reminds the author of APS publication policies; if the manuscript has been published, the Editor may require the author to publish an apology in the journal to correct the record. If, through the author’s actions, APS has violated the copyright of another journal, the Publications Chair writes a letter of apology to the other journal.

In serious cases of fraud that result in retraction of the article, a retraction notice will be published in the journal and will be linked to the article in the online version. The online version will also be marked “retracted” with the retraction date.

Updated March 2010.
GUIDING PRINCIPLES FOR RESEARCH INVOLVING ANIMALS AND HUMAN BEINGS

The research described in papers submitted to any of the APS publications that involve the use of human beings must adhere to the principles of the Declaration of Helsinki and Title 45, U.S. Code of Federal Regulations, Part 46, Protection of Human Subjects, Revised November 13, 2001, effective December 13, 2001 (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm). Research involving animals must adhere to APS’s Guiding Principles for the Care and Use of Vertebrate Animals in Research and Training. APS insists that all investigations involving humans or animals reported in its publications be conducted in conformity with these principles and that a statement of protocol approval from an IRB or IACUC or equivalent is included in the methods section of the paper. In describing surgical procedures, the type and dosage of the anesthetic agent should be specified. Curarizing agents are not anesthetics; if these are used, evidence must be provided that anesthesia of suitable grade and duration was employed. Editors/Associate Editors are expected to refuse papers in which evidence of the adherence to these principles is not apparent. They reserve the right to judge the appropriateness of the use of animals and humans in experiments published in the journals. Differences of opinion will be adjudicated by the Publications Committee.

WORLD MEDICAL ASSOCIATION
DECLARATION OF HELSINKI
Ethical Principles for Medical Research Involving Human Subjects

A. Introduction

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

2. It is the duty of the physician to promote and safeguard the health of the people. The physician’s knowledge and conscience are dedicated to the fulfillment of this duty.

3. The Declaration of Geneva of the World Medical Association binds the physician with the words, “The health of my patient will be my first consideration,” and the International Code of Medical Ethics declares that, “A physician shall act only in the patient’s interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient.”

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. Basic Principles for All Medical Research

10. It is the duty of the physician in medical research to promote the life, health, privacy, and dignity of the human subject.

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in compar-

ison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

20. The subjects must be volunteers and informed participants in the research project.

21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the subject’s information and to minimize the impact of the study on the subject’s physical and mental integrity and on the personality of the subject.

22. In research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject’s freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

C. Additional Principles for Medical Research Combined with Medical Care

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.

29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists. Note of clarification on paragraph 29 of the WMA Declaration of Helsinki: The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances: Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or Where a prophylactic, diagnostic or therapeutic method being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm. All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study. Note of clarification on paragraph 30 of the WMA Declaration of Helsinki: The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.

32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician’s judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

APS GUIDING PRINCIPLES FOR THE CARE AND USE OF VERTEBRATE ANIMALS IN RESEARCH AND TRAINING

As noted in the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training,1 “Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.” The use of animals is also justified to provide scientific, veterinary, and medical training that is not possible through other mechanisms.

Investigators should consider the appropriateness of the experimental procedures, the species of animals used, and number of animals required. Prospective approval of procedures on animal subjects should be obtained from an institutional animal care and use committee (IACUC) or similar oversight body as required under the relevant regulatory authorities. This review should also consider whether the use of animals in a given protocol could be replaced by other experimental approaches such as in vitro studies or computer modeling.

Only animals that are lawfully acquired shall be used in research and teaching. The procurement, transport, maintenance, and use of animals must in all cases comply with federal, state and local laws and regulations. In the United States, animal research may be subject to the Animal Welfare Act, the Public Health Service Policy on Humane Care and Use of Laboratory Animals, or other guidelines established by funding agencies. The PHS Policy requires institutions to use the Guide for the Care and Use of Laboratory Animals2 to develop and implement an institutional animal care and use program.

Analgesics and other techniques should be used to minimize discomfort and pain except when the intervention would compromise experimental goals. Appropriate anesthetics must be used to eliminate sensibility to pain.

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1 The Guiding Principles for the Care and Use of Animals in Research and Teaching were adopted by the American Physiological Society in 1953. They are based upon humane care principles formulated by Walter B. Cannon in 1909. The revision was approved by the APS Council on July 16, 2010.

2 URL: http://grants.nih.gov/grants/olaw/references/iphoph.htm#USGovPrinciples

during all surgical procedures. Drugs that produce muscle paralysis are not 
anesthetics. They must never be used alone for surgical restraint, only when 
animals are under anesthesia.

If the study requires the death of an animal, humane endpoints should 
be identified, and an approved method of euthanasia stipulated in the 
American Veterinary Medical Association’s Guidelines on Euthanasia⁵ 
should be used. Death is acceptable as the endpoint of a study only where 
euthanasia would compromise scientific outcomes and an IACUC or similar 
oversight body has approved the exception.

Animals used in research and education must be housed, fed, and 
maintained in a manner appropriate for their species and their condition. 
They should also be given appropriate veterinary care.

Personnel who care for or perform procedures on animals must receive 
training for these tasks. When students or trainees use animals in educational 
activities or for the advancement of science, such work shall be conducted 
under the direct supervision of an experienced teacher, investigator, or 
veterinarian.

The Publications Committee of the American Physiological Society gratefully acknowledges the services of the following reviewers who assisted the Editorial Board in the reviews of manuscripts.

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