

Guidelines for laboratory researchers at the Graduate School of Medicine of the University of Tokyo

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This document is intended as a guide to proper conduct by laboratory researchers affiliated with the Graduate School of Medicine at the University of Tokyo. It has guidelines in three main sections: planning laboratory research, conducting it, and reporting its findings. The increasing sophistication and diversity of research in medicine and life sciences has been accompanied by rapid growth in the complexity of the process of doing research. Many ethical, procedural, and organizational concerns are common to all the laboratory sciences, and the present Guidelines emphasize some that should be particularly important to scientists who are just beginning their research careers. In doing so, the present Guidelines are also intended to further improve the quality of the scientific research done at the University of Tokyo, to enhance the already-high regard in which the University is held, and to protect the University's rights to its research-based intellectual property.

SECTION 1: Planning laboratory research

What researchers should do before they begin their work (including applications for permissions, etc.):

Carefully read the "Code of Conduct for Scientific Research," which was developed by the Committee on Standards of Conduct in Scientific Research of The University of Tokyo. That document can be found at http://www.u-tokyo.ac.jp/public/pdf/180310_02.pdf and at <http://www.u-tokyo.ac.jp/ja/administration/codeofconduct/pdf/leaflet.pdf>. That Code of Conduct applies to all researchers who are affiliated with the University of Tokyo. To prevent and respond to violations of the Code of Conduct, a committee promotes compliance with the Code and prescribes actions to be taken if the Code is violated.

Appropriate use of research funds: It should go without saying that researchers must be careful to use research funds only in appropriate ways. This of course includes KAKENHI and other research funds obtained through competitions. Misuse of research funds is absolutely prohibited. For more information on this, carefully read the most recent edition of the KAKENHI handbook. A new

edition is released each year, and a version in English can be downloaded via the link at the bottom of http://www.jsps.go.jp/j-fellow/j-fellow_14/19_shorei_download.html or directly from http://www.jsps.go.jp/j-fellow/j-fellow_14/data/syorei/10.pdf.

Research involving humans: Everyone who expects to do research that involves human subjects (whether patients or healthy people) or samples taken from humans (including genetic material) must first attend the University of Tokyo's prescribed training in human-research ethics and must obtain a certificate of completion of that training. Before starting their research work, researchers must also understand the various Guidelines, etc. on this topic that are available via the Internet, which are introduced during the research-ethics training. Depending on the nature of the research, the researcher may need to first submit to the Faculty's committee on research ethics (<http://www.m.u-tokyo.ac.jp/ethics/ethcom/index.html>) the appropriate application for an examination of the proposed research from the standpoint of ethics, or for a research-ethics examination specific to studies involving human genetics. The Faculty's committee on research ethics must also give its approval before the research can start. After approval is obtained, if written informed consent of the people to be studied (the participants in the research) is needed, that consent must be obtained before the study begins. If circumstances require that the information in the application be changed before the study ends, the appropriate change-notification form must be submitted and approved.

Research involving (non-human) animals: Everyone who expects to do research that involves animals must first attend the designated training in animal experimentation and must obtain a certificate of completion of that training. Before starting any experiments on animals, the researcher must first prepare a written protocol, and must submit it to the Faculty's animal experimentation committee (researchers affiliated with the Center for Disease Biology and Integrative Medicine should submit protocols to the office of the Section of Animal Research within that Center). An experiment can begin only after it is approved by the department's animal experimentation committee and by the head of the department. Before planning animal experimentation, the researcher must carefully read the University of Tokyo's rules regarding animal experimentation and the University's animal-experimentation manual (refer to <http://www.adm.u-tokyo.ac.jp/gakunai/res/res1/kenkyoweb/bioscience/doubutuHOME.html>). The written protocol must clearly indicate that the researcher has fully taken into account the "three R's" of animal

experimentation: replacement (considering whether a substitution by another method is possible), reduction (using no more animals than necessary), and refinement (minimizing each animal's pain and suffering). If a change in the information provided in the application occurs before the study ends, the appropriate change-notification form must be submitted and reviewed.

Research involving recombinant DNA: All researchers who perform recombinant DNA experiments must do so with full knowledge of and in accord with both Japanese law (the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms) and the relevant University of Tokyo rules and regulations. Before starting any such experiments, the researcher must prepare the designated application form (application for approval of measures for containment) and must submit it to the Faculty's office in charge of bioscience research assistance, for consideration by the committee on genetically modified organisms. An experiment can begin only after it is approved by the Faculty's committee on genetically modified organisms and by the head of the Faculty of Medicine. Depending of the nature of the experiment, cabinet-level approval may also be required. Researchers must ensure that their facilities conform to standards. If a change in the information provided in the application occurs before the study ends, a change-notification form must be submitted. Researchers must attend all the necessary training sessions organized by the Faculty of Medicine and by the University, and must have full knowledge of the rules and regulations.

Research using ionizing radiation: As conditions for doing research involving ionizing radiation, researchers affiliated with the University of Tokyo's Faculty of Medicine and Graduate School of Medicine must register with the Faculty of Medicine's Office in charge of Radioisotope Control (*R.I.-kanrishitsu*), and must meet the following three requirements.

1. Twice each year they must undergo radioisotope handling training and practice (graduates of the University of Tokyo's Faculty of Medicine are exempt), and they must undergo the specified health examination.
2. Once each year they must attend the Faculty of Medicine's radioisotope lecture.
3. They must be included on the list of people who are planning to use radioisotopes, which is submitted once every three months by each laboratory's person in charge of radioisotopes to the office in charge of radioisotope control. Short-term users (i.e. users from the hospital or from other universities who will work in a laboratory for only a short time) must, every three months, submit a form requesting permission for short-term use of radioisotopes.

If you register for radioisotope use in a different Faculty or University and lose your eligibility to register for radioisotope use via your Faculty, you will automatically also lose your eligibility to use radioisotopes throughout the Faculty of Medicine, so be sure to attend the necessary Faculty's training sessions and to undergo the required health examinations. In addition, you will be required to attend the Faculty of Medicine's initial lecture and its additional radioisotope lecture once each year. For safe handling and use of radioisotopes, follow the three "C's": contain, confine, and control.

Contain: Keep radioactive materials in small spaces. Do not let them spread.

Confine: Use only the smallest amount of radioactivity necessary.

Control: Be precise and accurate when obtaining, using, and disposing of radioactive materials.

To avoid injury from exposure to gamma rays, X rays, and beta rays, follow these three guidelines: minimize the duration of exposure, stay as far away as possible from the radiation source, and interpose radiation-absorbing material between yourself and the source.

Invasive interventional studies done at the University of Tokyo Hospital: Before an invasive interventional study is done at the University of Tokyo Hospital, the Hospital's institutional review board (IRB) must be informed of the study's details, and permission to do the study must be obtained from the IRB. The IRB is part of the Hospital's Clinical Research Support Center <<http://www.cresc.h.u-tokyo.ac.jp/en/index.html>>.

Environmental safety in research: The Faculty of Medicine and Graduate School of Medicine has an office in charge of environmental safety (*kankyō-anzen-kanri-shitsu*) to ensure that appropriate and reliable safety measures are implemented. All faculty and staff involved in education and research must behave in ways that ensure not only their own safety but also the safety of others and of their surroundings, and they may be required to undergo safety-related training when they first become affiliated with the University. Also, before starting research you must be well-informed of the University's environmental-safety systems and all relevant national laws and regulations and University rules as indicated below.

1. Handling of chemicals and generation of waste from experiments:

To comply with the Industrial Safety and Health Act, the Basic Environment Act, and the law regarding the Pollutant Release and Transfer Register system, before starting research you must attend the environmental-safety lectures

organized by the Environmental Safety Research Center (*kankyou-anzen-kenkyuu-sentaa*), and you must have received a certificate of completion.

2. Storage of chemicals and waste management, safe handling of high-pressure gases and of laboratory equipment:

To comply with the Industrial Safety and Health Act, the University of Tokyo's rules regarding the handling of chemicals, the Narcotics and Psychotropics Control Act, the Pharmaceutical Affairs Act, the Fire Services Act, the High Pressure Gas Safety Act, the University's rules regarding the handling of high-pressure gases, and the University's own standards for handling high-pressure gases, you must attend the relevant lectures organized by the University's central Office of Environmental Safety (*kankyou-anzen-honbu*). These lectures cover the proper handling of chemicals, the proper handling of high-pressure gases, and the use of the University of Tokyo Chemical Registration Information System (UTCris), as well as the proper use, inspection, and maintenance of laboratory equipment (lasers, centrifuges, autoclaves, draft chambers). Because correct and thorough entries in the UTCris (for details, refer to https://utcris.adm.u-tokyo.ac.jp/CRIS_v1_0/index.aspx) are essential for the proper University-wide management of chemicals and high-pressure gases, even researchers who have completed the required formal training are strongly urged to receive instruction and guidance from their own laboratory's person in charge and manager of health and safety.

3. Ensuring safe working conditions:

Occupational-health physicians regularly inspect workplaces to prevent accidents, fires, environmental pollution, etc. in compliance with the Industrial Safety and Health Act and the Fire Services Act. Those employed at the sites of such inspections should cooperate with the inspectors' work and seek to comply with their instructions for improvement. The laboratory's health and safety manager is present during repeat inspection(s) and cooperates with the inspector(s) to ensure compliance with their instructions.

In the event of a fire, explosion, or other such accident or emergency, consider how urgent the situation is, and take appropriate action. As soon as possible, notify the proper authorities: the police or fire department, University Security, the Faculty of Medicine's Emergency Response Center (*bousai-sentaa*), the Faculty of Medicine's General Affairs Office (*shomu-gakari*), or the Faculty of Medicine's Office of Environmental Safety. Reports on accidents and

emergencies are submitted online via the University of Tokyo's Safety Management & Information System (UTSMIS, <http://utsmis.adm.u-tokyo.ac.jp/UT_Anei_User/Report/Accident/>) and approved by the Office of Environmental Safety.

Participation in consortia and other large-scale projects:

You should explain the present Guidelines to your collaborators and research partners and discuss them beforehand to ensure the credibility of the research findings and assign respective rights appropriately.

Important point #1: Begin experiments only *after* permission to do so has been granted.

The application procedures described in these Guidelines may take time, but you may not start experiments until *after* the applications have been approved. Even if an application seems to be simple or a mere formality, do not assume that permission will be granted, and never start an experiment without permission to do so.

SECTION 2: Conducting laboratory research

What researchers should do while their work is in progress (including Guidelines regarding laboratory notebooks, etc.)

- Confirmation of your research's originality and creativity: You should be constantly collecting information that attests to the originality and creativity of your research work.
- Experimental validity: New discoveries generally require confirmation via at least two different methods (for example, obtaining consistent results in biochemical, physiological, and histological experiments).
- Reproducibility: You should be able to obtain non-contradictory data from multiple experiments done separately.
- Appropriate controls: Any experiments done without the necessary controls will have to be done over.
- Appropriate statistical analyses: Use appropriate statistical analyses. Evaluate objectively the statistical significance of your findings.

Points to keep in mind regarding records of experiments (laboratory notebooks, etc.): Laboratory notebooks should include as much detail as possible. They should include enough information to permit a researcher who reads them to do follow-on studies. One can even go so far as to say that new discoveries depend on both deep insights and careful records.

What must be recorded?

- Laboratory notebooks (written accounts of each experiment's purpose, methods, results, and conclusions)
- Raw data (those that cannot be attached to a laboratory notebook, including long base sequences, image data, etc.)
- Information obtained from outside providers of materials or services (including records regarding the breeding and rearing of experimental animals, reports on the conditions under which purchased antibodies were manufactured, etc.)

Points to remember when writing in laboratory notebooks

- Use A4 paper for everything. Whatever format you choose, you will find it convenient to number all the pages and to begin with a Table of Contents. Each laboratory notebook should also have a serial number.
- In principle, laboratory notebooks should be bound (i.e., in book form). For simple day-to-day memoranda regarding experiments, a loose-leaf binder is appropriate.
- Entries in laboratory notebooks should be made in indelible ink. Do not use pencil.
- Your penmanship need not be attractive, but your writing must be legible. Undecipherable entries are meaningless.
- For each entry, be sure to include the date (years should be written AD) and, if it is not already printed on the page, the page number.
- Do not leave large blank spaces. To prevent blank spaces from being filled in at a later date, draw lines through them or write something such as "End of this note." or "No further notes on this page."
- If you need to correct a mistaken entry, draw two lines through the section to be corrected (ensuring that the original entry can still be read) and write the correction above, below, or to the right-hand side of it. Do not use correction fluid or correction paper.
- When you begin an experiment, write its title and purpose in the laboratory notebook: What are you trying to understand or clarify? What question are you trying to answer? How would you interpret the various results that you might obtain?
- If you need to attach any materials or documents, use paste or glue.
- Be sure also to record your interpretations. It is particularly important for you to record any ideas or other relevant thoughts you have while doing the experiment, even if they are not directly related to that study.

These written records of your ideas could prove to be very useful for planning future research and in obtaining patents.

Record the brand name and the lot number of any reagents used. This is particularly important for reagents not commonly used in that laboratory. Once the reagent's container is empty, you may remove the label and attach it to a page in the laboratory notebook.

If you receive any samples from someone else (whether that person is in the same laboratory or not), you must record what you received, how much of it you received, when you received it, and from whom you received it. If you received it together with a letter or other document, be sure to include that in the laboratory notebook.

Other important points regarding laboratory records

You must have a written protocol before you start any experiments. At the start of any new experiments, you should write a protocol that includes the following: the purpose of the study, the methods and procedures, the reagents and equipment required, and the approximate budget needed. Then you should fully discuss the protocol with the relevant staff members or directly with your advisor. That protocol must be attached to the laboratory notebook.

As much as possible, data that can be stored in electronic form should also be printed and stored on paper. This includes base sequences, data from fluorescence-activated cell sorting, data obtained by microscopy, etc. If the paper records of such data are too large to be attached to the laboratory notebook, they should be bound in files and the location of those raw data files should be recorded in the laboratory notebook. The name of the person in charge of the experiment should be written on those paper records. If the date on which the data were printed is not already on those records, that date must be written in by hand.

The date on which the data were collected, the name of the person doing the experiment, and any other information that might be needed to analyze the data or interpret the results must be included together with all raw data. Ideally, that information and the raw data should be included in or attached to the laboratory notebook. If that is not possible, then it can be stored by some other method: in a loose-leaf binder, bound in clear folders, etc. When stored separately from the laboratory notebook, a smaller-size (photocopier-reduced) copy of the raw data and other information should be attached to the laboratory notebook and the

location (file number, etc.) of the full-size paper copy should be written in the laboratory notebook.

If the experiment involves x-ray films, copies of them should be attached to the laboratory notebook and the originals should be stored in special-purpose clear files or other appropriate containers. Don't forget to record their storage location in the laboratory notebook. The date on which the film was exposed (including the year in AD) and the name of the person doing the experiment should be recorded on the film.

Of course it is also extremely important to preserve many files other than the laboratory notebooks described above. On the front cover of each file, be sure to record the name of the user, the topic or contents of the file, and the date (including the year in AD) on which the file was made.

Records kept in electronic form are particularly susceptible to loss (erasure), and thus require special efforts to prevent falsification through overwriting, etc. Some kinds of data (examples include image data and very long base sequences) would be qualitatively different if stored on paper, or would require extremely large amounts of paper. Because such data would be very inconvenient to store on paper, they may be stored in electronic form.

Important point #2: Remember that laboratory notebooks belong to the laboratory where they were produced.

All researchers should understand clearly that laboratory notebooks are not the property of any individual researcher; they are the property of the laboratory where they were produced. In principle, when a researcher moves from one laboratory to another, laboratory notebooks written by or used by that researcher must remain in the original laboratory.

SECTION 3: Reporting laboratory research findings: writing and submitting manuscripts

Author information: Be sure to enter every item of required information, including each author's affiliation with related research projects, etc.

Selection of co-authors: Decisions about co-authorship must take into account the degree to which the potential co-author contributed to the research. Consent to co-authorship should also be obtained (including agreement on the order in which co-authors are listed). Do not invite anyone to be a co-author until after that person has read the manuscript.

- Handle citations carefully. Ensure that your citations from previous research are fair and note the source explicitly.
- Be care when writing your Acknowledgements. Thank people who made your work possible (for example, anyone who provided you with samples), as well as any organizations that provided funding, but not co-authors. Before you include anyone in the Acknowledgements, obtain their permission for you to do so. If your research was supported by KAKENHI, be sure that your acknowledgement of that funding follows the example in the KAKENHI handbook. In the 2010 edition's Japanese version, the example is on page 21. In the 2010 edition's English version, this is covered in section 14, on pages 34 and 35 (slides 37 and 38 in some PDF viewers).
- Depending on the type of experiment you have done, you may need to include an explicit statement that your research was approved by the University of Tokyo's committee on research ethics or by the University's committee for evaluating the ethics of human-genome research. If your experiment involved (non-human) animals, you should include the statement "This research was done in accordance with the University of Tokyo's guidelines regarding animal research."
- Materials received from outside: When reporting results of experiments done using materials obtained from outside the University of Tokyo, be sure to adhere to the provisions (such as prior approval) of the relevant contract or material transfer agreement (MTA), and be sure to mention the source of the materials in the Materials section of the report.
- Obtaining consent to report results: Before reporting results of experiments done using materials obtained from a pharmaceutical company or similar organization, be sure to obtain the consent of that company or organization.
- The corresponding author takes full responsibility for matters related to a submitted paper, including the points mentioned above.
- Upon request, you may provide biological materials, recombinant genes, antibodies, reagents, etc. related to experiments and findings that have been made public. Keep in mind, however, that Japanese law may prohibit you from allowing certain samples to leave the laboratory or the University.

Important point #3: Handle data from experiments appropriately.

Reporting the same findings (which includes Figures, Tables, etc.) in more than one original research article (i.e. dual publication) is prohibited. Occasionally

one finds that a Figure showing control results has been used in more than one paper, but in an original article that is unacceptable. Be sure to avoid excessively retouching, altering, or manipulating Figures. Occasionally one finds that Photoshop® or other such software has been used to unnecessarily alter a Figure. For example, when SDS-PAGE is used a non-specific band may appear, but you are not allowed to erase that band. Some journals check for such alterations before a paper is published. If excessive alteration is detected, the journal may refuse to publish the paper in question and the journal may temporarily refuse to consider other papers by that author.

Important point #4: Keep in mind and disclose all conflicts of interest (COI).

Do your research in accord with the COI-related guidelines of the Japan Association of Medical Sciences and of all other relevant groups. When writing a manuscript and preparing it for publication, bear in mind and carefully consider any COI, and comply with the requirements for disclosure.

When researchers affiliated with an endowed department report the results of their work they should include the complete, formal name of the institution with which they are affiliated and they should clearly acknowledge, by name, the company that is the source of their funding. When writing in Japanese, include an acknowledgement such as this: “謝辞：X X X 寄附講座は、Y Y Y 製薬の寄附金にて支援されている。” When writing in English, include an acknowledgement such as this: “Acknowledgement: The department of XXX is an endowed department, supported with an unrestricted grant from YYY.”

If funding for the research being reported has been received from more than one company, then, to ensure transparency, the acknowledgment should list the name of every company from which funding was no less than a certain sum (e.g., every company that contributed 2 million yen or more).

What should be done when a report is submitted for publication: Long-term storage of laboratory notebooks and raw data (copies, etc.)

All of the following should be copied and kept on file in each laboratory: the findings used to make all Tables and Figures in all papers published or submitted for publication (including numerical findings in the text of the paper and data referred to as “data not shown”), all primary and secondary data, the experimental protocol(s) used at the time those data were collected, all records of materials used in the experiments, notes on the experiments, etc. Decisions regarding what is to be copied and kept should be made by the person in charge of the experiment in consultation with the principal investigator.

□ Preserving samples (for example, samples to be provided on request): When a report is submitted for publication, the principal investigator and the people in charge of the experiments should together decide which of the materials used in that study are important to preserve (e.g., genes, expression plasmids, antibodies, proteins). These materials become the responsibility of the principal investigator.

· Applying for patents: Applications for patents based on findings of your research should be filed as early as possible. If possible, they should be filed before the findings are presented at conferences or published in any form. Applications for patents should be reported to the Department of Intellectual Property (*chiteki-zaisan-shitsu*). For basic-science research, that is done via the Faculty of Medicine's Research Support Section (*kenkyuu-shien-gakari*). For clinical research, it is done via the University of Tokyo Hospital's Public Relations Center (*paburikku-rireshon-sentaa*).

· Bear fully in mind that once your research findings are made public through presentation or publication, they may lose patentability. In Japan, however, application for a patent can be made up to 6 months after research findings on which the application is based are presented at a meeting (within 6 months after distribution of an abstract) or published.

Further information (in Japanese) on the relevant patent law can be found at <<http://www.jpo.go.jp/index/tokkyo.html>>.

Important point #5: All co-authors must agree on a manuscript before it is submitted for publication.

Before a manuscript is submitted for publication, each co-author must receive a copy of the manuscript and must agree to be included as a co-author. Some journals require all co-authors to sign statements declaring conflict(s) of interest, agreeing to transfer of copyright, etc. To avoid trouble, ensure beforehand that you adhere strictly to the requirements of the journal to which you submit your manuscript. Remember that being included as a co-author is not necessarily desirable; some researchers may prefer not to be co-authors of your paper. If you are asked to be a co-author, be sure to read the paper before it is submitted for publication and to promptly inform the author inviting you to become a co-author whether you do or do not agree to be included among the co-authors. Bear in mind that co-authors share responsibility in the event that any problems should arise.