

1. Guideline for Conflict of Interest Management for Medical Research (proposal)

**The Japanese Society of Pathology
Medical Ethics Committee**

I. Introduction

In order to contribute to our society, through citizen educational programs, and by conducting educational programs for its members and providing its members with the opportunity to attend conferences and present the results of both basic and clinical research conducted by members, the Japanese Society of Pathology aims for improvements in the clarification of the etiology and pathology of diseases, as well as advances in the prevention, diagnosis and treatment of disease.

In Japan at the present, based on the policy of vitalizing the country through the establishment of Japan as a leader in the science and technology fields, there are a variety of programs and movements underway, being conducted as strategic government policies, and liaison between the industrial, academic, and government fields has been strengthened. The restoration of the results of research produced by universities, research organizations, and academic societies to society is of vital importance for the vitalization of the economy, as well as for ensuring security, safety and a good life-style standard for the citizens, and at the same time, it is significantly important for the vitalization of the source of those results, the education and research fields. In the local districts, as liaison between the industrial and academic fields increases, we have seen that the public organizations, such as universities and academic societies, develop deeper relationships with specific enterprises, and it is inevitable that the social responsibility of scientific organizations and foundations in the fields of education and research and the issue of personal benefit that arises along with liaison activities between the industrial and academic fields come into conflict. This situation is described by the phrase "conflict of interest" (COI), and there has been an increasingly strong demand for academic organizations and societies active in the fields of education and research to implement appropriate management of any latent COI situation for researchers employed at such organizations, in order to ensure that human rights and the safety of persons participating as the subjects of clinical studies are protected as part of the duties of those organizations.

The development of COI began in Japan in July of 2004, in a panel discussion sponsored by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), titled "COI Measures for Clinical Research and Clinical Trials," where the importance of the COI issue related to clinical research was confirmed. Accordingly, MEXT established a commissioned study group entitled the "Study Group on the Theory of Clinical Research and Conflicts of Interest," and in March of 2006, a "Guideline for the Drawing Up of Policies Related to Clinical Research and Conflicts of Interest" was announced. The aim of this guideline was to define rules of conduct aimed at researchers engaged in clinical research in situations where the researchers were operating under conditions of an economic conflict of interest, and by establishing these rules at each of the universities, research organizations, hospitals and academic societies, etc., concerned, maintain the prestige and results of the organizations and individuals involved in research employing human subjects while ensuring the related social trust. Accordingly, the aim of this guideline extends to ensuring that the researchers involved could be confident that they were operating in a just environment, and concentrate on conducting their clinical research freely at a high level of quality. Thereafter, in 2008, the Ministry of Health, Labour and Welfare announced a document entitled "A Guideline for COI Management for Scientific Research Related to Health, Labour and Welfare," which expressly stipulated the duties related to COI management aimed at researchers receiving grants or other funds for the research concerned.

Recently, there has been a trend seen worldwide for nations to implement strategic promotion of translational research applied in a clinical setting, rather than basic seed research, and in the midst of this transition, the type of research targeted for COI management has not been limited to just clinical research or clinical trials employing human subjects (including treatment studies), but rather expanded to include basic life-science research conducted through liaison between organizations in the academic and industrial fields. In other words, the trend is for persons involved in basic research conducted by private organizations or profit-based foundations or other organizations through liaison between the academic and industrial sectors to submit a report on their personal economic COI situation. In view of this trend, the Japanese Society of Pathology decided to define the types of research that require COI management as "Medical Research," covering a wide variety of research fields conducted through liaison between organizations in the academic and industrial fields, such as research on the improvement of disease prevention, diagnosis, and treatment methods, the improvement of the clarification of the etiology and pathology of diseases, as well as the improvement of patient's daily life, including life science research, basic medical science research, clinical medical science research aimed at human subjects (including research that employs personal information or other data from which individuals can be identified), and clinical trials.

In consideration of its social responsibility and the demand for a high standard of ethics, the Japanese Society of Pathology determined to produce this Guideline for Conflict of Interest Management for Medical Research (hereafter, the Guideline). Through the provision of appropriate COI conditions for its members, the purpose of the Guideline was to ensure that our efforts to create venues for the presentation of research results, and promoting the spread of those results, as well as for member education, will be appropriately continued honorably in conditions of neutrality and thus fulfill our social responsibility to contribute to progress in the prevention, diagnosis and treatment of disease.

The main point of the Guideline is to inform the members of the Japanese Society of Pathology of the fundamental concepts related to COI, and when members of the organization are involved in a project conducted by the Japanese Society of Pathology, ensure that the members submit a public COI report in order to maintain the COI conditions appropriately. Members of the Japanese Society of Pathology must observe the policies shown below, and actively promote progress in medical research.

II. Basic concepts related to COI

A COI situation in a medical research organization can impact the rights of patients, their life or safety. In addition, when treatment methods are devised in basic research or in an onsite medical treatment setting, if the researcher is performing basic medical research, a clinical trial or treatment trial under liaison between academic and industrial organizations, and especially considering the special circumstances that venture companies are often involved in when producing new products based on these plans, the inevitable result is the rise of a COI situation. However, the appearance of an economic COI situation is not an issue in itself, rather it is important to construct a system providing for appropriate management at the institute, organization or academic society concerned in order to ensure that inappropriate medical research is not conducted.

In the field of medical research, in regard to clinical research and clinical trials aimed at human subjects, transparency reliability and specialty aspects have already been guaranteed by the use of appropriate COI management. In the "Guideline for Ethics in Clinical Research" issued by the Ministry of Health, Labour and Welfare, the explanation is "Under no circumstances whatsoever should the nature of the research become warped due to a conflict with the interest of the researcher concerned," but based on the situation in regard to clinical research in Japan, "If all research that had a reciprocal economical interest with a private organization was shut down, it may be considered that

this would be an obstruction to the development of pharmaceuticals and drugs, etc." As shown here, in the field of medical research, especially clinical medical research and clinical trials, the ethics and specialty aspects are very important, and as the research is differentiated because it is aimed at human subjects, there is somewhat of a different characteristic involved, compared to the usual COI issue. Therefore, it may be considered that the major prerequisite here is first to overcome that different characteristic in an appropriate manner, and in order to prevent any potential COI situation from developing into a serious issue, assure that medical research aimed at human subjects is conducted appropriately with a high degree of transparency.

In COI management related to medical research, information regarding the economic interests (funds, etc.) or other related interests (status or concessions) offered to the researchers involved by enterprises, public organizations engaged in profit-making endeavors, or foundations must be disclosed appropriately within the system. In the performance of basic medical research, clinical medical research, or clinical trials (including treatment trials), it is desirable that this information is offered and disseminated appropriately and that the information offered by the researcher concerned can be objectively judged and evaluated. Furthermore, individuals in positions performing medical research who conduct themselves in any manner that damages the reliability of the research concerned or that threatens the safety of the subjects participating in a clinical medical research project must not be allowed to reap any personal benefits or proprietary rights. In order to assure this stipulation, COI situations must be avoided or a third-party supervision committee employed to assure that the medical research is performed appropriately. Furthermore, in regard to academic societies, the personal financial benefits of the researchers concerned or related interests must be disclosed appropriately, and accordingly, all educational and research activities must be promoted based on the principles of impartiality, independence, objectivity, and rigorous scientific procedures.

III. Persons subject to the Guideline

The Guideline will apply to any person in the following list, when a COI situation may arise.

1. Members of the Japanese Society of Pathology
2. Executives of the Japanese Society of Pathology (Chairman of the Board of Directors, Directors, Auditors), Chairperson of the General Assembly, the Chairperson of the various committees, members of special committees (Academic Affairs Committee, Editorial Committee for the Society's Journals, Committee for Diagnosis Guidelines, Medical Ethics Committee), and committee members of provisional work section meetings (subcommittees, working groups, etc.)
3. Persons giving presentations at the General Assembly of the Japanese Society of Pathology, persons appearing at scientific meetings sponsored by the Japanese Society of Pathology, and authors being published in the Society's bulletins or either of the Society's journals
4. Staff employees of the Japanese Society of Pathology

IV. Activities subject to the Guideline

The Guideline applies to all participants of all of the activities conducted by the Japanese Society of Pathology (hereafter, the Society) as enumerated below.

1. Academic meetings and conferences (including annual general assemblies), academic lecture meetings, and academic meetings sponsored by each of the Society's local branches
2. Bulletins, journals or books published by the Society
3. Diagnosis guidelines, and the drawing up of manuals, etc.

4. Authorization of certified pathologists and in-service training facilities, etc.
5. Performance of research or studies
6. Promotion of research and public prizes for research results
7. Promotion of international research activities
8. Other activities, and duties necessary to accomplish the goals of the Society

Furthermore, even when members of the Society are engaged in activities not related to the activities of the Society, members must observe the Society's COI policies.

V. Items that should be disclosed and open to the public

When persons subject to the stipulations shown below as items No. 1 through No. 7 find that they meet or exceed the criteria, defined elsewhere, for a COI situation, it is their duty to use the prescribed form for a COI situation, and voluntarily file a report disclosing the situation accurately. In addition, it is also the duty of persons subject to these stipulations to file an accurate report on the situation to the Society when they find that either one's spouse, any member of their immediate family, or a joint owner of any earnings or property, as applies to items No. 1-3 below, exceeds the criteria defined elsewhere. Furthermore, the person filing the report is responsible for its content. Details on the disclosure method will be separately defined in the subsidiary rules and regulations for subject activities.

1. Persons employed as an executive or an adviser for a private enterprise or a profit-making organization
2. A stockholder of the organization concerned
3. Persons who receive a patent royalty from a private enterprise or a profit-making organization
4. Persons who receive a daily allowance paid for attending a meeting (giving a presentation at the meeting) or any allowance for time or effort expended by a researcher from a private enterprise or a profit-making organization
5. Persons who receive a manuscript fee for writing a pamphlet, etc. for a private enterprise or a profit-making organization
6. Persons who receive any research funds offered by a private enterprise or a profit-making organization
7. Other remunerations (not directly related to research, such as travel expenses or presents)

VI. Avoiding COI situations

1. Items all subjects should avoid

The presentation of the results of medical research should be based purely on scientific conclusions and conducted solely in the public's interest. In regard to decisions on whether or not the results of any medical research should be presented in a written paper or verbally at a medical conference and also in regard to the essential nature of any medical research results and the interpretation of those results, members of the Japanese Society of Pathology must not be influenced by the arbitrary intention of any person or organization providing financial support for the medical research, or enter into any contract that would make it impossible to avoid any such influence.

2. Items the person responsible for a clinical trial or clinical research should avoid

Persons selected to be responsible for a clinical trial with decision-making authority in regard to the planning and performance of clinical research, including clinical trials and treatment trials (not applicable to the principal physician in charge of each of the facilities at a multi-facility clinical research project) should be free of all of the COI situations listed below, and after they are selected, they should avoid these situations.

1. The assumption of office as an executive or advisor or being a stockholder for a company or person providing funds for the medical research (excluding a scientific advisor without compensation)
2. Ownership of patent rights or the reception of patent royalties related to medicines or medicinal supplies, treatment methods or study methods, etc. related to the clinical research themes concerned
3. The reception of payment of travel or accommodation expenses for participation in an academic meeting not related to or necessary for the research concerned from a company or person providing funds for the medical research
4. The reception of expenses far exceeding that necessary for the research concerned
5. The reception of payment or gifts exceeding that considered fair compensation for the time and effort spent on the research concerned

However, even if the person concerned is applicable under the conditions listed above, if the person concerned is considered absolutely necessary for the planning or performance of said clinical research, and the research is considered extremely important and significant from an international viewpoint, the person may be assigned as the physician in charge of the clinical trial for the research concerned.

VII. Implementation methods

1. Roles for members of the Japanese Society of Pathology

When members of the Japanese Society of Pathology present research results at academic meetings, etc., they must assume the duty of appropriate disclosure of their COI situation related to the performance of the research concerned. The disclosure must be conducted using the prescribed forms specified in the subsidiary rules and regulations. When there is a question in regard to a COI situation going against the items specified in the Guideline, the Medical Ethics Committee in Charge of COI Management (hereafter, abbreviated as the Medical Ethics Committee) will deliberate on the issue, and submit a report to the Board of Directors.

2. Roles for executives and members of the Japanese Society of Pathology

The Directors, Auditors and the Chairpersons of each of the various committees of the Japanese Society of Pathology play important roles in all of the activities of the Society, carrying a heavy responsibility, and in regard to COI situations related to the activities of the Society, they are obliged by duty to submit a report on their COI situations from the time they assume their various positions.

In regard to meetings of the Board of Directors, the executives of the Japanese Society of Pathology (Chairman of the Board of Directors, Directors, and Auditors) are responsible for the execution of all of the activities of the organization, and when a serious COI situation arises, or when a report reveals an inappropriate COI situation, an inquiry will be submitted to the

Medical Ethics Committee. Improvement measures, etc., can be indicated based on a report from the Medical Ethics Committee.

When members of the Japanese Society of Pathology present medical research results, the chairperson and members of the Program Promotion Committee will verify whether or not the presentation is in accord with the Guideline, and the Committee can order the halt of any presentation that is not in agreement with the Guideline. When this occurs, the person(s) scheduled to give the presentation must be notified immediately of the action, along with the main relevant reasons. Furthermore, the Medical Ethics Committee will deliberate on this issue, and submit a report to the Board of Directors, which must approve the action before it is implemented.

When the results of medical research will be published in one of the Japanese Society of Pathology's journals, the Editorial Committee for the Society's Journals will verify that the paper is in accord with the Guideline, and the Committee can order the halt of the publication of any paper that is not in agreement with the Guideline. When this occurs, the author of the paper must be notified immediately of the action, along with the main relevant reasons. When it becomes clear that the paper concerned is in fact not in agreement with the Guideline after it has been published, the publication concerned may publish a public notification to that effect under the name of the Chairperson of the Editorial Committee for the Society's Journals. Furthermore, the Medical Ethics Committee will deliberate on this issue, and submit a report to the Board of Directors, which must approve any action before it is implemented.

The Chairperson and committee members of other committees of the Society must verify that the various activities of the Society and their performance are in agreement with the Guideline, and when there is any doubt that either goes against the Guideline, they must immediately study improvement measures. Furthermore, the Medical Ethics Committee will deliberate on this issue, and submit a report to the Board of Directors, which must approve any measures before they are implemented.

3. Filing an objection against a prohibition order

Persons who receive a prohibition order against a publication or presentation according to stipulation No. 1 or No. 2 above may file an objection with the Japanese Society of Pathology. When the Chairman of the Board of Directors of the Japanese Society of Pathology receives any such objection, he will immediately establish an Objection Judgment Committee, which will deliberate on the issue and report to the Board of Directors. The Board of Directors will deliberate on the issue and notify the person filing the objection of the results of their investigations.

VIII. Measures taken against the indicated Guideline offender and the responsibility for explanations

1. Actions implement against Guideline offenders

The Japanese Society of Pathology reserves the authority to deliberate on behavior in violation of the Guideline as specified in the rules and regulations specified by the Society elsewhere. An inquiry regarding related matters will be submitted to the Medical Ethics Committee and a report issued by the Committee will be submitted to the Board of Directors. When deliberations conducted by the Board of Directors based on that report indict that there has been a serious violation in conflict with the Guideline, actions may be implemented, in

accordance with the seriousness of the violation as shown below, either all items or in part, as required.

1. All presentations at academic and lecture meetings sponsored by the Society will be prohibited.
 2. All publications of any paper in printed material issued by the Society will be prohibited.
 3. The assumption of office as a Chairperson at academic and lecture meetings sponsored by the Society will be prohibited.
 4. Participation in the Board of Directors, any committee or work section of the Society will be prohibited.
 5. The person will be removed from the position as councilor, or the assumption of the post of councilor will be prohibited.
 6. Suspension of the qualification for membership in the Society, expulsion from membership in the Society, or prohibition of becoming a member
2. Filing an objection

Persons considered in violation of the guideline can file an objection against the ruling with the Japanese Society of Pathology. When the Chairman of the Board of Directors of the Japanese Society of Pathology receives any such objection, he will immediately establish an Objection Judgment Committee, which will deliberate on the issue and report to the Board of Directors. The Board of Directors will deliberate on the issue and notify the person filing the objection of the results of their investigations.

3. Responsibility for explanations

When it is considered that there has been a serious violation of the Guideline related to the presentation or publication of the results of medical research at locations involved with the Japanese Society of Pathology, a meeting of the Board of Directors must be held immediately to deliberate on the issue and fulfill its responsibility to issue an explanation to the public.

IX. Establishment of subsidiary rules and regulations

The Japanese Society of Pathology reserves the rights to establish the subsidiary rules and regulations necessary in order to implement the Guideline.

X. Enforcement date and revisions to the Guideline

The Guideline will be implemented and in force on Mar.28, 2011

In order to assure that it will remain appropriate considering the variations seen in social factors and stay in agreement as new laws and ordinances are passed or revised, and further, maintain its viability with the various conditions surrounding medical treatment and research, it is considered that revisions to parts of the Guideline will be necessary in the future. The Medical Ethics Committee of the Japanese Society of Pathology, through decisions concluded at meetings of the Board of Directors, the Councilors, and the General Meeting, reserves the right to deliberate on and conduct revisions to the Guideline.

Furthermore, this document, the "Guideline for Conflict of Interest Management for Medical Research," was drawn up based on the "Guideline for the Drawing Up of Policies Related to

Clinical Research and Conflicts of Interest" announced in March of 2006 by the Ministry of Education, Culture, Sports, Science and Technology, "A Guideline for COI Management for Scientific Research Related to Health, Labour and Welfare," announced in March of 2008 by the Ministry of Health, Labour and Welfare, and the "Guideline Related to COI in Medical Research (proposal)," announced in December of 2010 by the Japanese Association of Medical Sciences.