

The Guidelines Concerning Conflict of Interest of the Japanese Association of Medical Sciences

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I. Introduction

The industrial academic cooperation activity in the United States became strengthened with the introduction of the Bayh-Dole Act in 1980. For the past 30 years this has contributed greatly to practical applications in the fields of prevention, diagnostics, and therapeutics based on research in preclinical medicine. However the more academia becomes involved in profit-related activities and also with for-profit organizations, the more social responsibilities it shoulders in terms of education and research, and the personal development of individual conflicts of interest becomes unavoidable due to such industrial-academic cooperation (Figure 1). These conflicts of interest (COI) must be appropriately managed by academic institutions and societies and the safety and human rights of subjects taking part in clinical research must be zealously guarded. The Gelsinger incident that occurred in a US state university in 1999 was a great warning about the importance of the management of and supervision of an organization concerning COI regarding not only ethical aspects, but also state-of-the-art medicine. Since then more than 95% of all biomedical universities in the United States have established policies concerning research involving human subjects and have attempted to ensure appropriate clinical research and clinical trials.

This kind of movement was not limited to large general hospitals or medical schools who were actively promoting clinical research in association with industry,

but also involved institutions devoted to the publication of their research results to make them available for society at large, and they were also interested in making COI policy be understood by all researchers who were involved in clinical research and educational activities. Furthermore, awareness of the necessity of the declaration of COI status of researchers publishing in specialist medical journals increased, but, although the necessity for individual reporting of COI status increased, there is no uniform policy on, or management of, COI, as yet.

In Japan, the "Kagakugijutsu Kihonkeikaku" (Basic Plan for Science and Technology) was established in 1996. This was intended as an overall response to the wishes of the general populace regarding state-of-the-art preclinical research results. Thereafter, the second plan for basic research (2001) followed by the third plan (2006) advanced this philosophy and reflected the basic thinking concerning administration of scientific policies of our country. Furthermore, while attempting to establish the scientific and technological creativity status of our country, the importance of industrial-academic cooperation was emphasized. Not only universities, but also research institutes and scientific groups must return the benefits of the results of the research to society, thereby providing the Japanese populace with safety and good outcomes with regard to economic activity, and also ensure that education and research activity should be promoted. At the same time, the more that industrial academic collaboration increases, the responsibility of public institutions such as universities and research institutes also increases.

Therefore, the responsibility of disclosure of COI status concerning individual researchers and their affiliated institutions or universities becomes extremely important.

In addition, since medical research involves human beings, it is necessary to ensure ethical treatment of patients, who are generally in a weak position, and also ensure the scientific integrity of any project. Therefore, it is essential that the ethical aspect of any research be guaranteed. In the “ethical policies regarding clinical research” of the 2003 Declaration of Helsinki, it is clearly stated that COI regarding human subject research, especially concerning the individual profit that might be derived from research, should be treated with great care.

The first approach taken to COI in Japan was in August 2004 at a panel discussion sponsored by the Ministry of Education entitled “Clinical Research, Clinical Trials and Conflict of Interest: How to Handle the Problem”. This event established the importance of the question of COI. Thereafter, a committee entrusted to perform a survey by the Ministry of Education Research Group on the ethics of clinical research and COI was established. In March 2006 “Guidelines regarding Conflict of Interest Policy and Clinical Research” was published. These guidelines defined the regulations concerning universities, research institutes, hospitals and academic societies concerning clinical research on human beings. They also tried to

prevent any obstacle to the implementation of research involving human subjects and strove to establish the social responsibility and regulations for clinical research. The guidelines attempted to present basic policies on the management of COI problems involving clinical research and at the same time to promote a high level of clinical research and assist in the achievement of a high level of research. Then in 2008 the Ministry of Health and Welfare of Japan published their policy on the management of welfare, labor and health research concerning COI and clearly stated the duties of researchers in the field of clinical research who are receiving research grants.

One of the major worldwide movements of recent years is to perform preclinical research looking for seedlings that can be passed over by translational research to the clinical field and many countries use this approach in their national plan.

Because of this background, the research object of COI management is clinical research and clinical studies (including clinical trials). Industrial academic cooperation has expanded to the field of basic biomedical research and for-profit businesses, organizations, and groups are increasingly tending to demand financial COI status self-disclosures from basic researchers. Therefore, the Japan Association of Medical Sciences, wishing to improve approaches to prevention and methods for diagnosis and treatment, is seeking to gain better understanding of the causes and morphology of diseases and promote industrial academic cooperative research to improve the quality of life of patients. The biochemical research and

preclinical basic research both extend to human beings, and associated clinical research (including the use of specimens which can identify the individual from which they originated or data which can be used to identify the individuals from which they were generated), and defines all such activities up to and including clinical research as medical research, and therefore considers all such activities within this wide range as the target of COI management.

II. Basic thinking

Biochemical science universities, research institutes, hospitals, and similar institutes, specialists, or academic societies are hoping to help prevent, diagnose and treat intractable diseases through education and medical research by industrial academic cooperation. The medical research of these establishments and institutions, as well as their scientific educational programs and research concerning human beings, require the application of secure ethics and science. The publication of any results in academic meetings or academic journals requires transparency and neutrality. It goes without saying that such medical research, clinical research and clinical studies must strictly comply with ethical policies.

The COI status in medical research involves not only human rights, life and safety of the patient, but also preclinical research and health treatment in the healthcare environment. Researchers working in such an environment carry out research in

cooperation with industry, including basic research, clinical studies and trials, and moreover such researchers are involved with venture capital industries, which make commercial products of the treatment methods created by the researchers, and therefore the presence of COI is unavoidable. However, the fact that a COI status per se regarding financial aspects exists, is in itself not a problem. The institutions and organizations have to properly manage those aspects and it is essential that a system be developed in which inappropriate medical research is prevented. In our country, the response to the COI status, which has been taken up as an extremely important aspect of the Declaration of Helsinki and other ethical policies, has not been as rapidly developed and given as much importance as in the West.

In medical research, the necessity of transparency, reliability, and specialized aspects of clinical research and clinical studies in human beings require appropriate COI management. As reported by the Ministry of Health and Welfare in this interpretation of the "Ethical Policy in Clinical Research", they state that the conflict of interest of a researcher should not cause any "warping of the essential nature of the research", while at the same time, based on the status of clinical research in our country, they also state "if research related to for-profit industries were to be forbidden categorically, this would lead to hindrance in the development of drugs." As can be understood from this, even within the field of medical research, clinical medical research and clinical studies have an extremely high level of ethical

and specialized aspects, and since this means that the research concerning human beings is of a very special nature, this entails that COI status in this field is of a slightly different nature than the COI problem in general. By appropriately overcoming this problem and in order to prevent the COI status, which can develop latently to become a serious problem, all medical research regarding human beings must be particularly transparent and extremely appropriate.

In the COI management related to medical research, the foundation or organization which seeks to employ the data provided by the researcher should ensure that any financial profit deriving from the research (financial etc.) or other related profits (status or authority etc.) should be disclosed appropriately within the organization. In addition, the health science branch of such an organization must ensure that basic or preclinical information regarding medical research or clinical medical research, clinical studies (clinical trials) must be distributed appropriately and the researcher providing those data should ensure that objective evaluation is given to those data. In addition, in performing medical research or clinical research, it is important to ensure that there is no undue influence of considerations of financial profit. Furthermore, the individual researcher who is employed in medical research must ensure that the research does not lose any validity and that the safety of participants in clinical studies is not threatened. In addition, the researcher should not receive rights to ownership or profit. In order to attain this goal, the evaluation of the COI status should be enforced or supervised by a third party to ensure that

the appropriateness of the medical research is guaranteed. Furthermore, biomedical-related universities or scientific bodies should disclose appropriately any financial profit or other related profit. It therefore is essential to make progress based on an appropriate balance of education and research with an independent, objective and strictly scientific nature.

The guidelines concerning COI management of medical research of the Japan Association of Medical Science are intended to give guidance to the leaders of the societies affiliated with the Japan Association of Medical Sciences and members related to COI management. Each affiliated society manages all matters related to COI status, including distinct conflict of interest issues. The appropriateness of the medical research results should be verified, guaranteed and made public. The organization and modus operandi of the affiliated societies will differ, as will particular factors concerning each of the affiliated societies, therefore, we must state that these guidelines do not have legal power. These guidelines should consider many conditions related to each of the affiliated societies of the Japan Association of Medical Science and are intended to provide assistance in establishing COI policy and detailed regulations concerning medical research.

III. The special character of medical research and COI policy

Medical research differs from joint research, or commissioned research (for example, unlike engineering faculties etc.) and has the following particular features

which require extreme care in implementation:

1. Many researchers belonging to universities, research institutes, hospitals and other specialist societies are not only related to commercial ventures, but also are related to, or are involved with, doctor-patient relationships, protection of the rights of the subjects and guarantee of the safety of the health and welfare of the subject.
2. Data from medical research or clinical research are involved with the subsequent development of new diagnostic or therapeutic methods, therefore it is especially imperative for researchers to ensure the reliability of their data.
3. The publication of research results has a great impact on those involved in health care, those listening to presentations, or reading papers. Therefore, the interpretation of such publicized results has an influence on health care that is by no means small. In order to ensure a neutral objective self evaluation, it is necessary for the presenters to disclose all pertinent data concerning related commercial organizations and their COI status.

On the other hand, based on the following points of view, medical research and clinical research have the following special characteristics concerning the COI status of individuals and researchers.

1. Many areas of the most up-to-date medical research is related to developments in prevention, diagnosis and treatment. In many cases, the researchers themselves are the most appropriate persons to safely accomplish such basic and clinical research.
2. Concerning the development of new drugs, it would take a long time for society to benefit by relying only on technology transfer from existing commercial entities. Therefore, the role of researchers themselves regarding venture entities is large.
3. New drugs or new medical devices require basic research and clinical studies in order to be developed for clinical use. Therefore, it is very difficult for the researchers themselves to be completely uninvolved with this process.

In order to appropriately manage COI related to medical research (pre-clinical and clinical) in the environment of industrial-academic cooperation, the social situation in the specialty of each of the affiliated societies, must prepare detailed regulations concerning COI policy and COI management related to the above comments. As a result of that, the COI committee under the leadership of each of the affiliated societies should enforce suitable management of COI, thereby contributing to the return of benefit to the society, welfare of the people, promotion of health and the overcoming of intractable diseases.

IV. The basis of COI management related to medical research

In recent years, COI management related to medical research can be carried out at medical schools and research institutes and the specialist societies at which research results are made public can be largely divided into two stages (Figure 2).

1. Implementation of medical research by institutions and organizations

Various medical academic universities and research institutes are promoting the establishment of COI policies concerning medical research (including pre-clinical and clinical research and clinical studies and the systemization of management of COI at those institutions is gradually becoming better organized. In particular, concerning clinical studies, as in the case of other cooperative projects with industry, each researcher is required to submit not only clinical research program plans but also COI disclosure statements in order that the universities and research institutions can appropriately manage COI.

2. Specialized societies and scientific bodies at which medical research results are presented.

Specialty medical meetings of societies affiliated with the Japan Association of Medical Sciences at which the results of research are presented at institutions, often have duplication of researchers and therefore, it is necessary to establish a COI policy based on a common philosophy.

3. Items that should be avoided in medical research and their management

In cases of clinical research (clinical studies and clinical trials) involving human beings and the industrial medical cooperation system, the following items should be avoided by researchers involved in those projects, from the point of view of COI policy.

- (1) Being an intermediary or providing an introduction to the clinical study for the patient for which you will receive monetary remuneration
- (2) Receiving financial remuneration for accumulation of patients within a specified period of time
- (3) Receiving remuneration in regard to the results of the specific clinical study or result
- (4) Affecting the ability to report on the results at a medical society based on the influence of financial supporters or commercial organizations.

On the other hand, the principal investigator involved with clinical research, (including clinical studies and clinical trials) and who is involved with the planning and carrying out of the conditions of the study, must make clear whether the following conditions have been followed regarding the appropriate disclosure of any financial relationship regarding the financial sponsors or organizations.

- (1) Having responsibility as an executive member or financial support organization or venture regarding the clinical study
- (2) Having obtained any right to patent rights or patent fees regarding the medical products, diagnostic products or examination methods concerning the research topic
- (3) Receiving payment for travel or accommodation from the commercial societies or ventures in order to take part in medical meetings related to the research
- (4) Receiving financial remuneration that considerably exceeds the actual costs required by the research project reported
- (5) Having received money or gifts exceeding the actual value of the time or labor expended on the research.

V. The planning of detailed regulations concerning COI policy

Each affiliated society must establish its own policy concerning medical research-related COI and make that policy public, as well as establishing a management system based on that. In addition to making clear the extent of any profit to any individual taking part in this research, the management systems should also take into account the prevention of any breach of the COI policy, especially concerning the established policy (detailed rules). In order to implement management of COI the affiliated societies should have a predetermined policy on

how to deal with any breaches of the COI policy.

1. The procedure of COI management

Concerning the publication of the results of the medical research, all of the researchers involved in the given research must, in principle, submit a self-reported COI disclosure document to the president of the affiliated society (see appendix 2). The management process of COI concerning medical research can vary according to the particular conditions of the affiliated society, but basically the concerned researcher must describe the related commercial entities, foundation organizations, and any other groups which aim to derive profit, and this should be reported in the self-disclosure COI form which is submitted to the president of the affiliated society.

2. Businesses and corporate organizations and for-profit groups involved in industrial academic cooperative activity

Concerning medical research involving universities and research institutions, related to industrial academic cooperation with businesses, corporate organizations and for-profit groups (hereinafter, businesses, organizations, and groups) the following activities are included and should be disclosed.

- (1) Joint research: Research performed by dividing research funds and research personnel, involving businesses, organizations, groups. (with or without recompense or remuneration)

- (2) Commissioned research: businesses, organization, and groups commit themselves to contracts concerning methods of treatment, drugs and devices, and research is performed on the basis of such contracts
- (3) Technology transfer: businesses make practical use of the patent rights and other rights concerning the research results of universities and research institutes
- (4) Technology guidance: researchers of universities and research institutes etc. develop the research of businesses and give technological advice
- (5) University ventures: venture organizations are based on the results of the research of universities and research institutes
- (6) Donations: unrestricted donations are made to assist universities and research institutes by businesses, organizations and groups
- (7) Endowed departments: Departments are established for the promotion of research enabled by financial donations to universities from businesses, organizations, and groups.

3. Those subject to COI management:

- (1) When members present the results of research in scientific presentations etc., at the time of presentation, they must report the COI status in relation to the performance of that research and, in

accordance with the per se and detailed regulations of the affiliated society, must make such disclosures using the designated forms. If it is decided that the presentation in relation to the research is in contravention of the COI policy, then the president of the affiliated society is required to discuss with the COI committee and take appropriate measures based on the results of such discussion.

- (2) When publishing papers in scientific journals of the affiliated societies, not only members, but all authors, must submit self-disclosure COI forms.
- (3) All officers (chairpersons of the organization, regents, financial comptroller) those responsible for scientific meetings (meeting presidents etc.), all committee chairpersons, committee members of special committees (scientific organizing committees, editorial board committees, ethical committees, COI committees etc.) and temporary groups (subcommittees, working groups etc.) play a very important role and have responsibility for their activities in relation to the respective affiliated society. The COI status in relation to the given activity must be described by self-disclosure in the designated form at the time of appointment, and should the COI status change after the appointment, then according to the regulations of the society, there is a duty to adjust the form. The above officers and committee members are required to pay particular attention to the COI management responsibilities.

(4) Clerical staff employed by the affiliated societies. At the same time, each affiliated society should decide, based on its own individual situation whether to require COI disclosure of the spouses, immediate family or those who share income or property with those listed in 1 to 4 above. However, even if spouses or family are not considered subject to disclosure of COI, if they have an indirect effect or a non-financial effect on the implementation or the understanding of the medical research, or if such a possibility exists, they are required to disclose such relationships on the designated forms.

4. Activities subject to COI guidelines

COI policy should be applied to all those who take part in all activities of the affiliated society. To give individual examples:

- (1) Academic meetings (annual general meetings included), holding local or chapter meetings of the society
- (2) Publication of the academic journal of the society or academic publications
- (3) Implementing research or questionnaires
- (4) Those who provide encouragement for research or reward academic achievements
- (5) Certifiers of board-certified personnel or certifying institutions

- (6) Those promoting continuing medical education
- (7) Those promoting international research cooperation
- (8) Those involved with businesses enabling attainment of professional levels of various sorts.

In particular, the following activities require extreme care and respect for the policies of COI:

- (1) Making presentations at academic meetings held by affiliated societies,
- (2) Publication in scientific journals or affiliated society journals
- (3) Those planning health care guidelines or manuals
- (4) Work involving temporarily established investigation committees or advisory committees.
- (5) Making presentations at lectures, luncheon seminars, evening seminars etc. sponsored by businesses or for-profit groups

Furthermore, members of the affiliated societies must pay great respect to COI policies concerning academic activities, even if they are not directly connected to the activities of the given affiliated societies.

5. Items that must be disclosed

Among the items that must be disclosed, one of the most problematic and frequently discussed is that of grant contributions (entrusted funds), especially their interpretation and handling. The recipients of grant contributions from businesses, organizations, and groups, can be generally divided into two large groups. One of these includes the directors of institutions (school presidents or hospital directors) and department heads. In the case of the former, there is a tendency to make the interpretation that the grant is not related to individual researchers, but if the grant contributions are passed through the heads of an institution to an individual or to the section (department) of a person making a publication, or distributed to a research laboratory, it is necessary to clearly describe this in the disclosure. In order that there should be no suspicion or doubt on the part of society concerning the medical research performed through industrial academic cooperation, if it is considered that there was support from a related business, even if it be indirect, then it is desirable that this should be reported in the COI self-disclosure.

Another disclosure item, concerning which suspicions can easily arise includes those cases in which financial support (commissioned research, research funds) are made available from not-for-profit foundations (for example NPOs) or public foundations (for example public corporations). If grants from businesses are distributed to researchers via not-for-profit groups or public corporations then the greater the amount of the contribution the greater a third party will receive the impression that the objectivity of the research results might be lacking, thus this

deserves great attention. Therefore, the COI committees of each of the affiliated societies must consider the nature of the research funds and make an appropriate response to that.

Self-disclosure forms should be planned to be of three types (1) for officers, (2) those presenting at academic meetings, (3) those publishing in journals. All the above groups should be included but the above conditions should be made based on the situation of each individual affiliated societies.

6. COI management of each type of individual

(1) Officers

The president of the affiliated society must make it a duty for the individual officers to submit a self disclosure COI document with regard to their relations to businesses, organizations (not-for-profit organizations, foundations etc.), and groups. The method of disclosure is usually done on a printed form, but it could be worth considering a self-disclosure system established on a secured website for disclosure on application by a given day.

Businesses, organizations, and for-profit groups may present or may supply information on external finances including reimbursement for manuscripts, lectures, research funds (including clinical trials and clinical studies), commissioned

research, joint research, grant contributions, including trusts, and endowments) and these are all extremely important items from the point of view of COI management. It is therefore necessary to consider how to make these clearly understood by third parties. As a concrete example, for an item that should be declared by an individual researcher (see appendix 2) if the amount exceeds that described in the detailed regulations, it is necessary to disclose that to the president of the affiliated society. Furthermore, there should be detailed regulations concerning the concrete disclosure and method of publication of such information.

There has also been much discussion whether editorial board members or reviewers should be subject to COI management, although the Editor-in-Chief and members of the editorial board now have the duty to self-disclose COI. In the affiliated societies, there are frequently some unavoidable relationships among authors and those in the various specialized areas from which reviewers are selected, extending to even closer relationships between the reviewer and the submitting author (mentor-student, joint researcher, receiving grants from the same commercial entity). However, should it become necessary to request reviewers from among specialists who have absolutely no COI status problems with regard to the submitting author the number of potential reviewers could drastically reduce and it is even possible that it would be impossible to find suitable candidates to request peer reviews, based on this and other considerations, therefore it is

essential to give very careful consideration to the condition of COI management with regard to peer reviewers. As one example, if an editorial board member or reviewer feels reluctance to perform a review because of a COI issue with regard to the author or the individual reviewing peers they might not be able to take the responsibility to explain the result of the review, therefore it could be possible for them to refuse to review. This is one practical way of handling the problem. Be that as it may, the delivery of information from the results of research in academic journals is a very important means of the returning of benefit to society therefore it is essential for the COI committee to be closely involved in this process, in order to preserve public transparency and secure neutrality.

(2) Those publishing at scientific meetings

The president of the affiliated society can require all those with names attached to the publication or just the first presenter, whether they be a member or not, to self-disclose COI status with regard to businesses, organizations, and groups related to the contents of the research.

Concerning the amount of money that should be notified in the self-disclosure, this can be calculated according to the conditions of the individual affiliated society and standards should be prepared regarding disclosure. Furthermore, concrete standards should be established for the researcher's family (for example, immediate family etc.) that is, all those who are making a living together with the

researcher and these standards should be calculated and established by each of the affiliated societies.

(3) Authors publishing in scientific journals

The editorial boards of each of the affiliated societies must, under the leadership of the president of the affiliated society ensure that all authors, whether they be members or not, provide self-disclosure information concerning all publications in the scientific journals of the affiliated society. Usually the corresponding author should collect the statements concerning the COI status of all of the authors of the given paper and should take responsibility for the content of the paper. The information concerning the COI status of all the authors appears after the main body of the text, usually before the acknowledgment and references. Even if there is no definite rule about COI status reporting, there is usually a statement about COI status such as “The authors declare they have no conflict of interest”. Measures to be taken concerning those violating the principle of COI disclosure should be determined by each of the affiliated societies and the COI policy and detailed regulations should be clearly stated in the Instructions to Authors.

Recently the International Committee of Medical Journal Editors (ICMJE), in order to simplify matters for authors of papers, has proposed a standardized COI status disclosure form. The form for disclosure of potential COI that they are proposing will not only reveal the COI status of the authors but also require disclosure of the

COI status of the institutes and institutions to which they belong and, as a new development in this field, this is attracting much attention. Usually if the impact factor or citation index of a given journal is high, this has significant effect on the status and ability to attract research funds on the part of researchers. At the same time, the attention paid by society to the research results of medical research and clinical studies supported by business sponsors attracts much attention and has a great effect on society. Therefore, it is important that the journals and scientific societies not only ensure the transparency and the reliability of the COI status disclosures of the authors themselves; they must strive as much as possible for the security of the objectiveness and neutrality of the data. Because of that, there also should be close cooperation between the editorial board and the COI committee, 1) concerning authors in Japanese language journals, and 2) in English language journals of the societies. These two categories should be considered separately and description of the journal COI policy for each of those should be described in the manual for publication and appropriate handling of each is considered desirable.

1) Authors of papers in Japanese language journals

Since many of the authors in Japanese language journals of the affiliated society publishing in the journal are members, it is usually possible for the COI disclosure forms to have the same items as for the scientific meetings and lecture sessions of each of the affiliated societies. However, even in the case of non-members, it is

necessary that they should comply with the COI policy and detailed rules of each of the affiliated societies and clearly disclose their status using the given forms.

2) Authors in English language journals of affiliated societies

Concerning COI management regarding authors of papers in English language scientific journals, the COI self-disclosure forms required of the authors are, as in the case of Western societies, quite different according to the journal and there is as yet no standardization. It is considered that there will be a considerable number of papers from non-Japanese researchers (non-members) in the English language journals published by the affiliated societies. Therefore, since the situation in each country is very different from the industrial academic cooperation activity in Japan, ① the extent to which disclosure should be made by the authors, ② the disclosure items ③ the criteria for evaluation of the self-disclosure must be carefully considered and must be clearly described in the journal's COI policy.

7. Period required for disclosure

The medical research resulting from the industrial academic corporation is varied in nature. In preclinical research, it can often be performed within a short time, but for clinical studies, especially clinical trials, long periods of research are necessary. Therefore, in terms of the nature of the medical research and clinical research, the period for which disclosure is required in many cases covers several years. In

cases in which COI management has just begun to be addressed, it is possible to set the initial period for the preceding one year and then extend it year- by-year. In affiliated societies that are promoting COI policy and detailed regulations, they are requiring disclosure for the previous one year for members and employees of the affiliated society and will be carrying out management based on COI policy over several years, after which a complete system of several years (for example 3 years) may be required for disclosure as a disclosure period for self-disclosure. Clinical trial results can have a large influence on society and in cases in which such studies are carried out over long periods of time, extending beyond the limit defined by the industrial academic cooperation, it is desirable that individuals take responsibility to disclose their COI status appropriately.

8. Method of self-disclosure

The method of self-disclosure is clearly stated in the COI policy and detailed regulations according to subject. (See Figure 3)

(1) Officers

Officers must submit a self-disclosure form on their COI situation pertaining to the businesses, organizations, and groups every year at a set date (e.g. April 1) so that it may be updated for evaluation. In the event that a new COI situation occurs during the study period, there is an obligation to report this within a set time period

(e.g. within 6 weeks).

The following states the specific reporting process when commissioning officers to do research. 1) Candidates for director must follow the format and procedure determined by the affiliated society, and submit the COI self-disclosure form to the president of that society, and 2) a discussion will take place concerning the eligibility of the officer candidate at the COI committee meeting, 3) The results (written opinions concerning COI) will be reported to the head of the organization, and 4) The final decision concerning the approval/approval with condition/disapproval, etc. will be made by the head of the organization to the candidate.

(2) Authors presenting at scientific meetings

Presenters are obligated to self-disclose COI status with regard to businesses, organizations, and groups related to the theme of presentation using the form provided, both when submitting abstracts via the Website and also at the time of presentation. It would be an idea to construct a system which will not permit the presenter to submit the abstract via the Website unless all items of the COI form are answered. Moreover, speakers should disclose all existing and possible COI situations using the format prescribed by the affiliated society, either on the first or second slide (see Figure 4), and read the name of the business, organizations, and groups that are involved.

(3) Authors presenting publications in scientific journals

Authors giving presentations on publications in scientific journals are obligated to self-disclose their COI status regarding businesses, organizations, and groups and all coauthors, at the end of the publication in a style set by the committee. In recent years, some European and American scientific journals (e.g. the New England Journal of Medicine) have implemented a system whereby the COI status is undeclared at the end of the publication but instead, the reader can voluntarily access via the Website, the original self-disclosure form filled in by the author with regard to the COI status of all authors. In the future, if international standardization of the Form for Disclosure of Potential COI progresses along with the advances in electronic journal publications, this method of disclosure could be one possible method to consider.

9. Handling of COI self-disclosure forms submitted by officers

As COI self-disclosure forms submitted by officers may include very important personal information, they should be handled very carefully and a highly secure management by the secretariat of the affiliated society is needed to secure the protection of classified and personal information. A specific example would include, the necessity to keep and secure all COI related documents of those officers

whose term has expired and those who withdraw from the committee or terminate their commission, until the term has ended or for a fixed time period (e.g. 2-5 years), under the supervision of the president of the affiliated society.

Once a fixed time period has passed, the documents should be deleted or destroyed under the supervision of the Chairman of the Board of Directors. However, if the Chairman of the Board of Director decides that information should not be deleted or destroyed, a certain time period will be given, as necessary, to place a hold on such action. It is recommended that all COI information with regard to the president (including the president-elect), and the Chairman and organizing committee of the scientific meeting is handled in the same manner as COI information of officers. Methods to store or destroy such information should be clearly described in this policy.

10. Role and responsibility of the board of directors

The board of directors may consult the COI committee, ethics committee, and editorial committee to direct measures in the event that a serious state of COI problem arising from the need to accomplish the work of the affiliated society, may lead to a loss of social reliability, or if the COI self-disclosure of authors presenting at scientific meetings and in scientific journals is found to be improper. If an officer or member is accused of a suspected COI problem, the board of directors, on

behalf of the affiliated society, will act appropriately and in good time, and in the event that there is an unjust allegation or indictment, will give an opinion or make a statement to fulfill its social responsibility to explain the results of the verification of facts and to defend the individual member's rights.

It is clearly stated in the COI policy that the officer and members of the affiliated society, etc. when arranging contracts with businesses, organizations, and groups, will not agree to any activity or survey activity which may lack public transparency and appropriateness of research or announcements of the affiliated society.

11. Role and responsibility of the COI committee

The COI committee should be established independently from the ethics committee, to take measures against those who violate the policy. The COI committee should be supervised by the president of the affiliated society, taking into consideration that COI management must deal with the nature of the distinct content of self-disclosure, and the need to protect personal information. Moreover, for COI management to be conducted smoothly, it is recommended that the COI policy state a specific method in regard to how the COI committee, board of directors, Ethical Review Board, and the editorial committee should cooperate. The COI committee should play an advisory role to ensure that COI in medical research, clinical research, and clinical trials within the industrial-academic cooperation is

managed properly, from the researchers' standpoint.

1) Items of jurisdiction of the COI committee

The COI committee has jurisdiction over the following:

- (1) Handling all inquiries from individual members concerning their COI status (includes explanations, advice, and guidance).
- (2) Issues concerning COI management and educational activities.
- (3) Issues concerning COI investigations, discussions, management, proposals for measures to be taken, and recommendations.

2) Criteria for judgment of COI disclosure

Neither standard judgment criteria nor standard evaluation criteria exist in COI management since the COI status regarding medical research varies greatly according to the situation of the study in industrial-academic cooperation activity, social background, the patent and intellectual property, facilities and the situation the researcher is in (domestic or non-domestic residents).

Medical research in the environment of industrial-academic cooperation should be conducted in a proper and publically transparent way, regardless of the fact that the remuneration and grant support will differ depending on the businesses, organizations, and groups, therefore, a potential state of COI for the researcher is inevitable.

Therefore, the criteria regarding the content of the activity and the finances involved with the affiliated industry should be set, based on a policy decided by the affiliated society that can provide social accountability. An appropriate revision and update of this policy and detailed regulations should be done regularly, to improve handling of COI self-disclosure.

When a researcher is offered a large sum of money by businesses, organizations, and groups, either in the form of an honorarium, editing fee, or scholarship fund, there is a possibility that the interpretation and study results will be biased, and will be pointed out by the mass media since there is an increasing concern in society. At present, the need for disclosure is decided upon whether the monetary sum is over a standard amount, and in such case the corporate name of the sponsor must be disclosed.

However, regarding COI management of the officers and committee members, there has been a recent attempt to use a method of disclosure based on a standard amounts prescribed at 2 to 3 levels.

For example, a large scholarship fund with great interest in mass media has divided acceptance money into 3 levels, 2 million yen or more, five million yen or more, and 10 million yen or more, to facilitate COI management.

Moreover, there has been an attempt to introduce a point system to control management on different levels, whereby each item of disclosure is given a certain point, and one must disclose COI based on the total number of points. On the other hand, based on the Sunshine article of the U.S. medical insurance reform law (March 2010), pharmaceutical companies and manufacturing companies related to medical equipment are now obligated to disclose all payments made to physicians and medical institutions, and this information be made public via a Website from fiscal year 2013. If the financial relationship between the business side and the researcher becomes clear and open to the public, it can of course be expected to greatly affect COI disclosure criteria for researchers, and COI management in our country will need to be revised to meet the global criteria of industrial-academic cooperation. It is important to pay attention to the needs of the general public and set the disclosure criteria by selecting and entrusting officers and committee members so that the COI situation does not become more critical.

Concerning the COI disclosure criteria for overseas members and nonmembers, there is a need to consider the characteristics of the industrial-academic cooperation activity of each country, and the currency value in relation to its economic situation, thereby making it difficult to apply the same judgment criteria as domestic members.

In particular, with the vast increase of scientific speakers from developing countries experiencing rapid economic development, there is a need to construct an appropriate COI management structure from past cases. For this purpose, exchange of information between affiliated societies, in addition to collaboration, will be necessary in the future.

3) Structure of the COI committee

The COI committee will consist of those members who conduct the medical research, those familiar with COI problems, and those with legal knowledge concerning related laws and policies. However, concerning the nature of confidentiality of personal information, the number of members who handle this information should be limited (e.g. total of 5-7 committee members). In addition, it is preferred to have a fixed proportion of both men and women, and external members.

12. Role and obligation of the editorial committee

When scientific journals publish original papers, review articles, clinical guidelines, editorials, and opinions, the editorial committee of the affiliated society can, with the collaboration of the COI committee, verify COI policies have been followed, and in the case that there is a violation, can take appropriate measures such as prohibiting the publishing of such articles. In such circumstances, prompt contact

should be made with the author involved, to notify the author of the situation and reasons. If a violation occurred after the article was published, the editor-in-chief can publicize this fact in the scientific journal, and the editor-in-chief can consult the COI committee and take necessary measures based on discussions. In addition, for affiliated societies which publish English language journals, it is recommended that a separate COI policy be made available, stating clearly the specific measures to be taken for those who violate the policy.

13. Role and obligation of the ethics committee

The ethics committee functions independently from the COI committee, however, depending on the situation of the affiliated society, it is possible for the ethics committee to handle COI matters of committee members. The role and obligation of the ethics committee concerning COI management involves, receiving consultation from the Chairman of the Board of Directors, deciding on the appropriate measures to be taken by judging and considering the degree of violation, its effect on the affiliated society, and reporting this to the Chairman of the Board of Directors. As COI management deals with difficult ethical issues, daily exchange of information between the ethics committee, COI committee and the editorial committee is necessary to promote justifiable medical industrial-academic cooperative research.

14. Storage and release of personal data

The COI disclosure form of members and officers contain confidential personal information which must be stored securely. All personal information either in print or electronic data, should be secured by the secretariat of the affiliated society by an assigned manager, until it can be deleted or destroyed after a certain period of time.

This system allows the president of the affiliated society as well as the head of the COI committee to be able to access personal COI information of the member involved, at all times, in the event that measures need to be taken by the affiliated society in regard to COI management. However, access to this information should not be more than necessary, and information should not be disclosed for members, or for any other purposes, other than those who are required to disclose such information.

If the disclosure of COI status concerning officers and members is requested from the public (e.g. mass media), the appropriate information will be disclosed after carefully considering the confidentiality of individual information and privacy of the member. Furthermore, if disclosure of COI status is requested for specific officers and/or members through legal means, a board of directors meeting involving a personal legal counsel is necessary, and it is recommended that a manual be

prepared beforehand.

15. Monitoring, abiding by COI policy, and educational training

All members of the affiliated society and employees are obligated to follow the COI policy concerning medical studies. At the same time, it is important to implement COI policy in the training curriculum and programs for continuing education, lectures, and seminars for qualifications, for the purpose of increasing awareness of COI. In particular, if officers involved in medical research in the environment of industrial-academic cooperation have a serious COI status, regular reporting and monitoring, change in official post and avoiding inappropriate COI behavior, will ensure minimal effect on the conducted activity. Furthermore, in the event that an individual member's COI status is serious and may affect the affiliated society's activities, and if fairness and reliability cannot be assured, it is possible to implement a policy prohibiting all involvement (zero tolerance) in the activity. However, this kind of situation must be treated very cautiously as it may become a factor which hinders the general industrial-academic activity.

16. Handling requests for COI disclosure

If a request is made for disclosure of COI status of a member of an affiliated society, the procedure on how to respond should be stipulated from the understanding that

the request will be made from an external source. If the reason for request seems appropriate, the COI committee will, with consultation by the president of the affiliated society, respond to the request as quickly as possible, including conducting an investigation on relevant facts, and also by protecting the confidentiality of personal information. It is recommended that a structure for when the COI committee is unable to respond to a situation be made available.

17. Handling those violating COI policy

A serious violation of the policy concerning the affiliated society might cause the society to lose its reliability and moral standing in society. In order to prevent this from happening, it is necessary to increase the awareness of COI policy beforehand through publicity, scientific meetings and other activities that may educate those regarding this issue, and to create a COI management system centered around the COI committee. In the event that a member violates the policy, this policy clearly states that the president of the affiliated society will take the appropriate measures according to the degree of violation (e.g. prohibition of presenting at scientific meetings, prohibiting of publishing in a scientific journal of the society, prohibition of assumption of office or dismissal, withdrawal of qualifications as a member, expulsion from the society, and/or prohibition of admittance to the society). However, in the case of a serious violation of COI policy, the ethics committee (or appropriate committee) will be consulted and discussions

will be held, and based on the decisions made by the board of directors, appropriate measures will be carefully taken.

Generally speaking, since COI management is based on self-disclosure, if regulations for violations are too strict, there will be hesitation to disclose information, therefore attention should be paid to expressions used in violation regulations. On the other hand, it is necessary to state the procedure for appeal beforehand.

If a doubtful, social or moral problem arises concerning a society member, the COI committee will conduct a thorough investigation and hearing. If there is a serious COI situation, and if no explanation or responsibility can be taken, the president of the affiliated society will, based on the consultation with the ethics committee, discuss the situation at the board of directors meeting, and will retract the submitted publication or presentation of the author involved, or retract the publication. A structure such as this, stating the measures to be taken based on the policy of the affiliated society, should be prepared beforehand.

On the other hand, handling COI violations of nonmembers is most often difficult. It can be suggested that when requesting participation each time from a nonmember, each affiliated society should carefully explain the COI policy and the importance of following the policy, in writing. It can be assumed that for affiliated societies which

publish scientific journals in the English language, the number of nonmembers, especially from foreign countries, will increase and that correspondence in relation to COI violations can be expected to be more complicated than expected. It is recommended that a correspondence manual including measures such as prohibition of a presentation, retraction of a publication, and publishing an apology letter be made available to guarantee the integrity of the international society.

18. Response to an appeal

If an appeal is made, the president of the affiliated society must promptly set up a screening committee (hereinafter, the screening committee). The structure of the screening committee, in addition to the appeal procedure, is stated in the COI policy.

VI. Accountability to society

The presidents of affiliated societies are responsible for disclosing the COI status of their affiliated institutions and individual members, after discussions at the Board of Director's meeting. The COI committee should create a system in case a member's COI situation in the industrial-academic cooperation environment becomes serious, the related committees can collaborate regarding responding to the society and the mass media. For example, if a member has a COI situation in

which there is a need to take social and moral responsibility, the president of the affiliated society may disclose or publicize that information either within or outside the society after a final decision has been made by the Board of Directors.

In such cases, the member involved will be given an opportunity to present their own opinion either to the Board of Directors or to the designated officer, however in the case of an urgent situation leaving no time for consultation, then it will be noted as such.

VII. COI management of affiliated societies

The ways to handle COI problems of individual members and officers giving presentations on medical studies has been stated, however, it is important to state the policy concerning ways to handle serious cases of financial COI between the affiliated society itself and businesses, organizations, and groups. For example, if an affiliated society, receiving large remuneration from businesses, organizations, and groups, sponsors activities (such as special symposia, public lectures etc.), a possible COI status is likely to arise. When giving presentations under such circumstances, it can be predicted that COI evaluation and ethical aspects such as fairness, subjectivity and independence are difficult to maintain. This shows that we have entered an era in which a way to disclose remuneration and funds the affiliated society receives from businesses, organizations, and for-profit groups, is

needed. One method would be to have an external evaluation of the affiliated society.

VIII. Questions regarding the Q&A section and the homepage

The basis of COI management for each affiliated society is ① Informing members and participants of COI policy and detailed regulations ② making sure that members and participants abide by the COI policy and detailed regulations is important, however, questions and problems concerning the interpretation may arise. In that case, the COI committee should create a Question & Answer (Q&A) section in the society homepage, and make sure that each question is answered, in addition to publicizing the Q&A section of the homepage to members and other interested parties.

IX. Change in policy and detailed regulations

COI policy and detailed regulations should, generally, be updated every few years, in order to meet the revisions made to laws for social factors and industrial-academic cooperation, and various changes related to equipment, medicine, and clinical research.

Appendix 1) Definition of terms

① Investigator

The person conducting the medical research/study, or the subject individual.

② Immediate Family

The investigator's spouse (partner), underage children, children employed by a sponsor, a family member who is entitled to share equity (generally, first of kin), or those who are residing in the investigator's household.

③ Financial situations and related persons requiring COI disclosure

Since a COI situation may occur for various reasons, judgment may need to be made on an individual basis. For those employed, or in a position of leadership, regardless of whether it may be full-time or part-time, disclosure is required of all investment and licensing companies, all executive board members of for-profit organization, and officers.

④ Advisor or Consultant

This applies to those who act as advisors. For example, if a person acts as advisor or consultant in an investment, licensing, or for-profit organization, and receives income such as consulting fees etc. within a fixed term.

⑤ Equity (stocks etc.) holder

This applies if a venture company holds stock (includes stock options) whether it is a publicly held stock or unlisted stock, and is involved in investment, licensing, or is a for-profit organization, if it receives profit from such stocks (unless it is operated by a multilateral fund which cannot be managed or controlled by the correspondent)

⑥ Honoraria

A legitimate payment given for services such as giving lectures, seminar presentations and participation. This applies when the individual disclosing COI is given direct payment consisting of honoraria, investments, licensing fees from the authorities concerned, or from for-profit organizations. However, the maximum limit of lecture honoraria should be set by each affiliated society, in addition to other nominal income.

⑦ Funds for conducting medical research

This includes all funds related to conducting medical research projects, and applies even if the fund is paid by an agent hired by the sponsor. In addition, even if it is a scholarship fund from the sponsor of the medical research, with no specified expenditure, it must still be disclosed if it is over a certain amount. However, the total funds and duration when disclosing can be set by each affiliated society.

⑧ Other contributions (gifts, materials etc.)

Gifts and materials which are not directly related to research activity, such as travel expenses and gifts, are still subject to disclosure if they are received from investment, licensing, or for-profit organizations. In addition, disclosure is also necessary if such in-kind materials were received within a fixed term after the study activity was initiated.

⑨ COI policy

A structure which includes a basic system of COI management, such as, the basic policy related to COI of each affiliated society, the definition of COI, those subject

to COI and the extent of corresponding acts, foundation of a COI committee and self-disclosure forms.

⑩ COI management

A system to promote appropriate industrial-academic cooperative activities among the businesses, organizations, and groups related to medical research. According to COI policy, employees and members of each affiliated society must submit self-disclosure forms, to which an investigation is conducted by the COI committee, and in situations where COI status may cause damage to the corresponding affiliated society's activities, the COI committee will take necessary measures to ensure that education, research and publicity is conducted properly to society and the general public.

Appendix 2) Items to check when filling out self-disclosure forms

Items for self-disclosure for officers

① State if you have been an officer or consultant in a businesses, corporation or for-profit group (if the total annual income from the corresponding institution or facility exceeds a certain limit, e.g. 1 million yen), the type of income and amount. The preset limit of minimum income that must be disclosed should be decided by each institution or facility while considering the situation.

② State the type of equity (stocks etc.) of the industrial-academic cooperative

activity (e.g. either publicly held or unlisted stock, stock, investment, stock option, beneficiary rights etc.), and the amount. If the profit (total sum of the dividend or profit sales) from stocks within a fixed period from 1 organization totals more than a certain amount, e.g. 1 million yen or more, or if 5% or more of all stocks of the corresponding stock is owned then disclosure is needed.

③ Patent right fees from businesses, organizations and groups, of 1 million yen or more per patent fee, per year.

④ Remuneration for attending meetings (presentations) from businesses, organizations and groups, paid for the time and effort of the daily activity (lectures etc.) which is 500,000 yen or more from 1 organization or group per year.

⑤ Regarding manuscript fees paid for writing of pamphlets etc. by businesses, organizations and groups, 500,000 yen or more per organization, business or group, per year.

⑥ Regarding research funds for medical studies (trust research funds, joint research funds, clinical study funds) provided by businesses, organizations and groups, an annual total of 2 million yen or more for 1 organization or group.

⑦ For scholarship funds granted by businesses, organizations and groups, an annual total of 2 million yen or more from 1 organization or group, to the individual disclosing COI or to the affiliated department of the individual disclosing COI (department, field) or to the head of the department.

⑧ If the individuals disclosing COI is affiliated with the funded department

sponsored by the businesses, organizations and groups.

⑨ Concerning other travel expenses, gifts, or contributions unrelated to the research, an annual total of 50,000 yen or more by 1 business, organization or group.

However, whether the researcher's family members are subject to disclosure and if so, the specific range of disclosure, should be decided after consideration by each affiliated society.

Items for self-disclosure for speakers at scientific meetings

① For an officer or consultant in a businesses, corporation or for-profit group (hereinafter, businesses, organizations and groups) total annual honoraria of 1 million yen or more from 1 organization, business or group.

② State the type of equity (stocks etc.) of the industrial-academic cooperative activity (e.g. either publicly held or unlisted stock, stock, investment, stock option, beneficiary rights etc.), and the amount. If the profit (total sum of the dividend or profit sales) from stocks within a fixed period from 1 organization totals more than 1 million yen or more, or if 5% or more of all stocks of the corresponding stock is owned then disclosure is needed.

③ Patent right fees from businesses, organizations and groups, of 1 million yen or more per patent fee, per year.

④ Remuneration for attending meetings (presentations) from businesses, organizations and groups, paid for the time and effort of the daily activity (lectures etc.) which is 500,000 yen or more from 1 organization or group per year.

⑤ Regarding manuscript fees paid for writing of pamphlets etc. by businesses, organizations and groups, 500,000 yen or more per organization, business or group, per year.

⑥ Regarding research funds for medical studies (trust research funds, joint research funds, clinical study funds) provided by businesses, organizations and groups, an annual total of 2 million yen or more for 1 organization or group.

⑦ For scholarship funds granted by businesses, organizations and groups, an annual total of 2 million yen or more from 1 organization or group, to the individual disclosing COI or to the affiliated department of the individual disclosing COI (department, field) or to the head of the department.

⑧ If the individuals disclosing COI is affiliated with the funded department sponsored by the businesses, organizations and groups.

⑨ Concerning other travel expenses, gifts, or contributions unrelated to the research, an annual total of 50,000 yen or more by 1 business, organization or group.

However, regarding ⑥ and ⑦, if there are any research funds or scholarship grants received from organizations or groups where a COI situation exists between

the results of the study of the first author, the affiliation (department, field) of the first author, or the laboratory, disclosure is necessary.

Items for self-disclosure when publishing in a scientific journal

① State if you have been part of an activity where there is a possible COI situation regarding the corresponding clinical study and that business or group (if the total annual income from the corresponding institution or facility exceeds the limit, e.g. 1 million yen), the type of income and amount. The preset limit of minimum income to determine whether disclosure is necessary should be decided by each institution or facility while considering the situation.

② Give the same description as item ① for other parties related to the individual disclosing COI status. However, whether the researcher's family members (e.g. first of kin) are subject to disclosure and if so, the specific range of disclosure, should be decided on by each affiliated society.

③ State whether the applicant has been involved with industrial-academic cooperative activities related to the corresponding medical study (if the total annual remuneration exceeded a preset limit (e.g. 2 million yen) from the same external organization), type of remuneration received (e.g. joint research, funded research, consortium, conductance approval, transfer of rights, technological training, commissioned committee member, commissioned trips, visiting fellow and postdoctoral fellow appointment, acceptance of research grants and contributions,

request examinations and analyses) in the provided period. The preset limit of minimum income to determine whether disclosure is necessary should be decided by each institution or facility while considering the situation.

④ State the type of equity (stocks etc.) of the industrial-academic cooperative activity (e.g. either publicly held or unlisted stock, stock, investment, stock option, beneficiary rights etc.), and the amount.

⑤ State whether there is mention of COI in the informed consent (if so, attach explanation), the name of the applicant and personal seal.