The Japanese Association of Medical Sciences
COI Management Guidelines 2022

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I. Introduction

The industrial-academic cooperative activity in the United States became strengthened with the introduction of the Bayh-Dole Act in 1980. For the past 35 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 heads and researchers in research institutions become involved in profit-related activities and also with for-profit organizations, the more social responsibilities it shoulders in terms of education, research, and clinical practice, and the personal development of individual conflicts of interest becomes unavoidable due to such industrial-academic cooperation (Figure 1). These situations are called conflicts of interest (COI) and have caused some concern in the loss of independence of medical science research studies, publication of biased results in favor of industry (research bias, publication bias, reporting bias) due to close relationships and various activities with third-party organizations (regardless of for-profit or not-for-profit) and has become a social problem at times. The Gelsinger incident that occurred in a US state university in 1999 raised an alert about the importance of the management of and supervision of an organization concerning COI regarding not only ethical aspects in research but also state-of-the-art medicine.

There is a great demand for the heads of research institutions and academic organizations to ensure the safety and human rights of subjects taking part in medical science research is guarded, in addition to managing any COI of corresponding researchers (physicians) that may be embedded as an organization, so that medical science research is carried out appropriately by maximizing prevention of any bias risks in publication of results for constructing evidence-based medicine (EBM).

This kind of movement is not limited to research institutions who are actively promoting medical science research in association with industry, but also academic organizations involved in educational activities and medical journal publishers to appropriately manage the COI of researchers who are devoted to the publication of research results. Furthermore, the International Committee of Medical Journal Editors (ICMJE) which is a group of prominent international journal editors (Lancet, NEJM etc.) introduced the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals in 2013, which provides a common format for COI management by recommending specific instructions on how to prepare and publish a medical manuscript. This ensures not only the quality of research but the scientific integrity of the research, by clarifying the roles and responsibilities of authors, and over 6,000 medical journals currently adhere to the ICMJE Recommendations.

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 plan which has been carried over every 4 years, has advanced this philosophy and reflected the basic thinking concerning administration of scientific policies of our country. Furthermore, in 2014, the Japan Agency for Medical Research and Development (AMED) was established under national policies such as the "Health and Medical Promotion Strategy Act" and "Research and Development of Medical Organization as Independent Administrative Institution Law". The AMED emphasizes the importance of industrial-academic cooperation by developing groundbreaking pharmaceutical products, biologics, and medical equipment.

In medical science research involving human subjects, 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. In the Declaration of Helsinki (revised in 2013) and the "ethical policies regarding clinical research" by the Ministry of Health, Welfare and Labor, in 2003, it is stated that COI regarding human subject research, especially concerning individual profit (Conflict of Interest) that might be derived from research, should be disclosed, and subjects or legal guardians of the research must receive sufficient explanations and understand fully about the study to be conducted or continued, and informed consent should be obtained based upon their free will.

A full-scale approach taken to COI in Japan began when a committee entrusted to perform a survey by the Ministry of Education known as the "Research Group on the Ethics of Clinical Research and COI" was established and "Guidelines Regarding Conflict of Interest Policy and Clinical Research" was published in March 2006. These guidelines defined the COI regulations concerning universities, research institutes, hospitals, and academic societies concerning clinical research on human subjects. They also tried to prevent any obstacle to the implementation of clinical research involving human subjects and strove to establish social responsibility and regulations for clinical research. The guidelines attempted to develop basic policies on the management of COI problems involving clinical research and at the same time promote a high level of clinical research and assist in the achievement of a high level of research. 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.

The 2011 "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

neutrality of medical science research results should be verified, guaranteed and made public. Furthermore, these guidelines are intended to provide assistance so that results of medical science research activities can be published appropriately from the perspective of industrial-academic cooperation.

Amid such circumstances, a large-scale comparative clinical study on Valsartan (Diovan) conducted at five universities in Japan reported allegations of misconduct resulting from specific company intervention, and as a result of violations of COI disclosure and data manipulation in the interest of corporations, multiple articles were retracted.

In response to the publication of " Clinical Study Cases of Hypertension Treating Drugs and Measures to Prevent Recurrence" by the Review Committee, the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labor and Welfare, publicly announced the "Ethical guidelines on Medical Science Research Conducted in Human Subjects" in December 2014, that integrates ethical guidelines and epidemiological guidelines in order to clarify the responsibilities of the head of the research institution in addition to the researcher and to seek strict compliance with them. Subsequently, the Clinical Research Act came into effect in April 2018, and (1) Clinical research on unapproved or off-label drugs, etc. under the Law Concerning Quality, Efficacy and Safety Assurance of Pharmaceuticals, Medical Devices, etc. (Pharmaceutical Affairs Agency Law), and (2) Clinical research on pharmaceutical drugs funded by pharmaceutical companies are to be considered as designated clinical research; and in situations where clinical research is conducted to clarify the efficacy and safety of pharmaceuticals, procedures for conducting clinical research, management of conflicts of interest, measures for appropriate implementation of review and opinion work by an accredited clinical research review committee, and disclosure of information regarding the provision of funds for clinical research became mandatory. In 2019, the Guidance on Managing Conflicts of Interest in Clinical Research Act was introduced.

On the other hand, the Japan Pharmaceutical Manufacturers Association (JPMA) published the "Transparency Guidelines for Relations between Corporate Activities and Medical Institutions" (January 2011) which requires pharmaceutical companies to disclose all payments to physicians, medical institutions, and medical societies, and details of total scholarship payments, total manuscript fees and speaker remuneration fees for the previous fiscal year (total payments per researcher and number of payments, starting 2014) have been disclosed in detail on the website since fiscal year 2013. In recent years, the financial relationship between companies and the medical community, as well as the close involvement and activities of both parties, has often become a social

issue from the perspective of ensuring the quality and reliability of medicine and medical care. Therefore, COI disclosure and presentation of such information of not only researchers but medical institutions and medical societies need to be improved so as not to create misunderstandings or suspicion among society.

On the other hand, the Japan Pharmaceutical Industry Association, as a result of research fraud cases concerning Diovan, announced in April 2014, that in general, for clinical studies involving in-house pharmaceutical drugs, funding and support in providing goods would be carried out under a contract, and that donations would not be used as a method of support. It also made public the “Guidelines on Support for Investigator-initiated Clinical Research Using In-house Pharmaceutical Drugs”, in January 2016. As far as procedure, the pharmaceutical company will conduct an in-house review of the investigator-initiated clinical research protocol proposed by the researcher, and based on the " Investigator-initiated Clinical Research Contract (sample)" proposed by the pharmaceutical company legal research Group and the Japan Pharmaceutical Society, will draw up a contract, to clearly state how research funding can be made. However, because this way of forming a contract (model) can enable a company to have influence over an investigator-initiated clinical study and its results, maintaining neutrality and independence of the clinical research for the researcher is one major concern. For that purpose, compliance with research ethics and describing the details of corporate involvement and intervention in the publication are required in order to ensure the reliability and transparency of the research outcome.

In the United States, government agencies disclose details of funding and its amount from pharmaceutical companies via the open payment program. Recently, there has been news in the media about prominent U.S. physicians who failed to disclose serious COI situations in papers published in prestigious international journals. In Japan, details of financial relationships between companies and physicians can now be searched on the Web, and clinical societies are strongly required to manage the COI of participants who are involved with the formulation of clinical practice guidelines and are accountable if there are any discrepancies in the content.

Social contribution has become a major mission for medical universities in addition to education, research, and clinical practice, and research institutions are expected to give back to society for the public benefit through their own activities. However, the government's grant support to medical universities and affiliated hospitals has not only been decreasing every year since 2005, but competition for scientific research funds has intensified. In particular, industrial-academic cooperation is one of the important roles of the National University Act, and as a means to expand full-scale industrial-academic cooperation, organization to organization, joint research, funded

research, acceptance of scholarship donations, intellectual property, technology transfer, and establishment of collaborative centers are being strengthened with expectations for outcomes in research and development in methods for the prevention, diagnosis and treatment of diseases. However, potential institutional COI occurs when medical universities and research institutions receiving public funds receive large donations from companies that manufacture and sell pharmaceuticals, license patent rights to specific companies, or hold stocks and other assets. As a result, if senior executives of research institutions (e.g., chairpersons of the organization, presidents, hospital directors, and board members) who have decision-making or auditing authority in activities related to education, research, and clinical practice, make decisions that prioritize the interests of the research institution, the fairness and credibility of education, research, and clinical practice may be distorted, thereby increasing the risk of disadvantage of research subjects and patients. In addition, suspicion may arise among society if there is involvement with the preferential promotion of drugs and medical devices of these companies as an attempt to gain unjustified profits or to pursue more profits by publishing papers. Appropriate institutional COI management is required to prevent such suspicions or misunderstandings.

In the United States, in order to ensure the objectivity, fairness and integrity of research institutions, the American Association of Medical Colleges (AAMC) and the American Association of Universities (AAU) published COI guidelines specifically pertaining to research institutions in 2002. In 2008, a model policy for the management of institutional COI in clinical research involving human subjects, was introduced. The National Science Foundation (NSF) (2005) and the National Institutes of Health (NIH) (2013) each require researchers to disclose organizational COI. In 2013, the International Committee for Medical Journal Editors (ICMJE) published the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations), which have been adhered to by approximately 6,000 medical journals worldwide. In 2013, the ICMJE included in its disclosure form, not only the disclosure of the individual author’s COI but also the institutional COI of the research institution to which the author belongs at the time of publication. In Japan, the National Associate of Japan Medical Colleges Council published the "Guidance for the Management of Institutional COI in Medical Research Institutions" in 2018, emphasizing the importance of disclosure and management of institutional COI in clinical research. Furthermore, in 2019, it required not only the declaration of COI status for individual authors but also detailed disclosure of all professional or personal relationships and activities with third-party organizations and associations at the time of article submission. For-profit and not-for-profit organizations (entities) are defined as government agencies, foundations, corporate sponsors, and academic research institutions.

The Japanese Association of Medical Sciences has made extensive revisions to the Japanese Association of Medical Sciences' "Guidelines on COI Management in Medical Research" established in 2011, in order to incorporate both internal and external trends in COI management, revisions to ethical guidelines and other relevant guidelines. In 2019, the ICMJE published a significantly revised version of the ICMJE Disclosure Form 2021, which expands the concept of COI disclosure in articles submitted for publication. The Japanese Association of Medical Sciences has revised these guidelines in part, due to the fact that each subcommittee has fully adopted the ICMJE Disclosure Form 2021 in order to standardize its COI disclosure form with international standards for articles submitted to its medical journals.

II. Basic thinking

Academic organizations such as medical research institutions and specialist 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 institutions, as well as their scientific educational programs, medical research concerning human beings, and highly advanced medical treatment, require the application of secure ethics and science in order to protect the quality and integrity of the research. The publication of any results in specialist societies or academic journals require ensuring transparency and neutrality. It goes without saying that such medical science research must strictly comply with ethical policies, laws and regulations.

For researchers conducting medical science research, the first step to be taken is for the foundation or organization regardless of whether it is for profit or not, which seeks to employ the data provided by the researcher to ensure that any financial profit deriving from the research (financial etc.) or other related profits (goods, services, status or authority etc.) should be disclosed appropriately within the organization. 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. It is extremely important for research institutions and heads of specialist organizations, in addition to researchers, to properly manage those aspects and to amend any situations in which bias may be suspected from a third-person perspective, and to establish a structure which does not create any misunderstandings without reason regarding the researcher and research institution, to promote industrial-academic cooperation.

The supervision of research institutions and heads of academic societies becomes necessary to ensure that the medical and health, as well as clinical research and its results indicate no undue influence of considerations of financial profit in favor of the industrial side, as the COI situation of researchers is becoming an increasingly serious problem. In order to attain this goal, the evaluation of the COI status should be enforced to prevent serious COI situations, or be supervised by a third party to ensure that the quality and integrity of the medical science research is guaranteed. Furthermore, research institutions and heads of specialist societies should disclose and publicly release appropriately any financial profit or other related profit to create an environment which allows making progress based on an appropriate balance of education and research with an independent, objective, and strictly scientific nature.

In medical science research, clinical studies involving human beings as subjects and involving invasive procedures, which are expected to be the foundation of the development of clinical guidelines, demand an extremely high level of ethical and specialized aspects. Furthermore, since this means that the research concerning human subjects 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. For instance, a COI status can develop latently to become a serious problem, which can increase the risk of bias of the funding organization, and may lead to cause scientific misconduct, Furthermore, the individual researcher who is employed in medical science 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 funds, gifts, material compensation or unjust profits. Needless to say, researchers must adhere to COI policies and any other policies of research institutions or academic societies of which they are members, and from a global perspective these policies need to harmonize with editorial rules that conform to international standards.

III. The Special Character of Medical Science Research and COI Policy

Medical science 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 in medical science research belonging to research institutions and other specialist societies are not only related to commercial ventures, but also are related to, or are involved with, doctor-patient (subject) relationships, therefore the protection of the rights of the subjects and safety of the health and welfare of the subject must be guaranteed.
2. Data from medical science research are involved with the subsequent development of new diagnostic, therapeutic, or preventive methods, due to the Pharmaceutical Affairs Law enacted in

November 2014, therefore it is especially imperative for researchers to ensure the reliability of their data.

3. Researchers with clinical research experience are often required to participate in clinical trials conducted by the related companies and committees related to clinical trials, and often possess close relationships/activities/COI situations with specific companies.
4. The publication of research results has a great impact on those involved in health care, participating as an audience, or reading papers. Therefore, the interpretation of such publicized results has an influence on health practice that is by no means small. In order to subjectively determine whether there is a risk of bias or not in the content presented in relation to the relationships/activities/COI with third-party institutions and organizations, it is necessary for the presenters to disclose all pertinent data concerning related commercial organizations and their COI status at the time of the presentation.

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

1. Many areas of the most up-to-date medical science 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 relevant research.
2. Concerning the development of new drugs, medical equipment, and product development for regenerative medicine, it may be difficult or require a long time for society to benefit by relying only on technology transfer from existing commercial entities. Therefore, there are many cases in which the role of researchers themselves regarding venture entities is large.
3. New drugs or new medical devices require basic research, and medical science research in order to be developed for clinical use. Therefore, it is very difficult for the researchers themselves to be completely uninvolved with this process.
4. Physicians and researchers who possess the knowledge and experience to participate in the formation of clinical practice guidelines, often have relationships/activities/significant COI situations with third-party institutions and organizations.

IV. The Basis of COI Management Related to Medical Science Research

In recent years, COI management related to medical science research can be carried out at (1) research institutes and (2) conferences and medical journals of specialist societies at which research results are made public, and can be largely divided into two stages (see Fig. 2).

1. Implementation of Medical Science Research by Institutions and Organizations

Various research institutions have developed COI policies concerning medical science research (pre-clinical and clinical research involving human beings as subjects) and the systemization of management of COI at those institutions is managed by the heads to ensure the quality and integrity of medical science research when such research is conducted. In particular, concerning research involving human beings as subjects, each researcher is required to submit not only clinical research program plans (protocol) but also COI disclosure statements so that the head of the research institution can appropriately manage COI as an organization. The Guidelines for Investigator-initiated Clinical Trials introduced in 2015 by the National Associate of Japan Medical Colleges Council explains the methods and steps of COI management for clinical studies at research institutions.

When conducting investigator-initiated intervention-type clinical research which involves invasive procedures, the need to ask private sectors for financial support (donations, research grants, financial support for clinical research) increases as more research funding becomes necessary as the number of target cases increases.

In such situations, from the perspective of COI management, the relative researcher must self-disclose this COI to the COI Committee and in addition to making an application to the Ethics committee. Furthermore, the funding source and its purpose should be disclosed or published through publications. For intervention-type research to be conducted appropriately, the validity of whether or not the expenses are sufficient must be considered.

1) Investigator-initiated clinical research using drugs after marketing, particularly results of phase IV comparison tests, provide important information and grounds for the formulation of clinical practice guidelines. On the other hand, from the viewpoint of sales promotion, companies have a high interest in comparative clinical trials using in-house pharmaceutical drugs, therefore in many cases various forms of cooperation and support (funding, work positions, etc.) are often given to the researcher. However, if transparency between academia and industry is not secured, it can easily cause suspicion from society. Therefore, in order to ensure the quality and reliability of the research, it is essential for not only the contract, but COI disclosure of both sides to be made public.
2) Making the results of clinical research widely available to healthcare professionals, patients, and others will lead to public benefit. Therefore, it is necessary to register all clinical trials for human subjects via a public database, and test results should be, in principle, made public. When publishing the results, both the corresponding researcher and the supporting company involved

are responsible for disclosing and publishing all relevant COI related to the publication or presentation of the study.

3) When preparing the publication, it is necessary to clearly state the authorship criteria and if help was obtained from medical writers, statisticians, and any other persons regarding the interpretation and discussion, this should be mentioned. If such people do not satisfy authorship criteria, their contributions should be acknowledged in the Acknowledgement section by stating their names, affiliations, funding sources, and all COI.
4) In addition to investigator-initiated clinical research that is planned and financial sources obtained independently by the researcher, although there are other types of investigator-initiated clinical research, such as those requested by company (commissioned or entrusted research, joint research), and those contracted by a company after in-house reviews, from the perspective of complying with research ethics, the head of the research institution and the researcher must fulfill their responsibility to be accountable for the research.

Regarding the conduct of investigator-initiated clinical trials, the Clinical Research Act became effective in April 2018, and 1) clinical research on unapproved or off-label drugs etc. under the Pharmaceuticals Affairs Law, 2) Clinical research on pharmaceutical products funded by pharmaceutical companies is considered to be specific clinical research, and when conducting clinical research to clarify the efficacy and safety of pharmaceutical products, the procedures for conducting clinical research, management of COI, measures for appropriate implementation of work based on the review opinion of the Certified Clinical Research Review Committee, and disclosure of information regarding the funding etc. for clinical research are now mandatory. In addition, regarding COI Management Guidance under the Clinical Research Act (2019), it is clearly stated in the Q&A that "If, for example, you present the research results to an academic society after the research is completed, you must adhere to the COI management policy of the academic society to which you belong.

2. Specialized Societies at Which Research Results are Presented and Clinical Guidelines are Formulated

The 138 subcommittees belonging to the Japan Association of Medical Sciences have established COI guidelines based on a common philosophy with the COI guidelines of the research institutions to which researchers belong, and many members present their research results in relevant international medical journals using designated COI forms. We recommend that each subcommittee fully adopts the ICMJE DISCLOSURE FORM 2021, which is considered to be the standard, and utilize this form for disclosing the COI status of individual authors as well as institutional COI of institutions and organizations to which the authors are affiliated with when submitting papers to medical journals

(English and Japanese) of the subcommittees.

3. Items that Should be Avoided and Managed in Clinical Research Conducted by the Principal Investigator

In cases of research involving human beings conducted as an interventional study by the researcher for industrial-academic cooperation, the following items should be avoided by researchers involved in those projects.

(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 payment for travel or accommodation from commercial societies or ventures in order to take part in medical meetings unrelated to the research
(4) Receiving remuneration in regard to the results of the specific study or result

On the other hand, the principal investigator or research director (on behalf of collaborative research in multiple institutions) involved with clinical research, 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 relevant 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) Having received money or gifts exceeding the actual value of the time or labor expended on the relevant research.
(4) If the relevant research includes participation of temporary researchers, part-time instructors and graduate (working) students who belong to companies, are being dispatched to the research institution, suppressing the name of the relevant company in the research plan and published results.
(5) Affecting the ability in the collection and storage of data, statistical analysis, interpretation, and conclusion based on the influence of financial supporters or commercial organizations.
(6) Affecting the ability to report on the results at a medical society based on influence of financial supporters or commercial organizations

However, even if (1) and (2) are relevant to the researcher, in a case where the researcher is essential to the planning and conducting of the medical science research, and that the research is of extreme

significance in society, based on the understanding that the integrity and transparency are ensured, it is possible to nominate the researcher as the principal investigator or representative of the research. However, the head of the research institution has a duty to clearly state this fact to society. In addition, if accepting a contract whereby (5) and (6) are relevant, the funding source and its role must be disclosed at the end of the text of the manuscript at the time of publication.

V. Regulations Concerning COI Policy

Each affiliated society must establish its own policy concerning life sciences and medical science 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 and affiliated institution or organization taking part in this research, the management systems should also take into account any relationships/activities with third-party institutions or organizations to prevent any breach of the COI policy, especially concerning the established policy. In order to implement management of COI the affiliated societies should have a predetermined policy and penal regulations on how to deal with any breaches of the COI policy.

1. The Procedure of COI Management

Concerning the publication of the results of life sciences and medical science research, all researchers involved in the given research, must, in principle, submit a self-reported COI disclosure document to the president of the affiliated society at the time of presentation (Fig. 4). If it is pointed out that there is a violation of the COI guidelines in relation to the presentation, the researcher must understand and cooperate fully. If appointed as officers, chairpersons of committees, members of designated committees and members of working groups, the COI status in relation to the given activity must be described by self-disclosure in the designated form (Form B) at the time of appointment, and undergo appropriate evaluation, as they play a very important role and have responsibility for their activities in relation to the society.

2. Companies, Corporate Institutions and For-profit Organizations Involved in Industrial-Academic Cooperative Activity

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

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

(2) Commissioned research: companies, institutions, and organizations commit themselves to contracts concerning methods of treatment, drugs and devices, and research is performed on the basis of such contracts.
(3) Technology transfer: companies make practical use of the patent rights and other rights concerning the research results of research institutions.
(4) Technology guidance: researchers of research institutions etc. conduct business development and give technological advice.
(5) Research institute ventures: venture organizations are based on the results of the research of universities and research institutions and supported by the research institution.
(6) Donations: unrestricted donations are made to assist universities and research institutions by companies, institutions, and organizations.
(7) Endowed departments: departments are established for the promotion of research enabled by financial donations to research institutions from companies, institutions, and organizations.
(8) Joint research centers: activities such as opportunities for joint research, technical training, technical consultation, and providing information.
(9) Commissioned researchers: accepting current researchers from companies etc. and fostering them with research guidance to the graduate school level.

3. Those Subject to COI Management:

(1) Both members and non-members presenting the results of research in scientific presentations and publications etc., must report the COI status in relation to the performance of that research and its relationships/activities with the related third-party institutions and organizations and, in accordance with the per se and detailed regulations of the affiliated society, must make such disclosures (Fig. 4, Ref. 3) using the designated forms at the time of presentation. 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) 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 (CPG steering committee, scientific organizing committees, editorial board committees, ethical committees, COI committees etc.) and temporary groups (committees, working groups, teams 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 (Fig. 1) at the time of appointment, and undergo appropriate evaluation. Should the COI status change after the appointment, then according to the regulations of

the society, there is a duty to disclose any additional information, and such cases should be managed quickly and appropriately.

Whether to include spouses, first degree relatives, or subjects who share income or financial benefits (inherited benefits) of those above subjects should be determined depending on the situation of each affiliated society. However, in cases where the spouses, first degree relatives are not included as subjects of COI disclosure, if there is possibility of COI due to indirect or uneconomical factors that might affect the carrying out or interpretation of the results of the medical science research, they may be required to disclose such COI using the designated form.

(3) Affiliated Research Institutions

Regarding institutional COI, if the individual is affiliated with a research institution that has a COI relationship (e.g., patents, royalty ownership, etc.), or has been involved with the head of a research institution (university, hospital, department, center, etc.) as a collaborating or joint researcher that has a COI relationship with a specific company (e.g., personnel accepted from a company to a senior position, research funding, donations, patent ownership, etc.), either at present or in the past 3 years, if it is determined that there is a possibility of direct or indirect influence on the activities of the relative society that the individual is involved with, it is required that COI is disclosed for the items below using the designated COI disclosure form (Form 1). The amount set for disclosure will be determined by the following criteria for each item to be disclosed.

1) For research funds provided by companies, institutions, or organizations, disclose if the total amount of research contract funds used for medical science research (joint research, commissioned research, clinical trials, etc.) from a single company or organization is 10 million yen or more per year.
2) For donations provided by companies, institutions, or organizations, disclose if the total allotted amount for the affiliated institution or department of the individual, or the head of the affiliated institution or department from a single company or organization is 2 million yen or more per year.
3) Additionally, if the affiliated research institution or department of the individual, or the head of the research institution or department (has been involved as a collaborating or joint researcher in the past 3 years), owns shares (5% or more of all shares), receives royalties, or makes investments in venture companies, etc., these should be disclosed as institutional COI.

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, or public lectures 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 physicians, board-certified specialists, board-certified trainers or certified 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 COI policies:
(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 or co-sponsored by companies or for-profit organizations (includes online seminars via website, academic lectures)

Furthermore, members of the affiliated societies must disclose all COI situations using the designated form (Fig. 4) according to COI policies of the affiliated societies, concerning academic activities (regardless of being sponsored or co-sponsored by companies etc.), 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, we have established 9 items (Ref. 1, 2）concerning relations with industry. One of the most problematic and frequently discussed is that of grant (incentive) contributions, especially their interpretation and handling. The recipients of grant contributions from companies, institutions, and organizations, 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, field) 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 science

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 should be reported in the COI self-disclosure. In the latter situation, it has already been stated that COI self-disclosure is necessary.

Another disclosure item, concerning which suspicions can easily arise includes those cases in which financial support (commissioned research, research funds) is made available from fund management organizations and institutions such as not-for-profit foundations (for example NPOs) or public foundations (for example corporations, foundations) and investigator-initiated clinical trials are conducted. If grants from pharmaceutical companies 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 name of the funding company must also be listed in the COI disclosure form. For COI disclosure, when submitting manuscripts for publication, Item 2 of the ICMJE Disclosure Form (2021) corresponds to this. Self-disclosure forms should be of three types (1) for officers, committee members (2) those presenting at academic meetings, (3) those publishing in journals and used accordingly.

6. COI Management of Each Type of Individual

The subjects of COI management in affiliated societies include speakers (members, nonmembers), officers, committee members (including external members), and COI must be self-disclosed. All names of organizations and research institutions of which they hold full time positions must be listed during self-disclosure of COI when subjects are appointed as officers or committee members.

(1) Members

Members and non-members who are affiliated with research institutions must disclose all related COI when publishing or presenting academic achievements, however, members who are only affiliated with companies will not be targets of COI management. However, if the presenter is a full-time employee of a company but holds simultaneously a part-time position at a university or research institution etc. (e.g. lecturer, visiting professor, etc.), temporary researcher, graduate student (working), then the name of the affiliation where the presenter holds a fulltime position (including affiliation and title) should be given, or as another option, both the names of research institutions, etc. where both full-time and part-time positions are held. In principle, for the presenter, if the funding provider of the research funding of the presentation is company-affiliated, then only the name of the company (including affiliation and title) needs to be listed. If the funding is provided by a different company, the name of the related company should be disclosed in the self-disclosure form. 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 companies, institutions, and organizations related to the contents of the research.

On the other hand, if a member who is affiliated with a research institution has changed workplace in the past 5 years from a designated company or NPO to a fulltime or part-time position at a research institution (adjunct professor etc.) but the research theme is ongoing, the name of the present research institution to which the presenter is affiliated in addition to the previous affiliation (corresponding company name) related to the research must both be mentioned when presenting research results.

(2) Officers and Committee Members

The president of the affiliated society must, in principle, make it a duty for the individual officers and committee members to submit a COI self-disclosure document (online disclosure possible via website) with regard to their relations to companies, corporate institutions, (not-for-profit organizations, foundations etc.), and organizations（Ref.1）. Furthermore, if the subject was affiliated with related companies, or for-profit organizations in the past 5 years, this (period, name of company, position etc.) must be reported to the president of the affiliated society. The method of disclosure is usually done on a printed form, but a self-disclosure system established on a secured website for disclosure on application by a given day is also recommended.

Companies, corporate institutions, and for-profit organizations may present or may supply information on external finances including reimbursement for manuscripts, lectures, medical science research funds (including clinical trials and clinical studies), commissioned research, joint research, clinical trial funding, 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 who is an officers or committee member if the amount exceeds that described in the COI regulations, it is necessary to fill out the amount (3 levels) designated form (Ref. 1) and accurately disclose the situation to the president of the affiliated society. The president of the affiliated society must, in collaboration with the COI Subcommittee, determine the severity of the COI situation presented in the COI self-disclosure forms submitted by officers or committee members when selecting presidents or members for the respective committees.

1) Editorial Board Members

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 a duty

to self-disclose COI. In the affiliated societies, there are frequently some unavoidable relationships among authors and those in 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), and many may result in a COI situation. 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 be reduced and it is even possible that it would be impossible to find suitable candidates to request peer reviews. Based on this and other considerations, it is, therefore, 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 the reluctance to perform a review because of a COI issue regarding the author or the individual reviewing peers, they may 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 returning 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) Participants Involved in the Formulation of Clinical Practice Guidelines

The Clinical Practice Guidelines (CPG) are widely used not only by clinical societies, and clinicians but also by patient support organizations, funding institutions, medical experts, lawyers, and consumers. Recently, the clinical development of drugs and medical equipment is rapidly growing, and therefore the quality and credibility of CPG have brought much attention internationally. Based on the EBM technique, in order to formulate a trustworthy CPG, those involved in the establishing of the guidelines and the specialist societies as an organization must disclose COI situations and make them available publicly. Not only that, the criteria for those participating in the formulation of CPG must be made clear and COI management to avoid any bias risks is strongly desired.

The president of the affiliated society will establish a CPG Steering Committee as a standing committee. If new plans are established in the CPG regarding diagnosis, treatment, or prevention, and if revisions are to be made, measures such as budget and establishment of a systemic review team; SR team, and external evaluation (committee) should be established as part of the task to establish or revise CPG. It is possible for members of the CPG Control Committee, Guideline Formulation Committee, and SR team, to overlap partially, but in principle, the committees should be independent of each other to secure transparency of guideline establishment (Minds CPG Development Guide 2014). The president of the affiliated society will have participants involved with CPG formulation to self-disclose any COI using the designated form and will cooperate

together with the COI Committee beforehand to evaluate and manage this so that the most eligible members are chosen (Fig 3).

In general, the COI of those involved will not only include financial COI but expertise, preferences, promotions, and any other intellectual COI that might be considered to affect career development, or if the COI situation with the affiliated research institution or society and the specific company is strong, this can be seen as potentially affecting CPG formulation. In particular, when selecting the CPG Formulation Committee members, president (vice president), it is necessary to take a multifaceted approach and requires exceptional care. The Japan Association of Medical Sciences Guidance on Participants Involved in the Establishing of Clinical Guidelines (2017) can be used as referential material for specific measures to be taken in such situations.

In addition, if guidebooks, discussion articles, and special feature articles are to be published from member societies, any related COI must be disclosed by participants using the COI form and the information should be published at the end of the article.

(2) Management of Institutional COI and Effects on Research Institutions and Societies
In medical science research, especially when conducting and publicizing research results for clinical research involving human subjects, in addition to the process of establishing guidelines for clinical practice, and activities for clinical care and/or education, as it can be said that senior officials (chairpersons, presidents, directors, department heads, hospital directors, etc.) may directly or indirectly influence the relative researcher if they are their teacher, colleague, friend, or relative, the following have been reported as examples of institutional COI (institutional conflict of interest). For example, if a research institution (e.g., university or medical institution) or its senior officials receive a large endowment from a specific company, or if they own shares or receive royalties from a specific company, they may prioritize the acceptance of clinical trials using the company's drugs or medical devices or the procurement and purchase of products, and this may influence the review process. In addition, the content of contracts may be concluded in favor of a specific company. On the other hand, even if the head of the research institution takes all appropriate actions, it may not be possible to avoid society's suspicion that a bias may have occurred, disadvantaging research subjects and patients. In order to avoid or mitigate the occurrence of such situations as much as possible, if the affiliated research institution has a serious COI situation, or if the researcher has been involved with the head of a research institution, as a collaborating or joint researcher, that has a serious COI relationship either at present or in the past 3 years, it is necessary to disclose all institutional COI by referring to the examples below.

(1) Examples of institutional COI cases in medical science research involving human subjects (clinical trials, clinical studies).

1. AA University established the Clinical Research Support Center with a donation from TT Pharmaceuticals (900 million yen). TT Pharmaceuticals planned a large-scale comparative clinical trial of a new antihypertensive drug XX and conducted the trial at the Clinical Research Support Center. (TT Pharmaceuticals expected positive trial results from AA University: Management Example; AA University discloses the fact that funding to establish the Clinical Research Support Center was from TT Pharmaceuticals, ensure that the ethical review of clinical trials involving TT Pharmaceuticals and the monitoring of research implementation were conducted with neutrality and transparency without inappropriate corporate involvement).
2. The Hospital Director PP of AA University Hospital, is also the Chairman and Professor of the Department of Endocrinology at AA University Hospital, and accepted a contract of 20 million yen per year for a collaborative research fund with TT Pharmaceuticals, as Director of the hospital. Associate Professor RR, who is collaborating with Director PP, independently conducted clinical research on TT's drug YY as principal investigator, and published a paper (Director PP was not coauthor). (TT Pharmaceuticals expected that the research results would contribute to their sales promotion; Management Example: Associate Professor RR discloses all COI status of his mentor Chairman and Professor PP, institutional COI, in addition to his own COI disclosure with TT company)
3. The president of AA University, President PP, signed a 5-year (1 billion yen) comprehensive contract for drug development and research with TT Pharmaceuticals. President PP used the funds to start an in-house development project XX, and allocated 70 million yen to his former junior colleague Professor QQ as funding for clinical development research. Professor QQ conducted comparative studies on new combined effects mainly on YY, a marketed drug of TT Pharmaceuticals, and published the results in a paper. (TT Pharmaceuticals expected the results of Project XX to contribute to their sales promotion; Management Example: Prof. QQ discloses the funding source of 70 million yen as institutional COI).
4. AA University has invested heavily in TT, a venture company, for asset management. AA University Hospital is prioritizing a large-scale clinical trial YY, using TT's novel drug as a joint research (Both AA University and TT expect positive data: Management Example; AA University discloses the amount of investment in TT, COI management is necessary to avoid risk of bias in the process of conducting clinical trial YY and publishing the results).
5. TT, a manufacturer of cardiac catheters, offered 10% of its stock to medical institution AA and asked to conduct post-marketing clinical trials of its novel cardiac catheters and to publish papers on it (both TT and medical institution AA expect favorable results for sales promotion: Management Example; medical institution AA discloses stock ownership of TT company and

manages COI to avoid risk of bias in conducting the research and publishing papers).

6. AA University launches a venture company TT within their university, and Professor PP conducts a clinical trial of candidate drug XX at the university hospital using funding from the government's "Comprehensive Strategy for Strengthening Pharmaceutical Industry" (If successful, the results of the clinical trial will be well-acknowledged as the university's achievement and profits of the drug are expected after approval: Management Example; AA University discloses its COI interest with TT, Professor PP and joint researchers disclose not only financial COI but non-financial COI with TT to avoid risk of bias).

(2) Examples of institutional COI cases involving the purchase of pharmaceuticals and medical devices

When a research institution holds patents or receives royalties on pharmaceuticals or medical devices from a specific company or venture company, or when a large amount of funding (donations, grants, etc.) is provided by a company, it is likely that the affiliated hospital of the relative research institution will give priority to its purchase without objectively evaluating its efficacy and validity, and cases in which they are preferentially used in clinical practice may occur.

1. AA University has established a new Joint Replacement Research Center using donations from the former President PP, who contributed for the past 10 years. PP holds royalties for CC hip prosthesis, has been adopted in the hospital but the evaluation among orthopedic surgeons regarding the quality is low (the company selling CC expects AA university hospital to use and purchase CC: Management Example; AA University will verify that procurement of medical materials for the Joint Replacement Center is carried out objectively and competitively, and under no influence of former President PP).
2. AA University Hospital and a university venture company BB have succeeded in the co-development of a regenerative medicine product, human (autologous) organ-derived tissue sheet SS-10, and owns royalties. Professor PP who is affiliated with AA University has introduced clinical practice guidelines as head of the guideline committee of his affiliated academic society, that preferentially uses SS-10. (AA University and Professor PP expect favorable effects in sales promotion: Management Example; in principle, Professor PP who is affiliated with AA University who holds royalties should not be appointed as head of the guideline committee).

(3) Examples of institutional COI cases expected in medical science societies

When a large donation from a specific company is provided to a specific medical science society, or a contract is drawn for a specific drug, or if there is a financial relationship, such as a joint seminar with a company when hosting academic conferences, society may suspect that preferential treatment

is given to the relative company. In addition, the risk of bias increases if the officers of an academic society who are involved in projects related to the formulation of clinical practice guidelines have serious COI with relative companies (e.g., large honoraria, advisory board members, royalty holdings, etc.). In such cases, it is important to disclose and publish detailed institutional COI status of the society in advance. If such information is published after a questionable situation is pointed out and a request for disclosure is made, the credibility of the relative society may be damaged. Furthermore, by disclosing and making public information concerning institutional COI, the heads and officers of societies can act autonomously from a neutral standpoint for the relative activities, thereby reducing the risk of bias.

1. AA Society has a contract with medical journal JJ, which is fully supported by TT Pharmaceuticals, and uses it as the official journal of the AA Society for publication of review articles and original papers (TT Pharmaceuticals expect publicity effects: Management Example; AA Society needs to appoint members who have no COI with TT for its journal editorial board to ensure openness and neutrality and to avoid influence from TT as much as possible.
2. TT Pharmaceuticals donates 30 million yen to the AA society (with the expectation that TT will receive preferential treatment for activities related to the society: Management Example; the donation is placed into the general account, the chairman of the board of directors and other board members do not participate in projects related to TT, but only those members who have no COI with TT participate in such projects).
3. The President of the AA Society has a personal contract with TT as advisor, and the AA Society is promoting a multicenter clinical comparative trial of TT's drug (TT expects AA Society to be at an advantage in publishing papers and recommending guidelines: Management Example; the President of the AA Society declares at the board meeting that he/she will not be involved in any clinical trials involving TT's drugs, nor participate in any deliberations or voting, and this is recorded in the minutes of the meeting).
4. TT Pharmaceuticals donates 300 million yen to BB corporation (an academia founding fund management organization), and BB corporation provides a research grant of 90 million yen to the President of the AA Society for comparative studies of TT drugs (TT expects sales promotion of the relative drugs: Management Example; the author of the paper should list not only BB corporation but also TT Pharmaceuticals as the funding source, and to disclose appropriately if there are any authors who are also board members of BB corporation).
5. TT Pharmaceuticals sponsor symposia and luncheon seminars at meetings for the AA Society (TT expects sales promotion of its products: Management Example; the source and amount of funding from companies, in addition to COI of chairpersons and speakers should be disclosed).
6. An officer PP who is affiliated with TT Pharmaceuticals is appointed as the President of the AA society, which consists of members from both companies and research institutions and conducts

testing and research on HH testing equipment under a contract with TT Pharmaceuticals. (TT expects favorable research for the company: Management Example; the officer PP affiliated with TT is not to be involved in any tests or research on HH testing equipment and signs a written pledge that he/she will not participate in board discussions on related matters).

7. CC, who is the President of the AA Society holds royalties of TT's regenerative medicine product BB and participates in the development of guidelines for the appropriate use of the product BB (expects good sales promotion effect for TT: Management Example; the Chairman CC should not participate in development of guidelines and should appoint a member who is in line with the eligibility criteria for participation in the development of JAMS clinical practice guidelines).
8. The AA Medical Society has a contract with TT Pharmaceuticals for the analysis and presentation of results of post-marketing surveillance research on TT Pharmaceuticals' new drug ZZ, and receives funding from TT Pharmaceuticals to present the results at international meetings (TT Pharmaceuticals expects favorable sales promotion effect: Management Example; when the post-marketing surveillance research was requested by TT Pharmaceuticals, members with no COI should have been possibly appointed to the committee, and when the results are compiled and published, the funding source, TT Pharmaceuticals is disclosed).
9. TT Pharmaceuticals is a supporting member of the AA Medical Society (TT Pharmaceuticals expects to deepen personal relationships with the executive officials of the society, etc., and expects sales promotion effects: Management Example; TT Pharmaceuticals discloses on its website that it is a supporting member).
10. TT Pharmaceuticals is a sponsor of society awards established by the AA Society, which is a corporate organization (TT Pharmaceuticals expects public relations benefits from funding specific awards: Management Example; AA Society should clearly state that the Society awards are sponsored by TT Pharmaceuticals in the application guidelines and should publicize at the time of presenting the awards and also on the website, etc. Members with a serious COI with TT Pharmaceuticals should not be involved in the review of Society awards).
11. The Young Scientists Research Grant Program established by the AA Society is operated under the sponsorship of TT Pharmaceuticals (TT Pharmaceuticals expects sales promotion as well as publicity effects by providing grants: Management Example; AA Society should clearly state that the Society awards are sponsored by TT Pharmaceuticals in the application guidelines and should publicize at the time of presenting the awards and also on the website, etc. Research projects should not be related to TT Pharmaceuticals' products, and members who have a serious COI with TT Pharmaceuticals should not be involved in the review of research grants).

7. Period Required for Disclosure

The medical science 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 medical and health studies which require ethical approval, and in particular, interventional studies, long periods of research are necessary. Therefore, in relation to the contents of the submitted paper, all relationships/activities/COI situation with third-party institutions and organizations for support leading up to the submission of the paper should be disclosed without setting a time limit, and for any other disclosure items, a period of previous 3 years from the time the paper is submitted.

Clinical research using funds provided by a company, particularly large-scale invasive intervention type research, are often conducted over a long period of time, even after the time limit described in the research plan (protocol) approved by the Ethics Committee. Since COI self-disclosure is required according to the COI policy of the society or journal at the time of submission, it is desirable to keep records of all relationships/activities/COI situation with third-party institutions and organizations by year. In particular, the amount of donations and research support funding related to clinical trials should be recorded as part of the data together with the contract.

Furthermore, when a member publishes the results of a research, and when he/she is appointed as an officer, the period for the previous three years from the preceding year, is the target of COI disclosure.

8. Method and Timing of Self-Disclosure

The method of self-disclosure is clearly stated in the COI policy and detailed regulations according to subject. (See Fig. 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 8 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 affiliated society, and 4) the final decision concerning the approval/approval with condition/ disapproval, etc. will be made by the head of the affiliated society to the candidate.

(2) Authors Presenting at Scientific Meetings

The president of the affiliated society can require all those with names attached to the publication or just the first speaker, 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.

Speakers (of academic presentations) should disclose all existing and possible COI situations using the format prescribed by the affiliated society, either on the first or second slide (see Fig. 4 a, b). In addition to showing the slide for a certain amount of time, reading the names of companies, institutions and organizations in which a COI situation exists, is one significant way to manage COI. In addition, if a member participates in educational seminars or training seminars for the purpose of acquisition or renewal of professional qualifications/credits, and if handout materials which include contents of presentations are to be distributed, the COI information of the presenter should be disclosed using the designated form.

On the other hand, in luncheon seminars, evening seminars, research meetings and lectures organized or co-sponsored by companies or commercial organizations, the chairperson or MC must disclose the names of related companies and organizations to the audience and read out the names of companies by using the same slide format as academic speakers. If there are many company names to be read out, they should be disclosed by slide projection during the lecture on a separate projector or by other appropriate means.

Regardless of whether the lecture is sponsored or co-sponsored by a company, academic speakers must ensure the independence and fairness of the content of the lecture, and must be accountable for their own academic research. In particular, researchers who are requested to give company-sponsored academic lectures must comply with medical ethics and strive to communicate accurate information so that medical professionals can properly use drugs, medical devices, and regenerative medical products after approval (or certification).

(3) Authors Publishing in Scientific Journals: Relationships/activities/COI disclosure regarding third-party institutions and organizations

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 (both English and Japanese journals) in the scientific journals of the affiliated society for all support from third-party institutions and organizations and relationships/activities/COI situation from the start of the research leading up to the submission of the paper, using the designated form (ICMJE Disclosure Form 2021) (Ref. 3, 4). The term "related" to the

content of a submitted paper means any involvement or activities that may affect the benefits gained by a for profit or not-for-profit third-party institution or organization as a result of the content of the submitted paper.

① Authors

Authors of manuscripts should meet all four of the ICMJE authorship criteria as proposed in the ICMJE Recommendations: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; (2) Drafting the work or revising it critically for important intellectual content; (3) Final approval of the version to be published; and (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors must declare and disclose all relationships//activities/COI status with third-party institutions and organizations in accordance with the COI guidelines of the journal to which they are submitting papers. Usually, the corresponding author is the main contact person during the process of article submission, peer review, and publication, and is responsible for ensuring fairness by handling all administrative requirements such as author information, ethics committee approval, and collecting statements concerning the COI status of all authors of the given paper. After publication of a paper, he/she should respond sincerely to any criticisms or doubts about the research upon request from the journal publisher.

② Contributors

Although a researcher of a submitted paper who meets all authorship criteria with a is listed as an author, it is not clear what roles and contributions each author has made, especially in original papers that have multiple authors. From the perspective of taking responsibility for the action and accountability of each author, it is necessary to disclose such information as contributors. In particular, if an author has relationships/activities with a for-profit third-party institution, it is helpful for readers to understand the roles of each author in the process of the relative study to determine whether a bias exists or not.

③ Non-author contributors

For collaborators who do not meet all four authorship criteria, their contributions should be clearly acknowledged. Examples of such include acquisition of funding, general supervision of a research group, general administrative support, writing assistance, technical and language editing, and proofreading. Furthermore, academic contributions may include, for example, served as scientific advisor, critically reviewed the study proposal, data collection, provided and cared for study patients, and participated in writing or technical editing of the manuscript. Acknowledging the role of non-

author contributors assures the quality and reliability of the content of the relative paper, and therefore, the corresponding author should obtain written permission from all the individuals to be acknowledged to whom the acknowledgments are addressed. For relationships/activities/COI status related to the content of the submitted paper, each researcher should disclose detailed information using the ICMJE Disclosure form to disclose the role of funding sources, contributors, acknowledgments, and to clarify the roles and responsibilities of authors and collaborators (Fig. 5-A). On the other hand, to accept a submitted paper and publish it in a journal, proper management is required to ensure the neutrality and fairness of reviewers and editorial board members.

④ Editors

Editors (including visiting editors) who make final decisions on manuscript submissions should recuse themselves from participating in the editorial decision-making process if faced with the review of a manuscript with whom they have relationships/activities/COI with the author. Similarly, other editorial staff who participate in editorial decisions should disclose their relationships/activities/COI status to the editor, decline from making decisions if there is potential bias, and must not use any information from the work they are reviewing before publication for their own interests.

⑤ Peer reviewers

Reviewers should disclose whether they have any relationships/activities/COI status that could influence the review of a submitted paper. In cases where this could bias their opinions of a manuscript, they should recuse themselves from the review. Reviewers must not use any information from the work they are reviewing before publication for their own interests.

The following points should be brought to attention if there is a company-affiliated researcher among the authors. ①Name of the affiliated company of the researcher, department name, job title; ②Description of the contribution to the research; ③Investment amount from the company; ④ Where or whom the research results belong; ⑤Whether or not a contract exists that allows a relevant company to exercise influence regarding the presentation and publication of research results; ⑥Confirm whether there was labor provided from companies that may affect the results of the research, and publication of a manuscript should be a comprehensive decision made after considering whether the reliability and quality of the research are secured or not.

①Authors of Manuscripts in English language Journals

The International Committee of Medical Journal Editors (ICMJE) published the ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals in 2013, and introduced the ICMJE Disclosure Form to help standardize appropriate

disclosure of COI status conveniently of not only authors themselves but of their affiliated institutions and facilities. The form is, in principle, revised yearly.
In the case of English-language journals published by each subcommittee, it is expected that there will be a considerable number of papers submitted by overseas researchers (non-members), and there is a possibility that the content may differ from industrial-academic cooperation activities in Japan due to national circumstances. Therefore, the ICMJE Recommendations 2019 should be applied mutatis mutandis, and a declaration using the ICMJE DISCLOSURE FORM 2021 should be clearly stated in the journal COI guidelines regarding the relationship/activities/COI status with third-party organizations/associations limited to the content of the submitted paper.

For researchers, 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. In particular, the attention paid by society to the research results of medical science 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. For the convenience of contributors, it is necessary to harmonize the COI declaration disclosure forms for 1) Japanese journal presenters and 2) English journal presenters, and the Editorial Board and COI Committee of each subcommittee should work together and recommend the use of the ICMJE Disclosure Form 2021 (English version and Japanese translated version).

The policy of the "Guidelines for Support of Investigator-initiated Clinical Research Using Pharmaceutical Drugs" established by the Japan Pharmaceutical Manufacturers Association (abbreviated as Pharmaceutical Cooperative Clinical Research Support Guidelines) in January 2016, is that no research support by donation will be conducted, and research support will be provided as stated in the contract between the research institution. According to the content of this contract, the principal researcher will propose a research plan, and if the company finds it is advantageous for the company after review, it will approve the research which will be conducted through full responsibility of the research institution. It is obligatory to submit the details of the research results to the contract company, before publicizing them. The company will conduct a review of the results from an ethical, medical and scientific point of view, and will respond to the principal researcher. The principal researcher will take into account the response from the company, and will be responsible for making the final decision as to whether to make the content public, however the funding company is not liable for the research. Furthermore, in the event that it is not made public,

the contract allows the company to use or publish the research results, with a possibility of risk of bias towards the company side.

In order to ensure the fairness and reliability of research, principal researchers should make efforts to clearly state at the end of the publication any role or involvement of funding supporters (company related persons) in the planning, protocol making, conducting, monitoring, auditing, data compiling, statistical analysis, data interpretation, manuscript preparation, and review, to avoid this risk. Please refer to the example statement for English and Japanese manuscripts (Fig. 5-B), in reference to the ICMJE Recommendations created by the International Committee of Medical Journal Editors.

In order to ensure the fairness and reliability of the research, authors must self-disclose the COI status with companies etc. related to the content of the article using the designated form, and for medical science research conducted under contracts with companies, to clearly state the roles and involvement of funders (e.g., companies) in the planning, protocol development, implementation, monitoring, auditing, data collection, statistical analysis, data interpretation, manuscript preparation, and review, etc. as Role of the funding source or Acknowledgements in the article. In addition, from the viewpoint of authorship, the roles and contributions of each individual author during the process from the planning of the research to the publication of the paper must be clearly stated in the paper as Contributors.

Even if there is no definite COI status to be reported, there should be a statement about COI status such as “The authors declare they have no conflict of interest”. The action to be taken by the subcommittee against those who violate the COI disclosure will also be clearly stated in the COI guidelines or submission rules.

②Authors of Manuscripts in Japanese Language Journals

It is mandatory for member authors of Japanese journal articles (original articles, reviews, etc.) to comply with COI policy of the affiliated society for any non-member contributions, and must disclose COI status for all relationships/activities/COI situation with institutions and organizations using the Japanese translated version of the ICMJE Disclosure Form 2021 (Ref. 4). For publications in Japanese journals, including roundtable discussion articles, each author must disclose COI status with companies if it exceeds the base amount as shown in Fig. 6. Furthermore, if there is company involvement in the research contract, the details of the roles of the funding company must be stated appropriately in the paper, as shown in Fig. 5-A, 5-B.

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. 2-4 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.

10. Role and Responsibility of the Board of Directors

The president of the affiliated society may consult the COI committee, ethics committee, and clinical practice guideline steering committee, to and based on the response, the board of directors may consult 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 self-disclosure of relationships/activities/COI with third-party institutions 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 president of the subcommittee, on behalf of the subcommittee, 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 self and social responsibility to explain the results of the verification of facts and in response to excessive accusations of the individual member.

The president of the affiliated society, etc. should avoid arranging contracts with companies, institutions and organizations that will not agree to any activity or survey activity which may lack public transparency, neutrality and appropriateness of research or announcements of the affiliated society.

The president of the affiliated society should provide educational training on research ethics (bioethics, publication ethics, COI management, etc.) at academic meetings and lectures, and should make it mandatory to participate in order to educate members. Furthermore, attending a session on research ethics is mandatory and credits are given to board-certified physicians, board-certified

specialists, or board-certified trainers when obtaining and renewing qualifications. If a member participates in research ethics training at different affiliated societies or research institutions, there is a need for a compatible system to recognize the credits earned at different locations.

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, Editorial Committee and the Clinical Practice Guideline Steering Committee should cooperate.

1) The Role of the COI Committee

The COI committee should play an advisory role to avoid the risk of potential bias and ensure that COI of individual members as well as affiliated institutions and organizations which may affect the publishing of study results, and the formation of clinical practice guidelines is disclosed appropriately and managed properly to promote medical science research in industrial-academic cooperation. In addition, if in the event that a member's COI status is considered to be serious, or if the COI self-disclosure is found to be inappropriate or suspicious, a hearing will be conducted, and the results will be reported to the president of the affiliated society.

The COI Committee has jurisdiction over the following:

(1) Handling all inquiries from individual members concerning their COI status (creating Q & A).
(2) Judgment, management, and guidance concerning COI status of officers and presenters (including non-members) with risk of bias in business related activities (particularly, establishment of clinical practice guidelines).
(3) Cooperation and educational activities for the planning of training in research ethics and publication ethics.
(4) Investigation activities and recommendations for improving measures in the event of suspicions raised concerning COI disclosure of individual members.
(5) Gathering of information for revisions of COI policy and bylaws. The president of the affiliated society must provide an opportunity for commissioned external officers of the committee to participate in training of COI management and research ethics.

2) Criteria for Judgment of COI Disclosure

Neither standard judgment criteria nor standard evaluation criteria exist in COI management since the relationships/activities/COI status regarding life sciences and medical science 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 nondomestic residents). Life sciences and medical science research in collaboration with third-party institutions and organizations should be conducted in a proper and publicly transparent way, regardless of the fact that the remuneration and grant support will differ depending on the companies, institutions and organizations, therefore, a potential state of COI for the researcher is inevitable. Therefore, the criteria regarding the content of the activity and the finances involved particularly 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 companies, institutions and organizations, either in the form of an honorarium, editing fee, or scholarship fund, or research fund there is a possibility that the interpretation and study results will be biased in favor of industry, 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 the base amount, and in such case the corporate name of the funder must be disclosed. In this guideline, the base amount for disclosure has been set and proposed in order to prevent COI status from becoming severe for its members, officers, and when selecting committee members or commissioned personnel (Ref. 1, 2). It should be noted that, Disclosure Item 1 which states "officers and advisors of companies and for-profit organizations" refers to researchers affiliated with research institutions who are appointed as officers and advisors of a specific company, and is engaged in a contract where the researcher is regularly and continuously engaged receives remuneration.

If advice was requested by the other party (company) on a single occasion then this should be disclosed under Disclosure Item 4 “remuneration and daily wages received for attending meetings (presentations, advice etc.) from companies and for-profit organizations for the time and effort for which the researcher was detained. Furthermore, concerning the criteria for judgment of disclosure for research funding and donations provided by companies, etc., the actual amount that the researcher could have actually used, is shown based on the actual amount allocated from the total annual amount provided by the head of the research institution.

On the other hand, the Japan Pharmaceutical Manufacturers Association announced its "Transparency Guidelines for the Relation Between Corporate Activities and Medical Institutions" in January 2011, which obligates disclosure of all payments made by pharmaceutical companies to

doctors, and medical institutions, etc. From fiscal year 2013, the description of the total amount of scholarship donations, total amount of writing and lecture remuneration fees (amount and number of payments for individual researchers can be found from fiscal year 2014) for the previous fiscal year can be found on the website. 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 therefore this will need to be revised periodically.

Concerning the COI disclosure criteria for overseas members and nonmembers, there is a need to consider the unique 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, it will become necessary to establish a system to manage COI appropriately through a series of case studies.

3) Structure of the COI Committee

The COI Committee will consist of those members who conduct the medical science research, those familiar with research ethics and 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 expert external members.

12. Role and Obligation of the Editorial Committee

When publishing medical science research results in scientific journals as original papers, review articles, clinical guidelines, editorials, and opinions, the basic principle is to secure ethics and science in order to protect its neutrality. The editorial committee of affiliated societies regarding results of intervention studies, for example:

①Whether the medical science research is an invasive intervention study (clinical trial), ②For intervention studies, whether it is a registered clinical trial, ③Whether it is a contract or commissioned research, or an independent research, ④Whether the research funding is public or corporate (foundation grant, including nonprofit organization NPO), ⑤CONSORT（Consolidated Standards of Reporting Trials: Confirmation that it adheres to CONSORT (Consolidated Standards of Reporting Trials: Integrated criteria for clinical trial report). If funds from companies are used for the research, the author must disclose information about the funding source (provider) and the role of

the provider in the process of designing, data collection, analysis, interpretation, and manuscript preparation, of the research. In particular, for researchers who conduct intervention studies, if research support funding is obtained through contract with the company to conduct the research, this information must be disclosed regardless of what type of contract it may be (Fig. 5). This will in fact be one way to manage COI for third parties. For the basic way of thinking regarding medical editing, please refer to the Japan Association of Medical Sciences Editorial Guidelines (2015).

The Editorial Committee, with the cooperation of the COI Committee which clearly states the following, will confirm that COI related to the research contents are disclosed appropriately using the designated form (Ref. 2). The editorial committee of the affiliated society can, with the collaboration of the COI Committee, verify COI policies have been followed by checking to see if any COI related to the particular research has been disclosed appropriately using the designated form (Fig. 2), and in the case that there is a violation, can take appropriate measures such as prohibiting of the publishing of such articles or retraction. 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 (in English) 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 is a third-party organization that reports to the consultation of the president of the affiliated society and functions independently from the COI Committee. The role and obligation of the Ethics Committee concerning COI management involves, receiving consultation from the presidents of the affiliated societies 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 president of the affiliated society. As COI management deals with difficult ethical issues, daily exchange of information between the Ethics Committee, COI Committee, Editorial Committee and the Clinical Practice Guideline Steering Committee is necessary to promote justifiable medical and health industrial-academic cooperative research, and that each committee is established as an independent committee.

However, depending on the situation of the affiliated society, it is possible for the ethics committee to handle COI matters of committee members as an interim measure.

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 taking into account legal points of view is necessary and it is recommended that a manual be prepared beforehand.

15. Monitoring, Abiding by, and Educational Training of COI Policy

All members of the affiliated society and employees are obligated to follow the COI policy concerning medical and health 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.

As part of research ethics education, a system that includes educational plans to deepen understanding of bioethics, publication ethics, and COI management, and academic meetings (e.g. educational lectures, symposia etc.) where board-certified physicians, board-certified specialists, and board-certified trainers can earn credits necessary for acquiring and renewing certificates, should be established. Furthermore, in order to enhance the convenience of members belonging to multiple affiliated societies, it is also necessary to issue a common certificate for attending research ethics training sessions and credits among affiliated societies should be compatible.

In particular, if officers involved in medical science 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, is essential for minimal effect on the conducted

activity. Furthermore, in the event that an individual member's COI serious status may result in affecting 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 there is a possibility that 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 (e.g. mass media, public organization etc.). 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 investigations on relevant facts, and also by protecting the confidentiality of personal information. It is recommended that after consultation with the president of the affiliated society, the response is quickly passed onto the person requesting the disclosure.

If suspicions or doubt about industrial-academic cooperation are pointed out after the results of the medical science research have been published, the Editorial Committee and the COI Committee will work together to clarify the situation, and it is the responsibility of the president of the affiliated society to give an explanation. However, if it is decided that it cannot be dealt with by each committee, an investigation committee including external committee members (experts) will be established, and the committee will seek cooperation from the relevant university presidents to investigate the situation and to collect information. The committee will respond rapidly to clarify the alleged suspicion, and after receiving a response, the president of the affiliated society will be responsible for informing the person requesting the disclosure.

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 COI policy, the policy should clearly state 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, strict measures will be taken. On the other hand, it is necessary to state the procedure for appeal beforehand.

Generally speaking, since COI management is based on self-disclosure, however, in fiscal year 2013, in accordance with the transparency guidelines, it was decided that pharmaceutical companies would disclose the amount of scholarship donations made to every research institution. In fiscal year 2014, it was decided that details of writing fees, and lecture fees for each researcher would be disclosed, therefore it is possible that the information concerning disclosure may be different from that of self-disclosure. It may also be assumed that members of affiliated societies who are at question, may be considered to be problematic or a violator.

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 and stated in the COI policy.

On the other hand, handling COI policy violations of nonmembers is most often difficult. It is necessary 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 beforehand. It can be assumed that for affiliated societies which publish scientific journals in the English language, the number of nonmembers, especially the number of speakers from foreign countries, will increase and that correspondence in relation to COI policy 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 for those violating the policy, 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, and providing explanations to society as an organization to fulfill self-responsibility and ensure accountability. The COI Committee should create a system, in advance, so that in case a member's COI situation as a result of industrial-academic cooperation becomes serious, the related committees can collaborate regarding responding to various organizations 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.

VII. COI Management of Affiliated Societies

The ways to handle COI problems of individual members and officers giving presentations on medical and health 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 companies, institutions and organizations, 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. In the future, the detailed amount of remuneration and funds the affiliated society receives from companies, institutions and for-profit, should be disclosed in accordance with the format of the "Transparency Guidelines for the Relation Between Corporate Activities and Medical Institutions" of the Japan Pharmaceutical Manufacturers Association in the homepage of the affiliated society.

One method of COI management for affiliated societies as an organization would be to have an external evaluation of the affiliated societies. We will continue to pursue measures for COI management as the JAMS and also as a member of the affiliated societies.

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 the development of COI policy ②making sure that members and participants abide by the relevant COI policy 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. Changes 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.

X. Current Guidelines were Developed in March, 2011.

1. Partially revised in March, 2015
2. Substantially revised in March, 2017
4. Partially revised in March, 2020
5. Partially revised in March, 2022

Appendix 1) Items to check when filling out self-disclosure forms

A) Sample self-disclosure items for officers

① State if you have been an officer or consultant in a company, institution or for-profit organization (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.

②State 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 the standard 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.

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

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

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

⑥Regarding research funds for medical science studies (trust research funds, joint research funds,

clinical study funds) provided by companies, institutions and organizations, an annual total of 2 million yen or more from 1 company, organization or group.
⑦For scholarship funds granted by companies, institutions and organizations, an annual total of 2 million yen or more from 1 company, 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.
⑧If the individuals disclosing COI is affiliated with the funded department sponsored by the companies, institutions and organizations.
⑨Concerning other travel expenses, gifts, or contributions unrelated to the research, an annual total of 50,000 yen or more by 1 company, institution or organization.

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.

B) Items for self-disclosure for speakers at scientific meetings

①For an officer or consultant in a companies, institutions and organizations (hereinafter, companies, institutions and organizations) total annual honoraria of 1 million yen or more from 1 company, institution or organization.
②State 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.
③Patent right fees from companies, institutions and organizations, of 1 million yen or more per patent fee, per year.
④Remuneration for attending meetings (presentations) from companies, institutions and organizations, paid for the time and effort of the daily activity (lectures etc.) which is 500,000 yen or more from 1 company, institution, or organization per year.
⑤Regarding manuscript fees paid for writing of pamphlets etc. by companies, institutions and organizations, 500,000 yen or more per company, institution or organization, per year.
⑥Regarding research funds for medical science studies (trust research funds, joint research funds, clinical study funds) provided by companies, institutions and organizations, an annual total of 2 million yen or more for 1 company, institution or organization.
⑦For scholarship funds granted by companies, institutions and organizations, an annual total of 2 million yen or more from 1 company, institution or organization, to the individual disclosing COI or to the affiliated department of the individual disclosing COI (department, field) or

to the head of the department.
⑧If the individuals disclosing COI is affiliated with an endowed department where funding is provided by companies, institutions and organizations
⑨Concerning other travel expenses, gifts, or contributions unrelated to the research, an annual total of 50,000 yen or more from 1 company, institution or organization.

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.

Appendix 2)
An Analysis of the Current Status and a Proposal Toward Restoring Public Trust in Japan. The Committee for Medical Research Ethics and Integrity, the Japanese Medical Science Federation. July 20, 2017.

Appendix 3)
ICMJE Disclosure Form 2021
1) English version (Ref. 3)
2) Japanese translated version (Ref. 4)

Appendix 4) Definition of Terms
The definition of terms related to life sciences/medical science research is, in principle, based on the Japanese translation of the Helsinki Declaration prepared by the Japanese Medical Association, in reference to the "Ethical Guidelines on Medical and Biological Research Involving Human Subjects" (2021) of the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor and Welfare. We have attempted to try to ensure consistency with the content of our guidelines as much as possible.

1. Medical Science Research in Human Subjects
Activities involving human subjects for the purpose of A or B.
A. To obtain knowledge through ① through ④ to contribute to maintaining and promoting public health, and to the improvement of the quality of life and recovery of patients from injury or illness.
① the understanding of the etiology of the disease (including the frequency and distribution of various health-related events and factors affecting them) and its pathology, and ② understanding of the disease, and ③ improving and verifying the effectiveness of disease prevention methods, and ④improving and verifying the effectiveness in diagnostic and therapeutic methods.

B. To obtain knowledge about the human genome, gene structure and/or function, and gene mutation and/or expression by using specimens and information of human origin.
In this Guideline, for the term "human subjects" used in the Helsinki declaration published by the World Medical Association, we have used the Japanese term "human beings" translated by the Japan Medical Association.

2. Clinical Research
Medical science research that is conducted for the purpose of disease prevention, improvement of diagnostic and therapeutic methods, understanding the etiology and pathological condition of diseases, and improving the quality of life of patients, and is subject to ethical review.

① Interventional studies concerned with the prevention, diagnosis or therapeutic methods using pharmaceutical drugs or medical devices.
② Interventional studies (excluding those relevant to ①)
③ Studies without intervention using specimens etc. that do not include epidemiologic research (to clarify the frequency and distribution of various health-related events appearing in a clearly specified human group and the factors affecting them) (observational research).

3. Clinical Trials
Research with intervention designed and conducted in accordance with scientific principles, in human subjects, for the purpose of evaluating clinical effects of medical supplies (including vaccines, biologics), radiotherapy, psychotherapy, surgery, medical devices, alternative therapies. Classification of clinical trials according to purpose (general guidelines for clinical trials) include ① Clinical pharmacology trials, ② Exploratory trials, ③Confirmatory trials (comparative efficacy trials, randomized parallel dose-response studies, safety studies, evaluation of mortality / morbidity endpoints, large scale clinical trials, comparative trials) ④ Evaluation of therapeutic use (comparative efficacy trials, evaluation of mortality / morbidity) endpoints, tests for additional endpoints, large-scale clinical trials, and medical economics examinations.

4. Invasiveness
To cause stimulation for research purposes that exceeds the range covered by daily life such as puncture, incision, irradiation, and questions related to psychological trauma. “Minor invasiveness” refers to invasiveness that has little effect on the body and psychological state of the research subject.

5. Intervention
The act or practice for research purposes to control the presence or absence or degree of factors that

can affect a variety of events that occur in relation to human health (including actions to maintain and promote good health, medical practices, medication, examinations, etc.) for the prevention, diagnosis, or treatment of diseases. (This includes medical practice beyond the usual level, conducted for research purposes).

6. Research subject
①Individuals about whom an investigator is conducting research (including the individual asked to be enrolled in the research).
②Individuals about whom an investigator conducting research obtains existing specimens or information to constitute research. In cases where a surrogate is included in addition to the research subject, the term "research subject, etc." will be used.

7. Investigators etc.
This refers to the principal investigator and other individuals who are engaged in conducting the research (including collecting and providing specimens and information at organizations that collect and distribute specimens and information), excluding those who do not belong to research institutions but only engage in distributing existing data and information, and those who are partly engaged in entrusted research work.

8. Principal Investigator
An individual who is responsible for conducting the research, such as preparing the research plan, and who oversees all work related to the research at the affiliated research institution.

9. Research Director
An individual who is responsible for conducting the research, such as preparing the research plan, and who oversees all work related to the collaborative research at multiple facilities.

10. Head of the Research Institution
An individual who is a representative of a corporation, head of an administrative organization or an individual business owner, who is ultimately responsible for the research.

11. Third-party institutions/organizations
A for-profit or not-for-profit government agency, foundation, corporate sponsor, or academic research institution.

12. Sponsor

An individual, company, institution or organization having responsibility for the starting, administrating, managing and funding etc. of the medical science research. The Japanese Association of Medical Journal Editors has translated “sponsor” as "president" in Japanese and distinguishes it from Funder (funding provider).

13. Funder, funding agency

A government agency, foundation, corporate sponsor, academic research institution, or individual that provides necessary funding for conducting life sciences/medical science research. It also includes providing labor.

14. Serious Adverse Events

An event that ① results in death ②is life-threatening ③requires hospitalization or causes prolongation of existing hospitalization ④results in permanent or persistent disability or impairment ⑤ is a congenital anomaly or birth defect

15. Unanticipated Serious Adverse Events

Among severe adverse events, those not documented in the research plan, or informed consent documents, etc., or those that are described but whose nature and severity do not agree with the contents described.

16. Interventional Research

An invasive clinical trial involving human beings as subjects. A clinical trial conducted to collect data necessary for application for obtaining approval for the manufacturing and sales of new drugs is called a "trial". Interventional research that is initiated by the investigator to validate the clinical efficacy and safety of an approved drug is called an investigator-initiated clinical trial.

17. Randomized Controlled Trial

A type of research method of a large-scale comparative clinical trial which enables an objective evaluation of the efficacy of treatments by eliminating frivolous bias in evaluation.

18. Multi-institutional collaborative research

Research conducted at multiple research institutions based on a single research protocol.

19. Research Institution

A corporation, administrative institution, or individual business owner that conducts the research,

excluding cases where only a part of the work related to the storage of samples/information, statistical processing, and other research is entrusted.

20. Collaborative Research Institution
An institution, other than a research institution where research is conducted, that acquires new specimens/information from research subjects (excluding the acquisition of minor invasive specimens) and provides them to research institutions.

21. Informed Consent
Voluntary consent that is given by research subjects or their legal representatives etc. (hereinafter "research subjects") regarding the research (including the handling of samples and information) to be conducted or continued after receiving adequate explanations about the purpose and significance of the research, procedures, any discomforts research subjects may experience, and predicted results (including risks and benefits).

22. Informed Assent
The process whereby research subjects who are objectively considered unable to give informed consent regarding the research to be conducted or continued due to lack of cognitive maturity to understand, are informed of the research in words suited to meet their ability to understand, and express consent to participate in the research to be conducted or continued.

23. Legal representative, legal representatives etc.
An individual who can speak on behalf of the research subject's will and interests. If an occasion arises where the research subject is judged objectively that he/she does not have the ability to give informed consent to the research, the legal representative is able to give informed consent on behalf. In cases where the research subject is deceased, the term "legal representatives etc." will be used.

24. Industrial-Academic Cooperative Activities
Research institutions cooperate with companies, corporations, and for-profit organizations (hereinafter referred to as companies, etc.) related to the life sciences/medical science research. The following activities are included.

1) Joint Research: Research performed by dividing research funds and research personnel, involving companies, organizations, groups. (with or without recompense or remuneration)
2) Commissioned Research: companies, 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: companies make practical use of the patent rights and other rights concerning the research results of research institutions
4) Technology Guidance: researchers of research institutions etc. conduct business development and give technological advice
5) Research Institute Ventures: venture organizations are based on the results of the research of universities and research institutions and supported by the research institution.
6) Donations: unrestricted donations are made to assist universities and research institutions by companies, organizations and groups
7) Endowed Departments: departments are established for the promotion of research enabled by financial donations to research institutions from companies, organizations, and groups.

25. Monitoring

The principal investigator (research supervisor) will appoint an individual to determine whether a clinical trial is conducted properly in compliance with the research plan, and that progress, ethics and science of the research based on the research plan are ensured.

26. Audit

The principal investigator (research director) will appoint an individual to determine whether the clinical trial was properly conducted in order to assure the reliability of clinical trial results.

27. Definition of Terms Related to Conflict of Interest (COI)

①Entity (Third-party institutions/organizations)

A government agency, foundation, corporate sponsor, or academic research institution etc.

②Economic COI or related persons who need disclosure

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.

③Advisor 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.

④Equity (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)

⑤Honoraria

A legitimate payment is 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.

⑥Funds for Conducting Life Sciences/Medical Science Research

This includes all funds related to conducting life sciences/medical science 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 science 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.

⑦Other 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.

⑧COI 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.

⑨COI Management

A system to promote appropriate industrial-academic cooperative activities among businesses, organizations, and groups related to medical science research. According to COI policy, employees and members of each affiliated society must self-disclose all relationships/activities/COI, 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.

⑩Disclosure of COI status and definition of disclosure

Disclosure is disclosing relationships/activities/COI status of an individual with third-party institutions and organizations and transmitting the information to research institutions and members of academic organizations. Public COI disclosure means disseminating information to society as a whole, such as publishing this information in a manuscript in a journal.

⑪Institutional COI

If the institution itself or its affiliated senior officials (e.g., board of directors, presidents, vice presidents, directors and other officers, department heads, department heads of graduate schools, etc.) are involved with third-party institutions and organizations and have COI status, it could influence the process of making scientific, ethical or legal judgments or decision-making in academic activities (education, research, clinical care, etc.). This situation is referred to as institutional COI.

Appendix 5)

Websites that allow you to view relevant policies, guidelines, recommendations, etc.

①Helsinki 宣言：http://www.med.or.jp/wma/helsinki08_j.html

②CONSORT 2010.http://www.consort-statement.org/checklists/view/32-consort/66-title

③日本製薬工業協会「企業活動と医療機関等の関係の透明性ガイドライン」2011年2月
http://www.jpma.or.jp/about/basis/tomeisei/

④ ICMJE (International Committee for Medical Journal Editors): ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. 2013

⑤文部科学省・厚生労働省・経済産業省「人を対象とする生命科学・医学系研究に関する倫理指針」2021 年 3 月 title (mhlw.go.jp)

⑥日本学術会議「我が国の研究者主導臨床試験に係る問題点と今後の対応策」 平成26年３月 http://www.scj.go.jp/ja/info/kohyo/pdf/kohyo-22-t140327.pdf

⑦文部科学省「研究活動における不正行為への対応等に 関するガイドライン」2014年８月
http://www.mext.go.jp/b_menu/houdou/26/08/__icsFiles/afieldfile/2014/08/26/1351568_02_1.pdf

⑧一般社団法人全国医学部長病院長会議 「研究者主導臨床試験の実施にかかるガイドライン」2015年 https://www.ajmc.jp/pdf/guideline_01.pdf

⑨日本医学会 医学雑誌編集ガイドライン 2015年3月

http://jams.med.or.jp/guideline/jamje_201503.pdf
⑩日本製薬工業協会「医療用医薬品等を用いた研究者主導臨床研究の支援に関する指針」2016年１月
http://www.jpma.or.jp/about/basis/clinical_research/pdf/guideline.pdf
⑪Minds 診療ガイドライン作成の手引き2014.
http://minds4.jcqhc.or.jp/minds/guideline/handbook2014.html
⑫厚生労働科学研究における利益相反（Conflict of Interest：COI）の管理に関する指針
http://www.mhlw.go.jp/content/000799612.pdf
⑬臨床研究法 2018 年
https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000163417.html
⑭臨床研究法における利益相反管理ガイダンス 2021 年
https://www.mhlw.go.jp/content/10800000/000422858.pdf
⑮一般社団法人日本医学会連合研究倫理委員会「提言 わが国の医学研究者倫理に関する現状分析と信頼回復に向けて」2017 年
https://www.jmsf.or.jp/uploads/media/2020/02/20200212143618.pdf
⑯一般社団法人全国医学部長病院長会議「医学系研究機関における組織 COI 管理ガイダンス」2018 年 https://www.ajmc.jp/pdf/20190425_01.pdf
⑰COPE (Committee on Publication Ethics) https://publicationethics.org/
https://publicationethics.org/files/COI%20submitted.pdf
https://publicationethics.org/files/COI%20published.pdf

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Head of Committee

Saburo Sone	Professor Emeritus, Tokushima University

Committee Members

Chikashi Ishioka	Professor, Department of Clinical Oncology, Tohoku University School of Medicine
Kojiro Ueki	Director, Diabetes Research Center, National Center for Global Health and Medicine
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Shuji Terai	Professor, Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University
Yuichiro Doki	Professor, Department of Gastroenterological Surgery, Graduate School of Medicine, Osaka University
Masaomi Nangaku	The Japan Association of Medical Sciences Executive Committee Officer Professor, Division of Nephrology and Endocrinology, The University of Tokyo
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