

Organization of JDDW

“Guidelines on Conflict of Interest in Medical Research”

Introduction

A remarkable progress in medicine and healthcare from the latter half of the 20th century resulted in the development of many new methods of treatment and prevention. In Japan, the enactment of the Healthcare and Medical Strategy Promotion Act and the Act on Japan Agency for Medical Research and Development as a national policy in 2014, and subsequent establishment of Japan Agency for Medical Research and Development in April 2015, have expanded strategic approaches in the development of innovative drugs, biological drugs, and medical equipment and devices and in the promotion of regenerative medicine through academic-industry-government collaboration. The participation of the academia in regenerative medicine and entrepreneurship in relation to medical equipment and devices is beginning to bear fruits, further invigorating clinical development.

The Organization of Japan Digestive Disease Week (hereafter called the “Organization”) is engaged in activities involving human subjects (including their samples and data) towards maintaining and promoting national health and improving the prognosis and the quality of life of patients, through identification of causes of diseases, understanding of pathological conditions, prevention of diseases, and verification and improvement of the effectiveness of diagnostic and therapeutic methods used in healthcare. Further promotion of academic-industry collaboration is extremely important from the standpoint of evidence-based medicine and medical economics and in fulfilling our social responsibility.

On the other hand, the more researchers at public entities, such as research institutes and academic societies, promote academic-industry collaboration through medical research, the deeper they will become involved in the activities of specific companies. As a result, a clash or conflict inevitably and unavoidably arises between the researcher’s social responsibility to work for the public good and personal benefits obtained via collaboration between industry and academia. Such a situation is commonly referred to as a “conflict of interest (COI)”, and the academic organizations must manage and resolve such states of COI in their promotion of cooperative activities between industry and academia. If those engaged in medical research would fail to

declare appropriately a serious conflict of interest existing in relation to funding companies or organizations, it could increase the risk of bias, endanger the human rights and personal safety of the research subjects, and warp the research methods, data analysis, and interpretation of the results. In fact, a scandal over the antihypertensive drug valsartan in 2013 threw into doubt the credibility as well as the quality of clinical studies at five universities in Japan. The scandal came about as a result of obscure arrangements in corporate donations and acceptance of data management and statistical analysis services, and contracts and other safeguards were not used to appropriately manage bias risks. Data were willfully manipulated to fabricate a conclusion advantageous to the pharmaceutical company involved. A number of research papers published in international journals had to be withdrawn, tarnishing not only the quality but also the credibility of the medical guidelines in question. Partly to prevent such scandals, the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and the Ministry of Health, Labor and Welfare of Japan published the Ethical Guidelines for Medical and Health Research Involving Human Subjects, on December 22, 2014, by integrating existing ethical guidelines on clinical research and epidemiological research. The new guidelines, in particular, clarified the responsibility of the head of research institute and principal investigator conducting research on interventions, and sought to strengthen ethical review, monitoring, auditing, and COI management. Meanwhile, the Association of Japanese Medical Colleges (AJMC) also published the Guidelines for Investigator-Initiated Clinical Trials, in February 2015. The AJMC guidelines focused particularly on research on invasive interventions using approved drugs, and illustrated concrete steps from planning to appropriate conduct of clinical trials (including public registration of clinical trials, data management, statistical analysis, data interpretation, and preparation of theses). The AJMC guidelines also deal with COI management by using concrete examples, to assure quality and reliability of clinical trials that allow involvement of enterprises. Subsequently, the Clinical Trials Act came into effect as of April 2018. This law defined (1) clinical trials of unauthorized drugs, drugs for off-label use, etc. and (2) clinical trials of pharmaceutical companies' drugs, etc. conducted with funding from the same pharmaceutical companies as "specified clinical trials," and obligated, for clinical trials carried out to validate the efficacy and safety of the drugs, etc., a set of processes for the conduct of the clinical trials, management of conflict of interest, measures for ensuring

review and comments from a certified clinical trial review committee, and public disclosure of information about funding for the clinical trials.

Japan Pharmaceutical Manufacturers Association published the Transparency Guideline for the Relation between Corporate Activities and Medical Institutions in 2011, and its member companies began to disclose the amount of funding they provide to medical institutions, research institutes, other types of medical organizations, foundations, and healthcare-related individuals on their websites as from 2013. In the United States, a government agency discloses details about beneficiaries and amounts of funding from pharmaceutical companies in an “open payment program.” Last year, a stir was caused when the media reported on an omission by a well-known American physician to disclose a significant state of conflict of interest in a paper published in a world-class international journal. In Japan, too, it is possible to do online searches to find details about financial relations between companies and physicians. Academic societies in the field of clinical science are expected to meet a rigorous standard of COI management of individuals participating in development of medical guidelines and to fulfill its accountability if any discrepancies are found in the contents of their COI disclosures.

On the other hand, research institutes are also involved in development of approaches for prevention, diagnosis or treatment of diseases and are strengthening their efforts to use the results of such research to grant licenses to companies or to establish university spin-offs, and in that sense, research institutes are required to contribute to society and public good. If a publicly funded research institute has ownership of patents or stocks of a manufacturing company or a distribution company, a conflict of interest may potentially arise. As a result, if senior directors of that research institute who have authority over decision-making or auditing of the institute’s activities decide to give priority to the interest of the institute, it may distort the integrity and reliability of the research, increasing risk to the research subjects and patients. If the research institute becomes involved in promoting the distribution of such drugs and medical equipment preferentially over other drugs or medical equipment, it may be perceived with suspicion that it is trying to make wrongful gains or increase its revenues through publication of a thesis.

To ensure objectivity, fairness, and integrity of research institutes, the American Association of Medical College (AAMC) and American Association of Universities

(AAU) published guidelines in the United States regarding institutional conflict of interest of research institutes (hereafter called “institutional COI”) in 2002, and proposed a model policy for management of institutional COI in clinical research involving human subjects in 2008. The National Science Foundation (NSF) (2005) and the National Institutes of Health (NIH) (2013) each requires individual researchers to disclose institutional 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, which are now used as a standard in some 6,000 medical journals around the world. ICMJE also requires disclosure of the author’s personal conflict of interest as well as institutional COI of the author’s affiliated research institute in its COI disclosure form required for submission at the time of publication of a thesis. In Japan, the Association of Japanese Medical Colleges (AJMC) published the Guidance for Management of Institutional Conflict of Interest in 2018, in which it emphasized the importance of disclosure and management of institutional COI in clinical research. Considering these trends, the Japanese Association of Medical Sciences has published a partially revised version of the Guidelines on COI Management in Medical Research.

To ensure quality and reliability of medical research and fulfill our accountability to society, JDDW, which is a collaborative program of multiple gastroenterological societies, appropriately manages COI by enforcing participating members to thoroughly abide by the Organization of JDDW’s COI guidelines, which have been revised to maintain consistency with the Ethical Guidelines for Medical and Health Research Involving Human Subjects and in consideration of COI management trends in and outside Japan.

I. Purpose

Considering that the Organization is required to fulfill its social responsibility and maintain a high level of ethical standards in all of its medical research involving academic-industry collaboration, the Organization drew up the Guidelines on Conflict of Interest in Medical Research (hereinafter referred as the “Guidelines”). The Guidelines’ objectives are to have the member societies and participating societies of the Organization to appropriately manage their states of conflict of interest when engaging in medical activities, so as to manage bias risks in the conduct of research and in the

presentation, dissemination, and education of research results, to promote sound academic-industry collaboration while maintaining impartiality and integrity, and to fulfill its social responsibility by contributing to advancing progress in prevention, diagnosis, and treatment of gastrointestinal diseases. Accordingly, the Organization requires all academic societies partaking in JDDW to adopt and properly implement COI guidelines and bylaws of their own. Moreover, the Guidelines present basic principles on COI management to the member societies and participating societies of the Organization and others concerned, and requires them to voluntarily and properly disclose their states of conflict of interest as per the guidelines of the associated academic societies and abide by the Guidelines when making presentations for JDDW. Needless to say, members should also observe employee rules and regulations and COI guidelines of the research institutes, etc. they are affiliated with.

Basic concepts in COI management of research institutes and researchers are as follows:

- (1) Based on the presumption of ensuring ethical, medical, and scientific integrity of medical research through academic-industry collaboration, research institutes and researchers accepting external funding (donations or agreement-based research funds), drugs, medical equipment and devices, and/or services from companies, organizations, and individuals who have interest in the research, will do so in an appropriate manner by concluding an agreement where necessary (to clarify consideration and/or responsibility over research outcomes). However, while the Clinical Trials Act is applicable to a researcher-led clinical study that uses external funding obtained from a company or organization that refuses to take responsibility over the research outcomes, research institutes and researchers must avoid entering into an agreement that will enable such a funding organization to exercise influence on the interpretation of the results of a researcher-led clinical study or on the publication process, as such an agreement will compromise the independence and integrity of the study.
- (2) To ensure quality and reliability of the research results, research institutes and researchers will appropriately disclose the contents of the agreement (e.g. sources of funding, role of the funding organization, and the state of conflict of interest of the research institutes and the researchers), and take precautionary measures so that their state of COI does not develop into a problem. Research

institutes and researchers will accurately state and make public such information in research protocols, IC forms, and theses.

- (3) If a question is raised by society at large about the contents of a thesis, the corresponding author must fulfill their accountability jointly with related companies.
- (4) For a research institute to ensure the quality as well as reliability and integrity of its medical research, education, and medical practice, it must keep transparent its relations with interested parties by disclosing the institutional COI of the research institute as well as of the ties between its senior directors and specific companies and for-profit organizations.

II. Applicable Persons

These Guidelines apply to any of the below persons with a potential state of COI.

- (1) Persons making presentations at JDDW (including non-members)
- (2) Officers (presidents, directors, auditors, staff and advisors) of the Organization, chairpersons of the standing and special committees and vice chairpersons and members of the special committees of this Organization, and persons in charge of society meetings in JDDW (chairpersons of annual meetings of member societies and participating societies)
- (3) Personnel of the secretariat of the Organization
- (4) Spouses, first degree relatives of and persons sharing revenue or property with (1) ~ (3)

III. Applicable Activities

These Guidelines apply to all projects and activities of the Organization.

- (1) JDDW
 - (2) Joint seminars for medical education
 - (3) Dissemination of information on gastrointestinal diseases to the general public or related public outreach activities
 - (4) Other projects and activities necessary for attaining the missions of the Organization
- In particular, disclosure of the state of COI with related companies in the last three

years must be made using a prescribed form when giving presentation or making publication for the following activities:

1. Making presentations at educational lectures, etc. organized by the Organization during JDDW
2. Publishing articles in journals and other publicity papers
3. Work carried out by provisionally set up investigative committees and advisory committees
4. Making presentations at sponsored events, etc. hosted or cohosted by companies, corporate organizations, or for-profit organizations; as for sponsored events, etc. hosted or co-hosted by a company, the chair or moderator must also disclose his or her state of conflict of interest.

The “medical research” related to presentations means basic or clinical medical research, subject to ethical screening, implemented with the objective of improving methods for preventing, diagnosing or treating illnesses via medical care, understanding the causes and conditions of illnesses, or improving patient quality of life. Medical research for humans includes both subject-derived specimens and data that enable individuals to be identified, determined as per stipulations in the Ethical Guidelines for Medical and Health Research Involving Human Subjects published jointly by the Japanese Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Welfare and Labor (December 22, 2014).

IV. “Businesses, incorporated organizations or commercial enterprises associated with medical research” are any business, organization and enterprise related to medical research in any of the following ways.

- (1) Having requested or jointly implemented medical research (irrespective of whether research was financially supported or not)
- (2) Sharing patent rights or other rights for treatment methods, medicines, equipment or other material evaluated in medical research
- (3) Having provided medicines, equipment or other material used in medical research free of charge or at special advantageous prices
- (4) Having aided, donated to or otherwise supported medical research
- (5) Having provided unapproved medicines, medical equipment or other material for medical research

- (6) Having funded endowed chair, etc.

V. Matters for COI Disclosure and Disclosure Standards

Covered in this section are individuals required to make COI disclosure as well as such individuals' affiliated research institutes or the heads of the affiliated research institutes or divisions with whom the individuals, now or in the past, were in a relation of a co-investigator or research collaborator.

For the personal COI disclosure, applicable persons must, using a prescribed form, make a disclosure pertaining to the following activities (1) ~ (9) when they exceed the disclosure standards. Monetary amounts that must be reported in personal disclosure on COI shall be determined by the COI guidelines and bylaws of the associated JDDW member societies and participating societies. If a presentation is for an educational lecture or other event planned by JDDW, monetary amounts that must be reported shall comply with the standards set by the Organization. The Organization stipulates the below standard amounts for matters to disclose.

- (1) For officers and advisors of businesses, incorporated organizations or commercial enterprises associated with medical research (hereinafter referred to as “businesses, incorporated organizations or commercial enterprises”), remuneration from any one business, incorporated organization or enterprise that is equal to or greater than one million JPY a year.
- (2) Regarding stock ownership, annual profit (total of dividends and profits from sales) from stock of any one company that is equal to or greater than one million JPY or constitutes a quantity equal to or greater than 5% of all concerned shares.
- (3) Patent royalties from businesses, incorporated organizations or commercial enterprises that are equal to or greater than one million JPY per year per patent.
- (4) Daily allowances (lecture fee, etc.) paid by any one business, incorporated organization or commercial enterprise to a researcher to attend (speak, give advice, etc., at) a meeting as compensation for time and labor that total or exceed five hundred thousand JPY in a year.
- (5) Manuscript fees paid by any one business, incorporated organization or commercial enterprise for contributed articles for pamphlets, articles on round-table discussions, etc. that total or exceed five hundred thousand JPY in a year.
- (6) Research expenses for medical research (joint research, consigned research, clinical

trials, etc.) covered by any one business, incorporated organization or commercial enterprise, regarding which the total contracted amount for research that the reporting individual essentially has discretion over, total or exceed one million JPY in a year.

- (7) Scholarship donations provided by any one business, incorporated organization or commercial enterprise to the reporting individual or to the course, field, or research lab of the reporting individual, regarding which the total donated amount that the reporting individual essentially has discretion over, total or exceed one million JPY in a year.
- (8) The reporting individuals are participating as organizers, presenters, or lecturers in courses sponsored by a business, incorporated organization or commercial enterprise, and the total sponsored amount that the reporting individuals essentially have discretion over its use total or exceed one million JPY in a year.
- (9) Travel support or gifts directly unrelated to research, study or diagnosis/treatment provided by any one business, incorporated organization or commercial enterprise that total or exceed fifty thousand JPY in a year.

The “appointment as a board member or advisor of a company or for-profit organization” in (1) above applies when a researcher affiliated with a research institute assumes the office of a board member or advisor of a specific company under contract to regularly and continuously work for that company and receive remuneration. If advice, etc. is given at the request of a company in discontinuous, isolated instances, the COI disclosure should be made in accordance with (4) “per diem, honorariums, etc. paid by a company or for-profit organization for the time and energy spent by a researcher to attend or give a presentation or advice at a meeting” above.

In addition, as for (6) and (7) above, COI disclosure is necessary for all individuals if research expenses or scholarship grants were provided from a related company or organization to the department (course or field) or laboratory to which the reporting individual is affiliated with. It is also clearly indicated that the threshold for such disclosure of research grants or scholarship grants from related company or organization is based on the amount that the reporting individual essentially has discretion over their use. The specific methods for disclosure and publication will be as stipulated in the prescribed forms.

As for institutional COI disclosure, if the person required to make COI disclosure is

or was in a relation of a co-investigator or research collaborator either with the research institute the person is affiliated with or with the head of the affiliated research institute or division (e.g. university, hospital, faculty, center, etc.), now or in the past, and if such a relation may have an influence on the Organization's activities that the person is involved with, then that person is required to make the institutional COI disclosure using the prescribed form for the items shown below. The amount set for each item of institutional COI disclosure is based on the following standards:

- (1) As for research grants from a company or organization, the research grants are awarded by one company or organization to the research institute or division or the head of the research institute or division the individual is affiliated with and the total amount of the grants that the research institute or division or its head essentially has discretion over their use is ¥10 million or more in a year.
- (2) As for donations from a company or organization, the donations are awarded by one company or organization to the research institute or division or the head of the research institute or division the individual is affiliated with and the total amount of the donations that the research institute or division or its head essentially has discretion over their use is ¥2 million or more in a year.
- (3) In addition, if the research institute or division or the head of the research institute or division the individual is affiliated with owns a company's stocks (5% or more of the issued shares of the company), has received patent royalties from a company or organization, or has any investment outstanding in a company or organization, these must be disclosed.

VI. Notice on Medical Research and, in Particular, Invasive Intervention Research

- (1) Clinical trials for approval of new drugs must be carried out in compliance with the Good Clinical Practice (GCP). A researcher-led large-scale intervention study using a drug that has already been put on the market is conducted for the purpose of verifying efficacy and safety of the drug, promoting appropriate use of the drug in the clinical setting, and providing important information and evidence for standard treatment, and such research must be conducted based on ethical guidelines. As for the latter studies on already marketed drugs, it has been pointed out that companies, in view of promoting sale of their products, have a high level of interest in

supporting post-marketing clinical studies by way of funding or providing labor and services, and that this tends to increase bias risk in such studies and the potential for scandals. Presenters at JDDW must abide by the “Declaration of Helsinki,” the Ethical Guidelines for Medical and Health Research Involving Human Subjects, the Clinical Trials Act, COI guidelines, the AJMC Guidelines for Investigator-Initiated Clinical Trials, and related laws and regulations. Presenters at JDDW are required to pay special attention to protecting the human rights and lives of research subjects when conducting any intervention study.

- (2) When presenters at JDDW voluntarily conduct a researcher-led invasive intervention study, oftentimes they will have opportunities to use external funding, drugs, medical equipment and devices, and services of experts with technical knowledge and skills, provided by companies, organizations, and individuals. Where such clinical research is based on an agreement and has the institute of the member’s affiliation acting as the contact point, such research should be carried out as joint research or commissioned research, the responsibility of the fund provider on the research outcomes should be made clear, and any restrictions on the use of such funds, drugs, medical equipment and devices, and services, considerations, and division of roles should be clearly written down. On the other hand, where there are no restrictions on the use of scholarship grants or research funds, presenters at JDDW can accept such scholarship grants or research funds for use in a researcher-led clinical study. If external funding for joint research, commissioned research, or unlimited grant is to be used for intervention research and if such funding is equal to or above the Organization’s prescribed COI threshold, presenters at JDDW must clearly indicate the provider of such a funding source and such provider’s role in the clinical research, on the principle of making such information public and ensuring transparency.
- (3) Making results of medical research widely available for use by healthcare professionals, patients, and others benefits the public. Therefore, when conducting medical research involving human subjects, presenters at JDDW must register the research on a public database and publish the results of the research, in principle, in the form of a thesis.
- (4) When preparing and publishing a thesis, public relations material, or publication, presenters at JDDW must clarify authorship, bearing in mind international

standards on authorship, namely, the ICMJE Recommendations. Non-author contributors, such as medical writers, statisticians, and other contributors, their affiliation, and sources of funding should be mentioned in the “Acknowledgement.” In addition, if any interested party is providing labor or services based on an agreement to assist in the conduct of clinical research or in the preparation of a thesis and their involvement is anticipated to influence the contents of the thesis, the roles played by each of such interested parties must be clearly stated in the section “Role of the funding source” to ensure transparency. Existence of any other forms of interest must also be stated and disclosed. In addition, if suspicion of any wrongdoing is raised by a third party, both the principal investigator and the companies concerned must jointly fulfill their accountability.

- (5) When a researcher affiliated with a company is dispatched to work in a research institute as a researcher, graduate student, part-time lecturer, and the like, and such a researcher is to give a presentation on the research results or publish the research results in a thesis, such a researcher must also clearly state the name of the company he or she is affiliated with.
- (6) If a person who had been working for a company leaves his or her job to work for a research institute and such a person is to present or publish results of research that pertains to the company he or she had been working for, such a person must clearly state the name of such a company alongside the name of the research institute he or she is currently affiliated with, for a period of five years after leaving the company.

VII. Situations to Avoid Because of Potential Conflicts of Interest

1. Situations All Applicable Persons Must Avoid

The dissemination of medical research results (such as presentation at academic meetings), which contribute significantly to raising the quality of healthcare in our country, should be based purely on scientific evidence and conclusions, and public benefit. In reporting medical research results and interpretations, applicable persons must not be influenced by the selfish intentions of individuals or businesses that provide funds for the said medical research (such as unjust inducement of transactions or sale) and must not sign any contracts with said parties in which such influences cannot be avoided.

Specifically, the following should be avoided:

- (1) Receiving out-of-contract incentive payment for acting as an intermediary for or introducing human subjects in clinical studies
- (2) Receiving out-of-contract incentive payment for collecting cases within a specified period of time
- (3) Receiving out-of-contract performance-based payment for achieving specified research results

2. Situations Principal Investigators and Research Representatives Must Avoid Relating to Medical Research

Principal investigators and research representatives who plan and manage medical research, particularly clinical testing and trials (including those conducted to obtain government approval for drugs and medical equipment), must be selected from among researchers who are socially recognized to have no serious state of COI in relation to each of the items shown below (in other words, having relatively little overlapping interest with the provider of funding), and maintain such status after selection.

Specifically, the principal investigator and research representative, who have a duty to appropriately disclose monetary relations with the provider of funding, should take particular note of and avoid matters indicated below.

- (1) Possession of stock of the person or business providing funding for the medical research or is a director, etc. of such a business
- (2) Acquisition of patent royalties or rights for the drug, therapy, inspection method, etc. that is the subject of the research
- (3) Receiving of expenses for travel, accommodation, etc., other than for the legitimate reasons of participating in academic meetings, from the person or company providing funding for the research
- (4) Acquisition of money and/or gifts outside legitimate remuneration for the time and efforts expended on the research
- (5) A situation where a researcher affiliated to a company who is dispatched to work in a research institute and participate in the research as a researcher, part-time lecturer, or graduate student, engages in such an inappropriate act as concealing the name of the researcher's company in the research plan or when presenting or publishing the research results
- (6) A situation where the person or company providing funding for the research can

exercise its influence over the collection, storage, statistical analysis, interpretation, or judgment of the research data

- (7) Entering into an agreement that allows the provider of funds or interested company to exercise influence on decisions to present research results at a scientific meeting or publishing research results in a thesis

However, researchers that meet the criteria (1) ~ (4) above may serve as principal investigators and research representatives in medical research that has very important social significance provided that the said researchers are indispensable towards planning and managing the said medical research and the fairness, neutrality and transparency of their decisions and actions can be unquestionably ensured. In any event, accountability to society must be fulfilled.

If there is a possibility that a contract with a company contains matters described in (5) or (6) above, details on the role and involvement of the person or company providing funding for the research must be disclosed at the end of the thesis when publishing the research results.

VIII. Method of Implementation

1. Obligations of Presenters at JDDW

Presenters at JDDW must, upon presenting medical research results, etc., properly disclose in writing using the specified form as per the guidelines, etc., on COI of the associated academic society, any state of COI with regard to the said medical research. And, for educational lectures and other events planned by this Organization, presenters must properly disclose any state of COI with regard to the said medical research using the specified form as per the bylaws on COI of this Organization. If a violation of the COI guidelines of the associated academic society is indicated in the presentation of research, the Board of Directors of this Organization shall contact the respective society and demand appropriate action. If a violation of these Guidelines is indicated in the presentation at educational lectures and other events planned by this Organization, the Board of Directors of this Organization shall instruct the committee with jurisdiction over COI (hereinafter shortened as “COI Committee”) to weigh in on the matter and shall take appropriate action based on the Committee’s recommendation.

2. Obligations of Officers, Etc.

The officers (president, directors, auditors, staff and advisors), chairpersons of standing committees and special committees, vice chairpersons and members of standing committees of this Organization, the persons in charge of academic conferences of societies participating in JDDW (annual chairpersons of member societies and participating societies) and secretariats have important roles and responsibilities in all projects and activities related to JDDW. Upon assuming such positions, these persons must submit in writing using the specified form (Form 2), personal disclosures of any state of COI with regards to the said related projects and activities (covering the period of three years up to the year prior to the year of appointment). Moreover, if any new state of COI arises in the year of assuming the said position or thereafter, they must provide additional disclosure addressed to the President, using Form 2, within eight weeks of such new occurrence of COI. The Board of Directors must engage in the appropriate personnel management of board members, etc. in order to maintain fairness and impartiality of the said related projects and activities.

3. Roles of the COI Committee

In the event that a serious state of COI arises with an officer or presenter in projects or activities of this Organization, or an officer or presenter inappropriately reported COI in the personal disclosures, the COI Committee must notify the concerned person to that effect and instruct that person to follow the necessary procedures. Moreover, if suspicion is indicated over a personal disclosure on COI within an academic society, the COI Committee shall mandate the concerned society to appropriately manage the COI.

4. Roles of the Board of Directors

The Board of Directors must report to the COI Committee a serious state of COI or inappropriate personal COI disclosure made by an officer or other persons in the execution of the projects and activities of this Organization, and based on the Committee's recommendation, order the concerned person to improve the situation or take corrective actions.

The Board of Directors must, as an organization, appropriately and promptly deal with any suspicion of wrongdoing related to the state of conflict of interest of its officers and of any presenters at educational lectures and other events organized by the Organization, and if, as a result of an inquiry, it is deemed that the suspicion or

allegation is unfounded, the Board of Directors must fulfill the Organization's accountability to society and as for the allegation made against the particular individual in question, make efforts to regain and secure trust in that individual by issuing the Organization's views and statements to society (e.g. by publishing such views and statements on its website). On the other hand, if such suspicion or allegation is validated, the Board of Directors, needless to say, should disclose the results of the fact-finding inquiry and communicate the Organization's measures against recurrence.

5. Roles of Chairpersons of Member Societies and Participating Societies

Persons in charge of academic conferences of societies participating in JDDW (annual chairpersons of member societies and participating societies) must verify that the presenters (including non-members) reporting medical research findings at the annual meetings have appropriately completed their COI disclosure using a prescribed form. In particular, when a presentation is to be made on the results of research in which there is involvement of a company, it is the role of the chairpersons to provide an environment for the audience to judge whether or not the presentation of the contents of the research is being done in an impartial and equitable manner. The chairpersons may take steps to debar delivery of any presentation that runs counter to the Guidelines or that does not have COI disclosure. In such case, the chairpersons are required to promptly notify the candidate presenter thereof and explain the reason for said action. The chairpersons may refer such cases to the COI Committee, and based on the report of the COI Committee, instruct steps to be taken to remedy the situation.

As for breakfast seminars, luncheon seminars, satellite symposiums hosted or co-hosted by a company or for-profit organization, the chair or moderator must also disclose to the audience the names of the companies and organizations he or she has relations with, using slides in a similar manner as the presenters.

6. Institutional COI management of the Organization

Cases of institutional conflict of interest have been reported where senior directors (e.g. director general, director, etc.) in a relation of mentor-mentee, colleague, friend, or relative with the researcher in question, have been more liable to directly or indirectly influence medical research, particularly with regard to the conduct of clinical research involving human subjects and publication of those results. For example, if an academic

society or its senior directors have received substantial donations from specific companies or own stocks of, or receive royalties from, specific companies, it can be anticipated under such circumstances in regards to the research results as well as the publication of the results that it would be more challenging to guarantee integrity, objectivity, and independence from the point of view of COI assessment and ethics. The Board of Directors must centrally manage amounts paid by companies, corporate organizations, and for-profit organizations to the Organization by recording in each accounting year the number of instances of payments made and their total amounts for each company in each category of (1) donations and (2) income from academic conferences and meetings (e.g. company-related seminars and symposiums), and appropriately disclose such amounts as institutional COI.

7. Other

The chairpersons and members of other committees must verify that the projects and activities they are respectively involved in, are implemented in compliance with these Guidelines and, in the event a violation of these Guidelines arises, must promptly examine ways to improve that situation. In dealing with these matters, they may seek the counsel of the COI Committee and, based on the Committee's recommendation, the Board of Directors may order concerned persons to improve the situation or take corrective actions.

IX. Response to Request for COI Disclosure

If a request is made from outside the Organization (e.g. the mass media, citizens' groups, etc.) for disclosure of the state of COI of any applicable person and such a request can be considered reasonable, the Board of Directors will refer the matter to the COI Committee, which will look into the matter by conducting a fact-finding investigation while protecting the personal information of those concerned in the shortest time possible. After receiving a report from the COI Committee, the Board of Directors will promptly respond to those parties that have made the request for disclosure.

X. Action against Violators of These Guidelines and Accountability

1. Action against Violators of These Guidelines

The Board of Directors of this Organization has the authority to discuss violations of these Guidelines. In event of acts committed by officers or others of this Organization, the Board of Directors may seek the counsel of the COI Committee. If the Committee's recommendation and further discussions by the Board deem that the said act constitutes a serious failure to comply with these Guidelines, the Board may take necessary actions in accordance with the degree of the violation including but not limited to penalties. Moreover, in the event of acts by presenters at JDDW that violate these Guidelines, the Board of Directors may notify the associated academic societies and require them to take necessary actions with the violator as per their rules and regulations.

As for violation by presenters at educational lectures and other events organized by this Organization, necessary actions may be taken in accordance with the rules and regulations of associated academic societies. The Board of Directors deliberating on actions against the violator shall request participation of responsible officers from associated academic societies at such a meeting of the Board, as necessary, to allow persons from associated academic societies to take part in the deliberations.

2. Petition for Appeal

Persons subject to penalties may petition for an appeal by filing with the secretariat of this Organization an appeal addressed to the President, within seven days of receiving a notification of the decision of the Board of Directors.

Promptly upon accepting this petition, the president of this Organization shall form a board for reviewing the petition (Review Board), entrust that committee with reviewing the concerned matters, discuss the committee's report with the Board of Directors and notify the petitioner of a final decision.

3. Process for reviewing a petition

(1) Upon receiving the petition for appeal, the President must promptly establish a committee for the review of the petition (Review Committee). The Review Committee will consist of several persons from within the Organization and one or more members from outside the Organization, all of whom are appointed by the President. The committee members will elect the chair of the Review Committee from among themselves.

The members of the COI Committee may not concurrently serve on the Review Committee. The Review Committee will hold its meeting to deliberate on the

petition within 30 days of receipt of the petition.

- (2) The Review Committee may, where necessary, listen to the opinions of the chairperson of the COI Committee related to the petition and of the petitioner.
- (3) Except where special circumstances exist, the Review Committee will prepare its report on the review of the petition and submit it to the Board of Directors within a month of the first committee meeting held for deliberation.
- (4) The Board of Directors will make a final decision on the petition based on the recommendation of the Review Committee.

XI. Accountability to Society

If disclosure of COI information of any applicable person is necessary to fulfill social and moral accountability, the Board of Directors will, after adopting a resolution, disclose or make public, to the extent necessary, such information within and outside of the Organization to fulfill its responsibility and accountability to society. The individual to whom the COI information pertains will be given opportunity to express opinions to the Board of Directors or the director entrusted with the decision, except where the urgency of disclosing the information or making the information public precludes the possibility of listening to the opinions of the individual concerned.

XII. Coordination with Related Societies

This Organization shall coordinate closely with JDDW member societies and participating societies, and provide opportunities to share with them information on reviews of these Guidelines and bylaws.

XIII. Amendments to These Guidelines

This Organization may periodically review and amend these Guidelines in line with social factors, the establishment of or amendment to laws and regulations governing cooperation between industry and academia, and the various situations surrounding medical care and research.

XIV. Date of Enforcement

These Guidelines shall come into force as of April 19, 2013.

These Guidelines shall be revised on July 28, 2015 to take effect as of January 1,

2016.

These Guidelines shall be revised on March 2, 2018 to take effect as of the same day.

These Guidelines shall be revised on February 24, 2021 to take effect as of the same day.

Appendix 1. Definitions

In preparing the definitions of terms related to medical research, reference was made to the Japanese translation, by Japan Medical Association, of the Declaration of Helsinki and to the Ministry of Health, Labour and Welfare's Ethical Guidelines for Medical and Health Research Involving Human Subjects. Efforts were also made to ensure compatibility between these documents and the contents of the Guidelines as much as possible.

1. Medical research involving human subjects

Activity involving human subjects (including specimens and information acquired from them) carried out for the purpose of obtaining knowledge contributing to maintain and promote national health and improving the prognosis and quality of life of patients, through identification of causes of diseases (including the frequency and distribution of various health-related incidents and factors affecting them), understanding of pathological conditions, prevention of diseases, and verification and improvement of the effectiveness of diagnostic and therapeutic methods in healthcare.

2. Clinical research

Medical research listed below that is conducted for the purpose of improving methods of prevention, diagnosis, and treatment of diseases in healthcare, of understanding the causes of diseases and their pathology, and of improving the quality of life of patients, and is subject to ethical screening.

- (1) Clinical research that involves interventions and that is related to the use of drugs or medical equipment or devices in preventive, diagnostic, or therapeutic method
- (2) Clinical research that involves interventions (other than (1) above)
- (3) Clinical research using samples and the like and does not involve interventions. Epidemiological research (scientific research to elucidate the frequency and distribution of various health-related incidents in a clearly defined human population and factors affecting them; also called observational study) is excluded.

3. Clinical trial

Research involving human subjects designed and conducted according to appropriate scientific principles for the purpose of evaluating clinical effectiveness of drugs (including vaccines and biological drugs), radiation therapies, psychotherapies, surgeries, medical equipment and devices, complementary and alternative medicine, etc. Clinical studies can be classified according to their objectives (General Considerations for Clinical Trials) as follows: (1) human pharmacology studies, (2) exploratory therapeutic studies, (3) confirmatory therapeutic studies (comparative studies to establish efficacy, randomized parallel dose response studies, clinical safety studies, studies of mortality/morbidity outcomes, large simple trials, comparative studies), (4) studies on therapeutic use (comparative effectiveness studies, studies of mortality/morbidity outcomes, studies of additional endpoints, large simple trials, pharmacoeconomic studies)

4. Invasiveness

To cause stimuli exceeding those which research subjects may experience in their daily lives or injuries or distress to research subjects' body and/or mind by conducting a procedure for investigational purpose, such as puncture, incision, administration of drugs, irradiation, questions related to the subject's mental trauma, etc. Of various types of invasiveness, one causing minor effect on the research subjects' body and/or mind is called "minor invasiveness."

5. Intervention

A practice, conducted for investigational purposes, to control the presence of, or the level of the presence of, factors influencing various human health-related events (including activities to maintain and promote health and preventive, diagnostic, and therapeutic medication and examinations). Intervention may also include medical techniques beyond usual medical practice that are conducted for investigational purposes.

6. Research subject

Any individual on whom research is conducted (including individuals asked to be enrolled in the research) and any individual from whom existing specimen or information is obtained for use in the research.

7. Investigator, etc.

Principal investigator and other related persons engaged in the conduct of research (including collecting and providing samples or data at an organization engaging in such

activities). Individuals who do not belong to research implementing entities and are engaged only in the provision of existing samples or data or individuals who have been commissioned by another to take part in a portion of the research are excluded.

8. Principal investigator

Any individual engaged in the conduct of research, such as writing the research protocol, as well as in overseeing the research at the research implementing entity he/she belongs to.

9. Research representative

Any individual who, in addition to writing the research protocol and otherwise engaging in the conduct of research as a principal investigator, oversees joint research with other entities.

10. Head of the research implementing entity

A representative of an incorporated entity, a head of an administrative organ, or an individual business owner who carries out research and with whom the final responsibility for the research rests.

11. Sponsor

Any individual, company, institution, or organization that has responsibility over the initiation and management of clinical research and over funds for the research.

12. Institutional COI

A state where an individual making the COI disclosure is a co-investigator or research collaborator with the research institute the individual is affiliated with or with the head of the affiliated research institute or division (e.g. university, hospital, faculty, center, etc.), and as a result, it can be anticipated that such relations may influence the activities that the individual is involved in.

13. Funder, funding agency

Any individual, company, an incorporate entity, institution, or organization that provides the necessary funds for conducting clinical research.

14. Serious Adverse Event

Any adverse event that (i) results in death, (ii) is life-threatening, (iii) requires hospitalization or prolongation of hospitalization; (iv) results in persistent or significant disability or incapacity; or (v) causes congenital anomaly.

15. Unexpected serious adverse event

Of the above-defined serious adverse events, any event that is not listed in the

research protocol, the informed consent document, etc. or even if it is listed, is not listed at the specificity or severity stated therein.

16. Intervention research

Invasive clinical trial involving human subjects. Clinical trial conducted to collect data necessary for making an application for authorization of manufacture and sale of new drugs is called “chiken.” Intervention research designed by a research to verify the clinical efficacy and safety of approved drugs is called “researcher-led clinical study.”

17. Randomized controlled trial

Large-scale comparative clinical trial that enables objective assessment of therapeutic effect by eliminating arbitrary bias in the assessment.

18. Research implementing entity

Any incorporated entity, administrative organ, or individual business owner who carries out research. Those commissioned to take part in a portion of the research, such as storage of samples and data and statistical processing, are excluded.

19. Collaborative research implementing entity

A research implementing entity collaboratively conducting research in accordance with the research protocol. It includes entities to collect samples and data from research subjects for the research and to provide such samples and data to other research implementing entities.

20. Informed assent

Informed assent is given by a research subject who is objectively deemed incapable of giving informed consent. After such a subject is given an explanation, in language understandable to the subject, and made to understand about research that is about to be commenced or continued, informed assent may be given by the subject to express agreement to the commencement or continuation of the research.

21. Informed consent

Consent given voluntarily by a research subject or his or her legally acceptable representative (hereinafter collectively referred as “research subject, etc.”) with respect to whether the research may commence or continue (including handling of samples and data), having enough understanding after receiving adequate prior information with regard to the purpose and significance of the research, research methods, burdens on the research subjects, and predicted results of the research (including both risks and benefits).

22. Legally acceptable representative

Any individual expected to speak for the will and benefit of a research subject when the research subject is considered objectively unable to give informed consent. Such an individual can give informed consent to investigators, etc. on behalf of the research subject. When such a legally acceptable representative is speaking on behalf of any deceased research subject, the legally acceptable representatives for both living and deceased research subjects will collectively called “legally acceptable representatives, etc.”

23. Academic-industry collaboration

Academic-industry collaboration between a research implementing entity and any company, incorporated organization, and/or for-profit organization (hereinafter collectively referred as the “company, etc.”) in medical research, including:

- (1) Joint research: research conducted by the research implementing entity and the company, etc., with each contributing research expenses and researchers (regardless of whether or not payment will be made for the research)
- (2) Commissioned research: Agreement-based research on therapies, drugs, equipment and devices of the company, etc.
- (3) Technology transfer: Commercialization by the company, etc. of results of research conducted by the research implementing entity, including the use of patents and other rights
- (4) Technical guidance: Technical guidance provided by researchers from the research implementing entity or research and development of the company, etc. carried out by researchers from the research implementing entity
- (5) Venture business originating in research implementing entity: Establishment of a venture business based on the results of research conducted by the research implementing entity and with the support of the research implementing entity
- (6) Donation: Research grant from the company, etc. to the research implementing entity without any restriction on the use of the grant
- (7) Endowed chair: Chair established using donations from the company, etc. to the research implementing entity for the purpose of promoting research

24. Monitoring

Any act of overseeing the progress of research, and of determining whether a clinical trial is being conducted in compliance with the research protocol in ways that guarantee

the ethical and scientific integrity of the trial, in order to ensure that the clinical trial is properly conducted. Such an act is performed by an individual appointed by the principal investigator (research representative).

25. Audit

Any examination, performed by an individual appointed by the principal investigator (research representative), to determine whether a clinical trial has been properly conducted, in order to assure the reliability of results of the clinical trial.

Organization of Japan Digestive Disease Week

“Bylaws of the Guidelines on Conflict of Interest in Medical Research”

The Organization of Japan Digestive Disease Week adopted the “Guidelines on Conflict of Interest in Medical Research” (hereinafter referred to as “the Guidelines”) in order to fairly manage conflicts of interests (COI) of JDDW officers and presenters. The Guidelines were created based on the JDDW conference guidelines to maintain the fairness and neutrality of medical research, ensure the transparency and social accountability of presentations, and promote proper collaboration on medical research between industry and academia. The Bylaws of the Guidelines on Conflict of Interest in Medical Research (hereinafter referred to as “these Bylaws”) are stipulated as follows to facilitate proper and efficient implementation of the Guidelines.

Article 1. COI Reporting by Presenters at JDDW

When submitting an abstract on medical research at JDDW, all presenters and lecturers must disclose to the secretariat of the affiliated academic society, all financial relationships of self, a spouse, first degree relatives and other dependents with businesses or commercial enterprises associated with the medical research held over the past three years. The COI also has to be disclosed at the time of presentation using a slide or poster as per the bylaws of the affiliated academic society.

Prior to presenting or lecturing at educational lectures and other events planned by this Organization, the lead presenter or lecturer must disclose COI to this Organization using Form 1 as per reporting rules stipulated by this Organization, if a COI exists for any of presenters or lecturers, including co-presenters/co-lecturers. Similarly, the COI must be disclosed at the time of presentation as per the rules of this Organization. Presenters and lecturers must disclose such COI using Form 1-A in the first slide (that immediately after the slide that introduces the title, presenter/lecturer, etc.) of their presentations or lectures. Lead presenters must similarly disclose their COI situation using Form 1-C even if no such COI exists.

For poster presentations, COI must be disclosed using Form 1-B at the end of the presentation.

Article 2. Submission of Disclosure Statement on COI by Officers, Committee

Chairpersons, Vice Chairperson, and Members, Chairpersons of Participating Academic Societies, Etc.

Clause 1

The officers (president, directors, auditors, staff and advisors), chairpersons of standing committees and special committees, vice chairpersons and members of standing committees of this Organization, the persons in charge of academic conferences of societies participating in JDDW (the annual chairpersons of member societies and participating societies) and members of secretariats of JDDW member societies and participating societies must prepare and submit to the president of this Organization personal disclosures on COI over the past three years immediately prior to assuming their post and every year thereafter, regarding “V. Matters for COI Disclosure and Disclosure Standards” indicated in the “Guidelines on Conflict of Interest in Medical Research,” using Form 2. The chairpersons of member societies and participating societies must prepare and submit to the president of this Organization personal disclosure on COI over the past three years immediately prior to assuming their post at the time the Executive Committee is launched each year, using Form 2. Submission is unnecessary if the personal statement on COI has already been received. These personal disclosure statements on COI are limited to the relationships with businesses, incorporated organizations or commercial enterprises that are associated with projects or activities of this Organization.

Clause 2

Personal disclosure statements must report all matters stipulated in Article V. Matters for COI Disclosure and Disclosure Standards of the Guidelines as COI in Form 2. The standard amounts stipulated in Article 2 of these Bylaws apply to all disclosure requirements and must be itemized as per Form 2. The disclosure should cover a period of the last three years prior to the year of appointment, and a period of the last three years for each year thereafter, and the calculation period must be included in Form 2. Officers and others of this Organization are required to report any new COI that arises during their current term no later than eight weeks from such event, using Form 2.

Article 3. Handling of Personal Disclosure on COI

Clause 1

Personal disclosure statements on COI that are submitted at the time of abstract registration for presentation at JDDW must be retained under the strict supervision of the chairpersons of the respective societies for a period of two years. Personal disclosure statements on COI that are submitted for an educational lecture or other event planned by this Organization must be retained under the strict supervision of the president of this Organization for a period of two years. Similarly, documents with COI information on persons who have finished the terms as officer or committee member of this Organization or persons whose appointment as officer or committee member is withdrawn, must be retained under the strict supervision of the president of this Organization for a period of two years from the date that the final term ends or the appointment is withdrawn. In addition, personal disclosure statements that are submitted by the secretariats of JDDW must be retained under the strict supervision of the chairperson of JDDW for a period of two years after the date of retirement including incumbent periods. At the end of the two-year period, documents shall be promptly deleted and destroyed under the strict supervision of the president of this Organization. However, if document deletion or destruction is deemed inappropriate by the president of this Organization, a necessary extension may be granted to allow deletion and destruction of the COI information of the concerned person to be kept on hold. The COI information of persons in charge of academic conferences (annual chairpersons of member societies and participating societies) shall be handled in the same way as that of officers of this Organization.

Clause 2

The directors and officers of this Organization may use as necessary the COI information as permitted by these Bylaws in order to determine the existence or degree of COI between concerned persons and activities of JDDW, manage the said information, and take necessary action based on the said determination. The COI information must not be used beyond the intended objective of use and must not be disclosed to anyone other than those who require the said information for the said objective (obligation of confidentiality).

Clause 3

With the exception of the cases described in Article 4 Clause 2, COI information

shall not be disclosed in principle. COI information may within the necessary scope be disclosed and released within and outside this Organization after discussion and approval by the Board of Directors, if and when necessary towards demonstrating the social and ethical accountability of this Organization in pursuit of activities of this Organization or its committees. However, it is not precluded in this case that a special director is tasked with handling the concerned issue and bases any decisions made on the advice of the COI Committee. In such case, the concerned person whose COI information is to be disclosed or released may express his/her opinions to the Board of Directors of this Organization or the director tasked with making the said decision. This is not, however, imperative if disclosure or release is urgent and there is not adequate time to hear the opinions of the concerned person.

Clause 4

If a request for disclosure (including legal requests) is made to a specific officer, the president of this Organization shall consult the COI Committee, and given an adequate reason the Committee would respond in appropriate manner while protecting the personal information of the concerned person. If deemed that the matter cannot be handled by the COI Committee, the president of this Organization shall form a COI Inquiry Commission consisting of the one special director tasked with handling the concerned issue, a few participants of this Organization and one or more outside persons. The said COI Inquiry Commission shall convene no later than thirty days from the date that the request for disclosure is received, and shall provide a response as soon as possible.

Article 4. Conflict of Interest Committee

The president of this Organization shall form a Conflict of Interest (COI) Committee consisting of a few Organization members and shall appoint a person to chair the committee. The members of the COI Committee are obliged to keep confidentiality of COI information they handle as committee members. The COI Committee shall manage, in coordination with the president of this Organization and in line with the Guidelines and these Bylaws, the COI of members so as to prevent development of serious situations, and shall deal with violations. The COI Committee shall, in the event of

serious COI associated with projects or activities of this Organization or inappropriate disclosure of COI, notify the concerned person to that effect either through the associated academic society or directly, and instruct that person to take necessary action, i.e., to correct their personal disclosure statement. The reporting and handling of COI information shall comply with the stipulations of Article 3.

Article 5. Action against Violators

Clause 1

In the event that social or ethical issues are suspected or arise in the personal statement on COI submitted by a candidate presenter for JDDW, the COI Committee shall contact the associated academic society and request appropriate action to be taken in order to demonstrate the social accountability of this Organization. Moreover, the Board of Directors of this Organization may take appropriate action if acts by concerned persons significantly damage the social responsibilities of this Organization.

Clause 2

The chairperson of the COI Committee must, in the event suspicion is indicated over a personal disclosure on COI of an officer, committee chairperson, a committee member with a duty to submit personal statement on COI, or any candidate to any of the above posts prior to or after assuming the said post, notify the president of this Organization thereof in writing. The president of this Organization must then promptly convene the Board of Directors, which must then determine whether to acknowledge or disavow the said indication. If the said indication is acknowledged, the president must notify the parent society that nominated the said person of the issue and, after sufficient discussion with the said society, take appropriate action, i.e., demanding that the nomination be withdrawn and membership revoked.

Article 6. Action against Violators of the Obligation of Confidentiality

Personnel of the secretariat of this Organization have the same obligation of confidentiality stipulated in Article 3 Clause 2 for the directors and concerned officers of this Organization with regards to COI information of individuals learned in the course of managing COI cases. The Board of Directors may punish concerned persons and secretariat personnel who deliberately release COI information to outsiders by

expulsion and dismissal etc. without following proper procedure.

Article 7. Amendments to the Bylaws

These bylaws may need to be amended in part in line with social factors, amendment to laws and regulations governing cooperation between industry and academia, etc. The Board of Directors may seek the counsel of the COI Committee with regard to reviews of these Bylaws and determine amendments based on their recommendations.

Supplementary Provisions

Article 1. Date of Enforcement

These Bylaws shall come into force as of April 19, 2013.

Article 2. Amendments to These Bylaws

These Bylaws shall be reviewed, as a rule, every few years to keep pace with social factors, the establishment of or amendment to laws and regulations governing cooperation between industry and academia, and the various situations surrounding medical care and medical research.

Article 3. Special Provision for Officers, etc.

Persons serving as officers or other posts of this Organization at the time these Bylaws go into force shall promptly submit reports, etc., in compliance hereto.

Partial Revisions:

- These Bylaws shall be revised on July 28, 2015 to take effect as of January 1, 2016.
- These Bylaws shall be revised on March 2, 2018 to take effect as of the same day.
- These Bylaws shall be revised on February 24, 2021 to take effect as of the same day.