The JAMS COI Management Guidance on Eligibility Criteria for Clinical Practice Guideline Formulation
March, 2017

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1. Background

Industrial-academic cooperation is indispensable for promoting clinical development and clinical research in disease prevention, diagnostics and therapy.
Clinical research is the origin of evidence-based medicine (EBM), as it enables validation of the effectiveness and adverse events of multiple treatment methods, and furthermore allows a systematic comparison of the cost effectiveness, and therefore this contributes greatly in the formulation and revision (hereinafter, formulation) of the Clinical Practice Guideline (CPG) that suggest optimal medical care and treatment for patients.

However, while the national medical expenditure in 2014 expanded to 40 trillion yen, and the total amount for pharmaceutical products was 10 trillion yen, close to a quarter of that amount, the foundation for clinical research in Japan is extremely poor compared with other countries. Furthermore, the number of clinical epidemiologists, clinical biostatisticians, and clinical coordinators, establishment of data centers and public funding support are insufficient. The quality and number of clinical research papers are unsatisfactory, and it is difficult to say that optimal treatment or CPG formulation based on medical economics is being carried out adequately.

On the other hand, the interest of pharmaceutical companies is extremely high because the formulation of CPG is related to the sales promotion and the positioning of their products. Therefore, it is more likely for pharmaceutical companies to become deeply involved in clinical research publications and public relations, which form the foundation of CPG formulation. In addition, researchers conducting clinical research develop stronger financial ties with for-profit companies.

For this reason, it causes suspicion among those in society and raises questions such as, “Can independence of the research be kept?” “Can a fair judgement be made?” and “Will a certain company be unjustly favored?”
It has been reported that in fact, when conducting or publishing intervention research involving companies, bias, that is to say, trial bias (research unfavorable to companies are not conducted), publication bias (adverse results are unpublished), or reporting bias (efficacy is overrated, side effects are underrated), are likely to occur.
Recently, an incident in Japan of fraudulent clinical research involving companies, has been brought to attention, and there have been other cases which have led to the loss of international credibility of CPG, creating a social problem.

CPG is widely used by clinical medical societies, patient support organizations, payment agencies, medical specialists, clinicians, lawyers, and consumers. With the rapid growth in the clinical development of pharmaceutical drugs and medical equipment, efforts to secure the quality and credibility of CPG has raised much interest as an urgent issue both domestically and internationally, and specific rules have been formulated.
In order to formulate a trustworthy CPG based on the EBM technique, it is necessary not only to disclose and publicize the conflict of interest (COI) of the relevant participants and societal organizations involved, but also to clearly state the eligibility criteria for those taking part in the CPG formulation, to prevent and manage any risk of bias. In addition, to ensure the quality and credibility of CPG, verification must be conducted through regular and appropriate reviews and revisions.
This must be done through the cooperation of the CPG Steering Committee, a standing committee of the affiliated society, and the COI Committee, in order to properly manage COI of the participants.

Based on the COI management guidelines of the Japanese Association of Medical Sciences (JAMS), we have established guidance on the requirements for Eligibility for participation for individuals participating in CPG formulation. This guidance exemplifies guidelines for appropriate management of bias caused by various COI situations of those participating in CPG formulation and sets an example of securing the quality and credibility of CPG.
Although each affiliated society of the Japanese Association of Medical Sciences (JAMS) can be expected to have different circumstances, organization and operation methods, by taking into account the domestic and international trends, we hope this will contribute in some way to improve COI management of the affiliated societies.

2. Those subject to COI management

The president of the affiliated society will establish a CPG Steering Committee as a standing committee.
In order to newly formulate or revise CPG concerning diagnosis, treatment and prevention, the establishment of umbrella committees such as the CPG formulation committee (group for guideline formulation), systematic review team, external evaluation committee (committee). All individuals who participate in these committees, groups, and teams, in addition to spouse, first degree relatives or any persons who share income or property assets are subject to COI disclosure.

3. COI disclosure items and self-disclosure of participating individuals and spouse, or persons who share income or property assets

Those who are engaged in CPG formulation will self-disclose COI status using the COI self-disclosure form for CPG formulation participants (Fig. 1-A) for the past 3-year period starting from the previous year, for each year (January 1 to December 31) from when the individual takes office and CPG is announced.

1)COI self-disclosure of participating individuals

(1) Position as an officer or advisor of a company or for-profit organization, and amount of remuneration.
(2) Stock ownership and profit from stock (profit from stock for the previous year)
(3) Remuneration received for patent royalties or licensing fees from companies or for-profit organizations.
(4) Honoraria such as lecture fees, attending conferences (presentations, providing advice etc.) received from a single company or for-profit organization.
(5) Manuscript fees received for writing articles for pamphlets, roundtable discussion articles, etc. from a single company or for-profit organization
(6) Research funding (joint research, commissioned research, clinical trials etc.) provided by a single company or for-profit organization
(7) Scholarship (incentive) donations provided by a single company or for-profit organization
(8) Endowed departments established through donations by a company
(9) Other remuneration (travel expenses, gifts etc. not directly related to research)
The amount declared in (6) and (7) is the actual amount allocated from the head of the research institution, and can be considered to determine the actual expenses and donations the researcher could have used for the research.

2)COI disclosure of spouse or first degree relative of the participant, or persons who share income or property assets

(1) Position as an officer or advisor of a company or for-profit organization, and amount of remuneration.
(2) Stock ownership and profit from stock (profit from stock for the previous year)

(3) Remuneration received for patent royalties or licensing fees from companies or for-profit organizations.

3) COI disclosure regarding the participant's affiliated organization or division

Two items including research expenses and scholarship (incentive) donations accepted by the head of the organization or division (research institution, hospital, department or center etc.) in relation to the participant's research contents are subject to COI disclosure as an organization (Fig. 1-B).

Fig. 1-A. Base amount for disclosure and amount of COI self-disclosure items for CPG formulation participants and first-degree relatives

Fig. 1-B. Base amount for disclosure and amount of COI disclosure items for organizations related to CPG formulation participants

4. Amount classification for COI disclosure items
Participants involved in CPG formulation will disclose COI items and fill in the corresponding number for amount in accordance with the COI self-disclosure form for participants involved in CPG formulation (Form 1).

5. Basic thinking of eligibility for CPG participation
As a basic approach to determining eligibility for CPG participation, if the COI status of the candidate for CPG formulation is found to exceed a socially acceptable range, and if, after CPG is formulated, there is a possibility of a large financial benefit from recommending the CPG for the CPG participant, spouses, first degree relatives, or persons sharing income or property assets either directly or indirectly, then in principle, the candidate should not be able to participate.

1) If any of the following apply to the candidate for CPG formulation, or spouse, or first degree relative or persons who share income or property assets, in principle, the candidate will not be able to participate.

(1) Income as an officer or advisor of a company or for-profit organization (1 million yen or more /company /year)
(2) Profit from stock ownership and stock (5% or more of all shares /company, or 1

million yen or more/company/year)
(3) Remuneration received for patent royalties or licensing fees from a company or for-profit organization (1 million yen or more/company/year)
(4) Affiliation to endowed departments provided through donations from a company or for-profit organization

Participants taking part in CPG revision work, including spouses, first degree relatives, and persons who share income or property assets, should avoid creating the above mentioned conditions while participating in the revision work.

2) Evaluation and management of eligibility for participation in CPG formulation participants according to amount

The following illustrates the procedure for COI management for those participating in the CPG formulation committee and systematic review team (Fig. 2).
Eligibility for participation is determined according to the amount classification and base amount for each, based on COI self-disclosure for the past 3 years (Table 1). However, in principle, eligibility is given to those who have items to disclose in amount②, and those who have items to disclose in amount③ should not be eligible to participate in work related to CPG formulation.

Fig. 2. Procedure for COI management for those participating in CPG formulation

Specifically,
(1) Eligibility for participation for the head of the CPG formulation committee is based on COI self-disclosure and COI disclosure of the organization. If the items in amount① do not exceed the base amount, then it is possible to participate in the CPG formulation with voting privileges. However, taking into consideration the great influence the head will have on CPG formulation, if a situation arises where there are several items in amount①from a specific company or for-profit organization that would be considered to be perceived to affect the promotion of its pharmaceutical drugs and medical supplies, then measures such as having the deputy head act on behalf of the head should be taken.

(2) Eligibility for participation of committee members is considered if each item in amount② does not exceed the base amount. If this is the case, it is possible to

participate in the CPG formulation with voting privileges. However, if a situation arises where the formulation committee member has items in amount② that exceed the base amount and also relevant items in amount③, if the individual is indispensable to the formulation of CPG, and if the transparency and neutrality can be ensured, participation can still be granted in the CPG formulation process.

However, the president of the affiliated society must take measures such as not giving power to make a final decision in CPG formulation and fulfill obligations to explain and be answerable to society. In the event that a CPG formulation participant during their term of formulation, has items in amount②(head of committee, deputy head of committee) or ③ (committee member), the president of the affiliated society must promptly report the case and take appropriate measures.

Table 1. Eligibility criteria and base amount per item for those participating in the CPG Steering Committee, CPG Formulation Committee, and Systematic Review Team

6. Structure of the CPG Formulation Committee

Participants for the CPG formulation committee will be selected as members based on related eligibility criteria but the following points should be noted in the structure of the committee.

1) The number of members having items to disclose in amount② should not exceed the majority of the total number of members.
2) The committee should be structured so that diversity of the participant's area of expertise is emphasized, including epidemiologists and statisticians, and that it is not biased toward members who have a COI situation with a specific company or for-profit organization.
3) Since CPG serves as a source of information to support the decision-making by patients and healthcare workers in the medical setting, those representing patients and civic groups should be invited as members of the CPG formulation committee and aim for a committee that is structured so that different values can be shared.

7. Responsibilities of the head of the CPG formulation committee

At the time of CPG publication, the head must disclose the COI status of each participant including the affiliation and title for the past 3 year-period starting from the previous year, by classifying the participants into guideline steering committee, guideline formulation committee, and systematic review team, using the designated COI form (Table 2). This information must be placed either at the beginning or end of the CPG text.

Table 2. Example of COI disclosure for participants of CPG formulation

In addition, the source of the funding used for CPG formulation must also be disclosed. That is, at the time of CPG publication, 1) the name of the company that provided funding (donations etc.) for activities of the affiliated society (academic lectures etc.), and 2) the name of the company that provided funding (includes labor) in relation to the formulation of CPG, must be disclosed using the designated form (Table 3) for the past 3 year-period starting from the previous year.

Table 3. COI disclosure (example) for an affiliated society related to the formulation of CPG

When recommendations of the CPG are publicized through media, the COI status of participants in the formulation should be disclosed. In particular, the same applies to publications in company-related public relation brochures or commercial magazines.

8. Points to consider when formulating CPG

In order to improve the quality of CPG content and ensure credibility, the head of the committee involved in CPG formulation should handle the following items appropriately.

1) Obtaining beforehand the name of the company or for-profit organization involved with the manufacturing and sales of pharmaceutical drugs or medical equipment mentioned in the CPG to be formulated.
2) Assessment of CPG contents with a cost-effective perspective
3) Verifying and securing the neutrality and fairness of CPG contents

4) Managing and recognizing any COI between the participant in CPG formulation, spouses, first degree relatives or persons who share income, and the company or for-profit organization involved.
5) The sharing of COI information of each participant by all those participating in the CPG formulation committee.
6) Acceptance and appropriate handling of comments received from other related institutions and organizations of which a COI exists
7) Acceptance of an external evaluation to improve the credibility of CPG
8) Disclosure of funding sources related to expenses required for CPG formulation and publication
9) Disclosing the contents of any financial support from a company etc. involved in the contents formulated, to the related organization
10) Acceptance of advice etc. for CPG formulation (revision) based on evaluation results of a third-party organization (e.g. Japan Council for Quality Health Care, Medical Information Network Distribution Service (Minds))
11) Establishing disciplinary guidelines for guideline violations

(Form 1)

COI Self-Disclosure Form for Participants in CPG Formulation

20 (01.01～12.31)

Name of Individual Disclosing COI (Member Number) : ______________________ (   )

Affiliation (Institution, Department, Hospital Department), Title:

____

Official Title in Society: ☐ Member ☐Councilor/Representative ☐Board member ☐Non-member

A. Items to be declared for COI self-disclosure (COI status with a company or for-profit organization related to CPG formulation)

1. Position as an officer or advisor of a company or for-profit organization, and amount of remuneration
 (☐Applicable ・ ☐Not Applicable)
 (Disclosure to be based on annual payment from a single company or organization)

	Name of Company/Organization	Title (Officer, Consultant etc.)	Amount
1			
2			
3			

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

2. Stock ownership and profit from stock (profit from stock for the previous year)
 (☐Applicable ・ ☐Not Applicable
 (Disclose if annual profit or ownership is 5% or more of all stocks of the corresponding stock from a single company or organization)

	Name of Company	Number of shares	Share price (per share)	Amount
1				
2				

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

3. Remuneration received for patent royalties or licensing fees from companies or for-profit organizations.
 (☐Applicable ・ ☐Not Applicable
 (Disclosure to be based on annual patent fees for a single patent)

	Name of Company/Organization	Name of Patent	Amount
1			
2			

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

4. Honoraria such as lecture fees, attending conferences (presentations, providing advice etc.) received from a company or for-profit organization for the time and labor given by the researcher
 (☐Applicable ・ ☐Not Applicable
 (Disclosure to be based on annual payment from a single company or organization)

	Name of Company/Organization	Amount
1		
2		
3		

4		
5		
6		
7		
8		
9		

Base amount for disclosure: 500,000yen/company/year

Amount: ①500,000 yen or more ②1,000,000 yen or more ③2,000,000 yen or more

5. Manuscript fees received for writing articles for pamphlets, roundtable discussion articles, etc. from a single company or for-profit organization

（☐Applicable ・ ☐Not Applicable

(Disclosure to be based on annual payment from a single company or organization)

	Name of Company/Organization	Amount
1		
2		

Base amount for disclosure: 500,000yen/company/year

Amount: ①500,000 yen or more ②1,000,000 yen or more ③2,000,000 yen or more

6. Research funding provided by a company or for-profit organization

（☐Applicable ・ ☐Not Applicable

(Disclose if research contract funds received from a single company or organization allocated for medical science research (joint research, commissioned research, clinical trials etc.) is 1,000,000 yen or more)

	Name of Company/Organization	Research Funding Classification	Amount
1			
2			
3			

Research classification: ①Industrial-academic cooperative research, ②commissioned research, ③clinical trials, ④other

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②10,000,000 yen or more ③20,000,000 yen or more

7. Scholarship (incentive) donations provided by a company or for-profit organization

（☐Applicable ・ ☐Not Applicable

(Disclose if scholarship (incentive) donations provided by a single company or organization allocated to the affiliated department or division is 1,000,000 yen or more)

	Name of Company/Organization	Amount
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

8. Endowed departments established through donations by a company

（☐Applicable ・ ☐Not Applicable

(Disclosure to be made if donations received is 1 million yen or more)

	Name of Company/Organization	Name of Endowed Department	Installation Period
1			
2			

9. Other remuneration (not directly related to research such as travel, gifts etc.)

（☐Applicable ・ ☐Not Applicable

(Disclosure to be based on annual payment from a single company or organization)

	Name of Company/Organization	Details of Remuneration	Amount
1			
2			
3			

Base amount: 50,000 yen/company/year

Amount: ①50,000 yen or more ② 200,000 yen or more ③500,000 yen or more

B. COI disclosure for spouse, first degree relatives or any persons who share income or property assets with the declarer.

Please check the box applicable.

☐No items to disclose: There is no need to fill out the rest of this form

☐Items to disclose: Please check the following items. If not applicable, check 'Not Applicable'.

1. Position as an officer or advisor of a company or for-profit organization, and amount of remuneration

(☐Applicable ・ ☐Not Applicable

(Disclosure to be based on annual payment from a single company or organization)

	Name of Corresponding Person	Relationship with declarer	
	Name of Company/Organization	Title (Officer, Consultant etc.)	Amount
1			
2			
3			

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

2. Stock ownership and profit from stock (profit from stock for the previous year)

(☐Applicable ・ ☐Not Applicable

(Disclose if annual profit or ownership is 5% or more of all stocks of the corresponding stock from a single company or organization)

	Name of Corresponding Person		Relationship with declarer	
	Name of Company	Number of Shares	Declared share price (per share)	Amount
1				
2				

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

3. Remuneration received for patent royalties or licensing fees from companies or for-profit organizations.

(☐Applicable ・ ☐Not Applicable

(Disclosure to be based on annual patent fees for a single patent)

	Name of Corresponding Person		Relationship with declarer
	Name of Company/Organization	Name of Patent	Amount
1			
2			

Base amount for disclosure: 1 million yen/company/year

Amount: ①1,000,000 yen or more ②5,000,000 yen or more ③10,000,000 yen or more

C. Concerning disclosure items of the head of the declarer's affiliated institution or division (research institution, hospital, department or center etc.)
(Applicable if the head of the institution or division is involved in joint or collaborative research with the individual who is disclosing COI)

Please check the box applicable.

☐No items to disclose: There is no need to fill out the rest of this form

☐Items to disclose: Please state the amount if the amount exceeds the base amount of disclosure for the corresponding items

1. Research funding provided by a company or for-profit organization

（☐Applicable ・ ☐Not Applicable

(Disclose if research contract funds received from a single company or organization allocated for medical science research (joint research, commissioned research, clinical trials etc.) is 1,000,000 yen or more)

	Name and Title of Head of Declarer's Affiliation	Name of Company/Organization	Research funding classification	Amount
1				
2				
3				

Research classification: ①Industrial-academic cooperative research, ②commissioned research, ③clinical trials, ④other

Base amount for disclosure: 10 million yen/company/year

Amount: ①10,000,000 yen or more ②20,000,000 yen or more ③40,000,000 yen or more

2. Scholarship (incentive) donations provided by a company or for-profit organization

（☐Applicable ・ ☐Not Applicable

(Disclose if scholarship (incentive) donations provided by a single company or organization allocated to the affiliated department or division is 1,000,000 yen or more)

	Name of Company/Organization	Amount
1		
2		
3		
4		
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10		

Base amount for disclosure: 2 million yen/company/year

Amount: ①2,000,000 yen or more ②10,000,000 yen or more ③20,000,000 yen or more

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Pledge: I hereby declare that there is no discrepancy in my conflict of interest status described above. I have no other COI that may impede my work for the Society other than those I have stated. I agree that the contents of this disclosure form may be made public if subject to social or legal requests.

Date: / / (month / date / year)

Signature:

Use this form if you require more space to disclose items. **(Additional Form)**

Name of Individual Disclosing COI: _____

＜Items to Declare＞

1. Position as an officer or advisor of a company or for-profit organization, and amount of remuneration.
2. Stock ownership and profit from stock (profit from stock for the previous year)
3. Remuneration received for patent royalties or licensing fees from companies or for-profit organizations.
4. Honoraria such as lecture fees, attending conferences (presentations, providing advice etc.) received from a single company or for-profit organization
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7. Scholarship (incentive) donations provided by a single company or for-profit organization
8. Endowed departments established through donations by a company
9. Other remuneration (travel expenses, gifts etc. not directly related to research)

Name (A・B・C)	Disclosure Number	Name of Company/For-profit Organization	Applicable (Title, Patent name, Type of research etc.) *If #2, give the total number of shares and share price	Amount (refer to each item)

*Please make copies if more space is required