



Istituto Superiore di Sanità

The ISS process of assessing and managing conflicts of interest for MSIF Essential Medicine Panel (MEMP)

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Introduction and purpose

The Multiple Sclerosis International Federation (MSIF) promotes and coordinates a multidisciplinary international working group called the MSIF Essential Medicine Panel (MEMP) aimed at developing evidence-based recommendations for the choice of disease-modifying drugs for multiple sclerosis in low resource-settings, which will also be proposed to the World Health Organization (WHO) for inclusion in the Essential Medicines List (EML), whose periodic update is scheduled for 2023.

The National Center for Clinical Excellence, Quality and Safety of Care (CNEC) of the Istituto Superiore di Sanità is in charge of examining the declarations of interests of each member of the panel and of the people involved in the project (evidence review team, expert consultants and observers), as independent external institution.

This document describes the process of evaluating the interests of all subjects engaged in the development of the above-mentioned recommendations for identifying cases of conflict of interest for each clinical question and the measures to be undertaken for their management.

The evaluation process is based on the policy for the conflict of interest management in the development of the ISS guidelines described in the *Methodological Manual for the production of clinical practice guidelines* (available at https://snlg.iss.it/wp-content/uploads/2021/08/MM_v1.3.2_apr_2019.pdf) and on the principles set out by the Guidelines International Network -G-I-N (Schünemann *et al.* 2015).

Definition of Conflict of Interest (Col)

A Col arises in "any circumstance in which a secondary interest influences or could unduly influence the impartiality of professional judgment" (IOM, 2009).

Types of interest

In line with the policies of the main organizations that produce clinical practice guidelines¹ and with international standards (NICE 2017; WHO; IOM, 2009; IOM 2011; Schünemann *et al.* 2015) a distinction is made between:

- *financial interests* – that is the financial relationships with organizations that invest directly in products or services relevant to the subject matter. It refers to any monetary value related to the direct payment for services, shareholdings, stock options or other shares, intellectual rights properties (patents, copyright royalties). Within this type, a distinction is made between:
 - *personal financial interest*, referring to opportunities for economic gain for the declaring person;
 - *family financial interest*, referring to opportunities for economic gain for people with whom the declaring person has habitual relationships - including the spouse, cohabitant, minors and adults (cohabiting and not) for whom the subject is legally responsible, relatives or kin up to the second degree;
 - *institutional financial interest*, referring to a payment or other benefit received not personally by the declaring person but by the department or structure in which he/she operates and/or has managerial responsibilities.
- *non-financial or intellectual interests*, which relate to career advancement, social prestige and personal beliefs.

Both *financial* interests and *non-financial or intellectual* interests can be:

- *specific*, or directly associated with the topic on which the subject must give judgement (i.e. relating to the producer or owner of the good or service assessed by LG)
- *non-specific*, or not directly associated with the topic on which the subject must give judgement (i.e. related to the sector of the good or service but unrelated to the subject under consideration).

Finally, the interests are considered:

- *current* – that is existing at the time of participation in the work for the preparation of the recommendations;
- *previous* - or present in the last 4 years and concluded.

The evaluation of the declaration of interests

Declarations of interests are evaluated by two independent reviewers with specific technical-scientific and ethics skills who assesses each individual interest to determine the extent to which

¹ National Institute for Health and Care Excellence (NICE), National Health and Medical Research Council (NHRMC), Io Scottish Intercollegiate Guidelines Network (SIGN), US Preventive Services Task Force (USPSTF), World Health Organization (WHO) and others.

the interest could reasonably be expected to influence the expert's judgment. Possible discrepancies will be resolved through discussion.

The assessment considers the following information:

- type of interest
- relevance in terms of specificity with respect to the topic on which the subject must express himself
- period and duration
- role of the declaring person in the relevant structure and / or activity and the amount of funding (in the case of institutional interest).

Col risk levels and mitigation actions

Based on the evaluation, each interest is assigned one of the three following risk levels:

- Level 1 - minimal or irrelevant
- Level 2 - potentially relevant
- Level 3 - relevant.

At each of the three levels of conflict, there are corresponding measures to be taken for their management, as illustrated in Table 1.

Table 1 Possible measures to be taken by level of conflict of interest

Level of risk		Measure	
1	<i>Minimal or irrelevant</i>	1a	None (full participation in the work)
2	Potentially relevant	2a	full participation in the work with public disclosure of interest
		2b	partial exclusion from the work
3	Relevant	3a	partial exclusion from the work
		3b	Total exclusion

Interest is considered minimal or irrelevant (level 1) if it is unlikely to influence the subject's judgment. In this case, no action needs to be taken: a) No measure.

In the case of potentially relevant interest (level 2), the application of one of the following measures for the management of the conflict is indicated:

2a: full participation in the work with public disclosure of the interest in the final document of the guideline or on the website following the publication of the recommendation to which the interest refers. It applies for interests considered relatively minor.

2b: partial exclusion from the work, such as exclusion from the part of the meeting or work relating to the declared interest and from the related decision-making process. It is used to

allow Panel members to access the knowledge or opinion of the most qualified experts, while bearing in mind their potential biases.

In the case of significant interest (level 3), the application of one of the following measures for the management of the conflict is indicated:

3a: partial exclusion from the work, such as exclusion from the part of the meeting or work relating to the declared interest and from the related decision-making process.

3b: total exclusion, i.e. the limitation to participation in any part of the meeting or process. It applies when the nature of the interest is too significant with respect to the general objectives or where limiting the involvement of the expert to a part of the work would not make sense.

Mitigation or abstention actions in the presence of potentially significant or significant risk levels

In the event that a declared interest is considered potentially or clearly relevant (level 2 and 3), in taking a decision towards mitigation or abstention of a subject, the "balancing test" is applied.

In carrying out such a "balancing test", the reviewers, while fully considering the contribution, tasks and function of the expert as well as the availability of alternative experts with the required expertise, must weigh:

- the nature, type and magnitude of the expert's interest and therefore the degree to which the interest may be reasonably expected to influence the expert's judgment

against:

- the adequacy of measures/options available to protect the independence and integrity of the decision-making process.

In cases of inclusion in the Panel of Experts of members with level 2 or 3 Col, the evaluation commission will be asked to decide on the participation of these members in some phases of the process, for example by excluding their participation in the formation of judgments on the GRADE EtD criteria or voting on recommendations for individual PICOs.

Box 1 provides an example of how the Chairs of Experts Panel should manage the involvement of Panel members with or without Col during the guideline development process.

Box 1. Guide for Chairs on the involvement of panelists with and without Col

All Panel members are invited to participate to:

- the critical evaluation of the evidence, providing any additional considerations deemed important;
- the discussion that will take place after the formulation of the recommendation. That is because it is very unlikely that there will be any changes to be made to the recommendation, unless there is new evidence or the panel realizes that relevant evidence was eluded.

Only Panel members without Col are invited to participate to:

- formulating judgments on the GRADE EtD criteria;

- online voting by responding to the electronic survey to express opinions on the GRADE EtD criteria;
- the consensus stage or voting on the conclusions and on the recommendation formulation.

Panel members with CoI will be asked to remain silent during meetings and to intervene only when questioned.

References

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