Policies for Conflicts of Interest

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In its role of think tank and within the framework of the "Assises du Médicament", the LIR considered useful to make realize by the researchers of the ESSEC an international study on the policies of management of conflicts of interests.

Four reglementations were studied : United States, Great Britain, Germany and Sweden.

Contents

Introduction

Each country and even each regulatory body has its own approach to cope with conflicts of interest (COI) in the health system. A systemic review of the policies and rules of COI was done for the United States of America (USA,) for the European Medicines Agency and for three European countries (United Kingdom, Germany, and Sweden) by searching the official websites of their health agencies and institutions:

- In USA, the department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), the National Institutes of Health (NIH) and the Office of Extramural Research (OER);
- In UK, the Department of Health (DH), the National Institute for Health and Clinical Excellence (NICE), the Medicines and Health Care products Regulatory Agency (MHRA) and the National Health Services (NHS);
- In Germany, the Institute for Quality and Efficiency in Health Care (IQWIG) and the Federal Joint Committee (G-BA);
- In Sweden, the Swedish research council and a common guidance for the Dental and Pharmaceutical Benefits Agency (TLV), the Medical Products Agency (MPA), the National Board of Health and Welfare, the National Food Administration, the Swedish Council on Health Technology Assessment (SBU), Swedish Institute for Communicable Disease Control (SMI) and the Swedish National Institute of Public Health.

The focus of this study is to analyze the policies and guidance in the field of conflicts of interest. Thus, a list of questions was elaborated.

1. What is a conflict of interests?

A conflict of interest is a situation in which financial or other personal considerations have the potential to compromise or bias professional judgment and objectivity. It involves the abuse - actual, apparent, or potential - of the trust that people have in professionals. [1]

According to the Institute of Medicine, “a conflict of interest is a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.” Primary interest varies according to the purpose of a professional activity and secondary interests may include not only financial gain but also the desire for professional advancement, recognition for personal achievement, and favors to friends and family or to students and colleagues. [2]

2. Who is covered by the COI policies?

The entire chain of the health system and specially the decision makers are target for conflicts of interest. Policies and regulations are implemented by institutions in order to ensure the impartiality of individuals and to avoid bias decisions. The COI policies apply to two different groups: internals and externals to the institutions. (See Table 1)

Table 1 – Individuals covered by COI Policies

Internals	Externals
All Employees of institutions	Clinical investigators when applying for a marketing authorization
Scientific committee members	Clinical investigators conducting / participating

Commissions	in the studies
	Applicable manufacturers or applicable groups purchasing organization that provides payment or other transfer
Chairman and other non-executive members of boards	Patients and consumers invited to attend and take part in advisory board meetings, committees activities or oral debates
Chairs and members of the advisory boards to the institution	Experts and independent contractors
Working Groups	Physicians

3. What are the interests that should be declared?

Based on the literature review, the kinds of interests that need to be declared can be classified as follows:

- Specific or Non Specific to the question under discussion:
  This classification is defined in the NICE code of practice for declaring and dealing with conflicts of interests. The interest is regarded specific when it is related to the product or service being evaluated; and non-specific when it is unrelated to the matter under consideration.
  NB: The FDA classified the question under discussion and not only the interest. The FDA has a decision's tool for participation of special and regular government employees. In the first question of the tool, the subject matter of the meeting has to be defined as a particular matter or not. "Will the meeting itself or governmental action of which it is a part involve deliberation, decision, or action that is focused upon the interests of specific persons, or a discrete and identifiable class of persons?" [3] The topics could potentially affect such a large number of persons or organizations, that they would not be considered a particular matter. In this case, the participation and voting of an employee is permitted without a waiver. (See Appendix 1)

- Personal/ Non-Personal:
  This classification was shown in the context of the MHRA Code of Practice. "A personal interest involves the payment, in any form, to an individual personally, by a pharmaceutical company whose business may be directly affected by the advice of the advisory body". [4] "A non-personal interest involves payment that benefits a department for which an individual is responsible, but is not received by the member personally". [4]

- Direct / Indirect:
  For the EMA, the interests in pharmaceutical industry are divided into direct and indirect interests. The first one includes employment, consultancy, patent, and financial interests, and the second one includes investigator and funds.

- Pecuniary / Non-pecuniary:
  The nature of the interests declared is mainly financial. In fact, all agencies requested the disclosure of the pecuniary interests and only NICE enquires the declaration of non-pecuniary interests. These latter may be difficult to measure and to be quantified, but have a real influence on individuals. NICE defined the non-pecuniary interests as clear opinion, public statement about the matter under consideration, holding office in a professional organization or advocacy group with a direct interest in the matter under consideration and other reputational risks in relation to an intervention under review.

- Family interests:
  The FDA requests the financial interests of the immediate family of the government employee (spouse, minor child or general partner). NICE and MHRA enquires the declaration of "family interests". The Swedish common guidance for the 7 institutions also requires the disclosure of the

interests “of family members and close relationships”. However, this is not the case for the EMA; this type of declaration is not requested.

4. When and how should interests be declared?

The declarations of interests are made on appointment, before meetings, or / and annually. It depends on the status of the person declaring the interests. In USA, the regular and special government employees at the FDA need to declare their interests prior to each meeting. In Sweden, it is required from the external expert to update his declaration whenever a change occurs. The EMA has a special approach for the declaration of the COI. First, all members and experts should be included in the EMA Expert Database. A disclosure of interests is then required prior to the first appointment. Based on the information provided, the level of COI risk is evaluated. If the information on individuals deemed to have ‘high risk’ COI, the case is referred to the Declaration of Interests Assessment Group (DIAG), which assesses their acceptability for involvement in EMA activities.

The declarations are mostly reported on papers such as the FDA and NICE declaration forms. The electronic form (eRA) is used by the US institutions that are applying for grants from the NIH. It also applies for the companies to disclosure their payments to physicians and others, according to the Sunshine Act.

The control of declarations is not mentioned by any agency. The disclosure of conflicts of interest is a declaration of honor.

5. What are the limits for the interest’s declaration?

It is complicated to identify what are the limits for the interests’ declaration and when the ties could have an effect on the agency’s ability to act objectively and impartially [5]. Two limits can be observed.

Firstly, the thresholds of financial interests differ leading to question about the appropriate financial limit to fix. The EMA experts for example, are asked to indicate if the value of financial interests exceeds 50 000 Euros. [6] The FDA enquiries from the clinical investigator who conducts any clinical study submitted in a marketing application, to declare any equity interest that exceeds 50 000 dollars in value and other sorts of significant payments that have a cumulative monetary value of 25 000 dollars or more. Financial conflicts of interests are tangible interests but how to define the threshold from which the value of the financial interest becomes a risk for conflict. A financial interest does not have to be greater for a bigger influence. Social science research suggests that the influence may operate without an individual being conscious of it and that gifts of small value may influence decisions. [2]

Secondly, the time limits requested for the declarations also vary. In Sweden, a fixed time limit of 2 to 3 years is proposed, while the EMA requested information for the last five years. The Swedish common guidance highlights that it is difficult to specify the time required for “neutralization” of an experts past assignment, once regarded as an unacceptable conflict of interest, in order to allow a new assignment in a similar issue from an agency. The length of such a period must however be dependent on the type and scope of the relationship, the nature of the assignment, and its economic significance. [5] In UK, the annual declaration of the chairmen and members of the MHRA must include all the financial interests in the pharmaceutical industry currently held or held in the last 12 months but not restricted to this period.

6. Are the conflicts of interests information published?

In the literature review, the COI information is made public for all institutions. However, the kind of information provided differs. Interests declared to the MHRA are published each year in the Annual Reports of the Commission on Human Medicines and Section 4 Committees. This publication will provide only the name of the committee chairman or member, the source of the interest (e.g. the company name); it will not provide any financial information nor numbers (e.g. for shares) nor identify the family member or other holding the interest by name. Furthermore, the decisions on participating in the committee meetings are recorded in the minutes that are publicly available on the MHRA web site. [6]

Declarations of interest made by experts to the EMA are accessible to public, either on the agency's website or in its offices. Also, certain information about the outcomes of EMA COI policies and procedures, such as assessments made by the Declaration of Interests Assessment Group (DIAG), is made available on request. [6]

In Germany, IQWIG declarations of interests are presented and published in a tabular summarization.

7. Who is responsible of managing conflict of interests? How is it handled?

When reviewing the policies on conflict of interests, it is hard to identify for some agencies the entity responsible of managing the declaration of COI. For example, the EMA does not specify in the procedure of the handling of the COI, the entity that assigns preliminary the risk level of COI before referring the individual to the DIAG. As well, NICE does not specify the responsible entity of handling COI. Yet, the IQWIG has a committee for the conflicts of interest to evaluate the declaration of experts. As for the FDA, the FDA ethic's staff handles the declaration of the COI.

The actions listed below are the main measures taken by the health authorities in order to handle the COI:

- Exclusion from the meeting / the project:
  The FDA is using a decision making tool to evaluate the risk of COI in the participation of an individual. It is an Algorithm of 10 steps. At each step, a decision is taken to authorize or not an employee to assist to FDA meetings. At the last step, a waiver can be issued if the need for the special government employee's services "outweighs the potential for a conflict of interest", and if the financial interest of a regular government employee is "not substantial as to be deemed likely to affect the integrity of the services provided by that individual".

- Requesting additional information:
  A conflict of interest may exist for the clinical investigator conducting studies that the FDA relies on to establish that the product is effective. In this case, the FDA can request that the applicant for marketing authorization submits additional data.

- Suspension of funds:
  The NIH in USA may suspend the grants for an institution if a conflict of interest appears.

- Money penalties:
  According to the Sunshine Act, a manufacturer or organization is subject to civil money penalties for each payment or other transfer not reported as required. The penalty is not less than $1,000, but not more than $10,000 if failure to report, and not less than $10,000, but not more than $100,000 if knowing failure to report.

- Imprisonment:
  According to the Department of Health in UK, any person who contravenes Medicines (Advertising) regulation 21 is guilty of an offence, and liable, on summary conviction to a fine not exceeding £5000, and/or to imprisonment for a term not exceeding two years.

Recommendations

It is an established fact that it is easy to damage an agency's credibility, but extremely difficult and time-consuming to repair the damage. [5] Relying on a disclosure of financial and non financial interests rather than managing or eliminating them is a problem. [7] Thus, managing a COI is essential ; but, handling COI is a major challenge because of the complex relationships between government, academia and industry. [8].

There are three main problems that can affect the efficacy of a policy: (1) the individuals' failure to declare on purpose or not, (2) the control of the declarations and (3) the handling of the COI. Success in implementing rules and standards is only possible if the different conflicts of interest systems are shaped to the needs of the specific administration, taking the particularities of the administrative culture and political context into account. [9] The Institute of Medicine suggests a list of criteria for Evaluating Conflict of Interest Policies. [2] (See Table 2)

Table 2 – Criteria for evaluating conflict of interest

Criterion	Description
Proportionality Transparency	Is the policy most efficiently directed at the most important conflicts? Is the policy comprehensible and accessible to the individuals and institutions that may be affected by the policy?
Accountability Fairness	Does the policy indicate who is responsible for enforcing and revising it? Does the policy apply equally to all relevant groups within an institution and in different institutions?

The following list of points can be considered:

- A standard and single declaration to a unique receptor but specific rules per institution;
- Double declaration by the donor and the beneficiary;
- An identified committee for handling conflicts of interest;
- An "Algorithm d'aide à la décision" (or assessment tool) to evaluating the COI and managing them.

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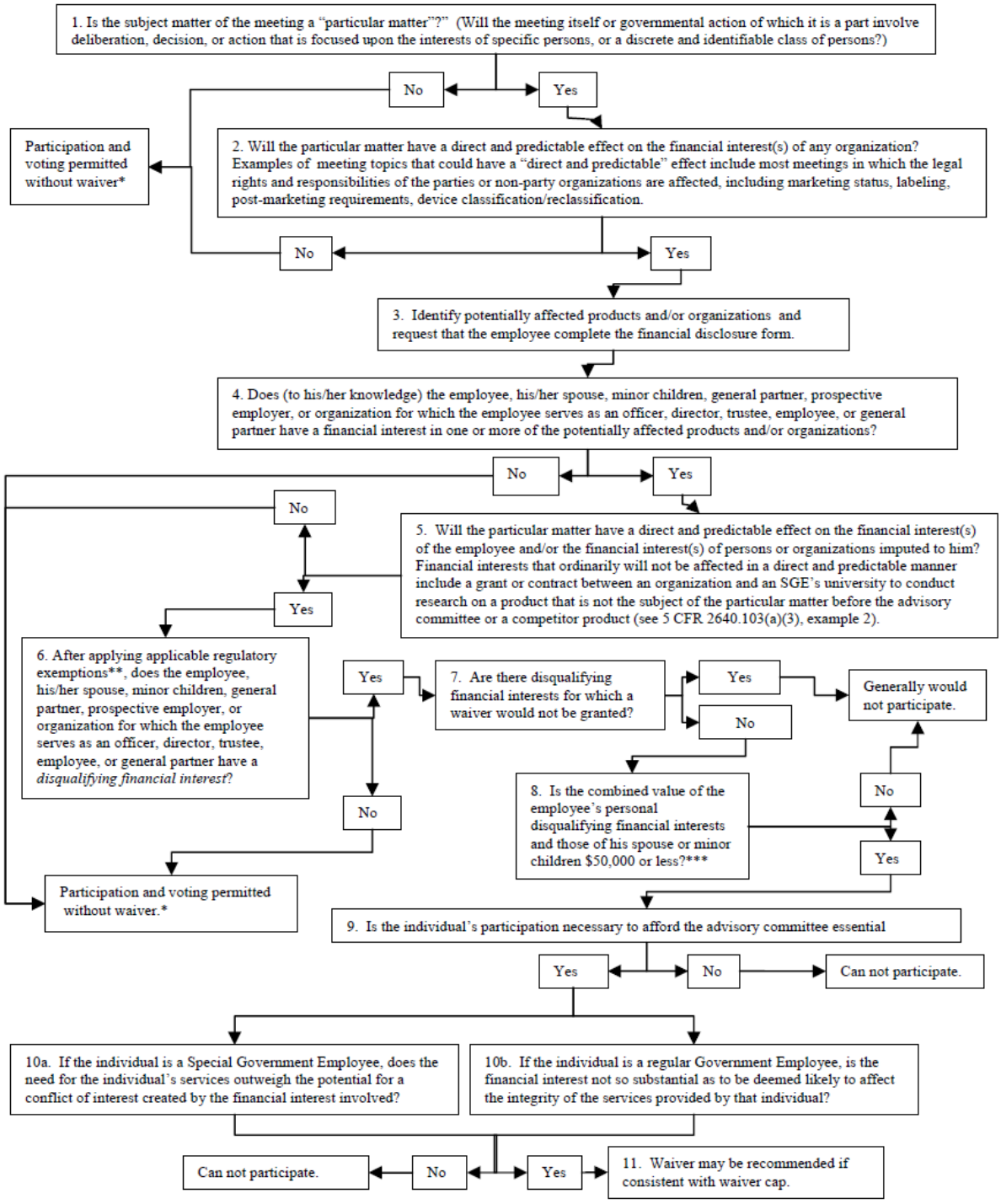
Appendix 1: FDA's Algorithm



*In some cases, an employee will have a financial interest or relationship that, while not a disqualifying financial interest, may cause a reasonable person with knowledge of the relevant facts to question his impartiality in the matter. *See* 5 CFR 2635.502. Such matters should be evaluated under that regulatory standard and, if appropriate, an impartiality determination should be requested.

**The applicable regulatory exemptions are found in 5 CFR 2640.201-206.

***In rare cases, staff may pursue whether a conflict of interest waiver is appropriate where the combined value of the employee's personal disqualifying financial interests and those of his

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