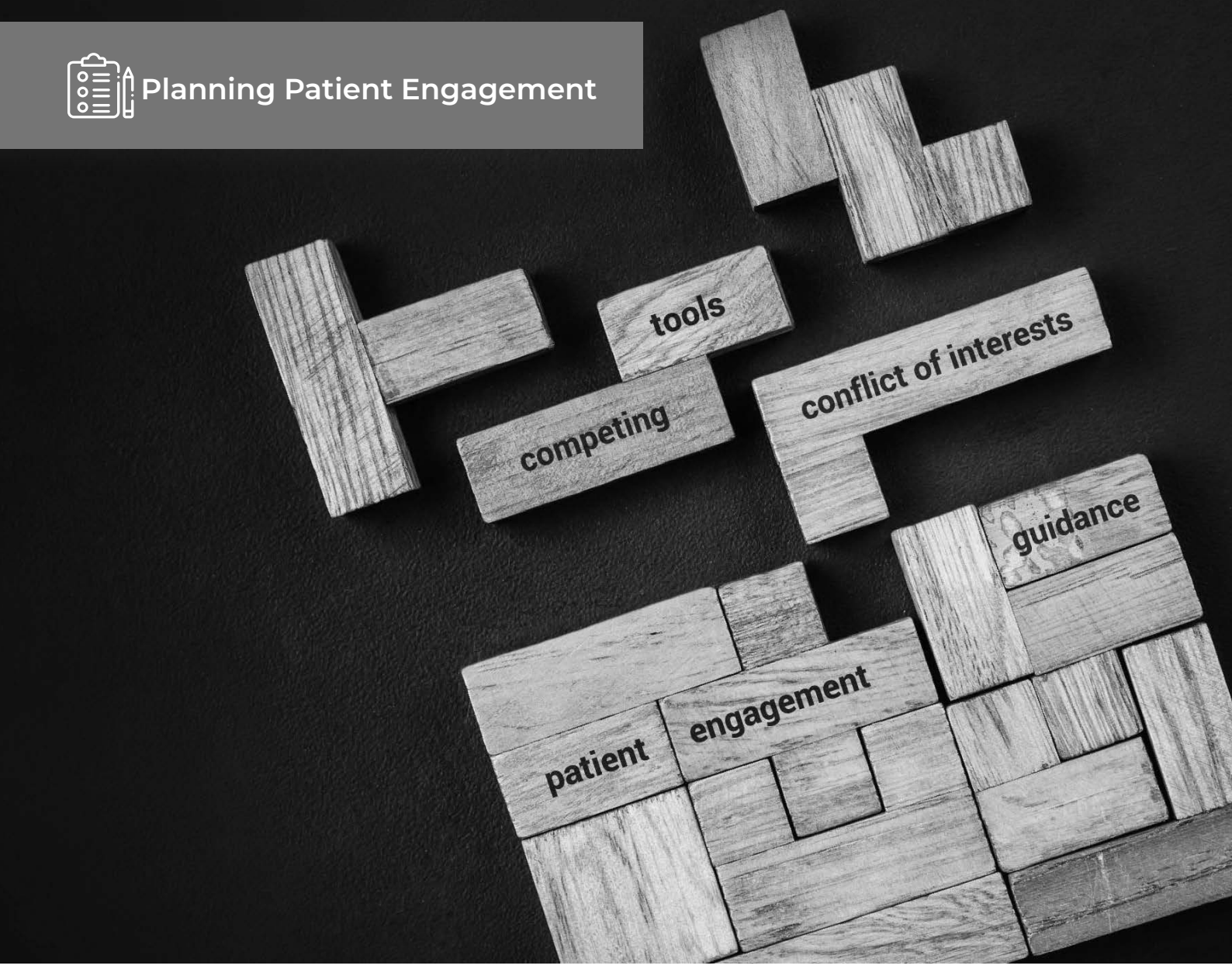
PARADIGM
Patients Active in Research and Dialogues for an Improved Generation of Medicines

innovative medicines initiative

Planning Patient Engagement



Raising awareness on managing competing interests in a multi-stakeholder environment:

Guidance to patients and engaging stakeholders

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders
PARADIGM is receiving funding from the Innovative Medicines Initiative Joint Undertaking 2. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA

Contents

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Introduction

PARADIGM (Patients active in research and dialogues for an improved generation of medicines) was an IMI funded multi-stakeholder consortium to provide a framework for structured, effective, meaningful and ethical patient engagement along the lifecycle of medicines.

The project focused on three decision-making points: research priority setting; clinical trial design; and early dialogues with regulators and health technology assessment (HTA) bodies. The result of the consortium/the output of the consortium is a comprehensive set of tools and practices to support the integration of the patient perspectives into medicines development beyond the focal areas of the project.

Patient engagement should be a standard practice to improve medicines development and deliver results that are focused on patients' needs.

What is this tool?

The present document aims to raise awareness among patients (in their role of experts by experience) and the engaging stakeholder organisations of the consequences that the act of engagement might have on patients during multi-stakeholder interactions.

The interactions between the patient community and the engaging stakeholder should be based on transparency, respect, autonomy and independence.

This document promotes best practices and highlights how each stakeholder could better prospectively manage competing interests, and to help avoid/minimise conflict of interest by suggesting risk mitigation strategies.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

1. Definitions and types of interests

1. 1. Definitions of competing interests and conflict of interest

Everyone has interests. Interests generate responsibilities and one should be aware of those responsibilities. Different interests can come into competition or conflict if undisclosed or unmanaged as they can result in potentially biased decision-making, a lack of objectivity and serious damage to the reputation of individuals or organisations, and ultimately cause incorrect decisions during medicines development.

In the case of patient engagement (PE), it is essential to protect the process and integrity of the parties involved (i.e. the patient and the engaging stakeholder). It is the engaging stakeholder who/that defines what constitutes a conflict of interest for a particular process.

In any case, the right of the patient to receive treatment (and potentially be cured) can never be understood as a personal interest competing with the interests and objectives of any other stakeholder.

For the purpose of this document, we have reviewed several definitions of competing and conflict of interest applicable to various fields (See Annex 1) and inspired by those. We define:

- **Competing interests** as those that may affect an individual's impartiality but that do not constitute a conflict per se. They should be declared for transparency purposes.
- **Conflict of interest** as a situation in which the individual's judgement may be affected by a secondary interest, as defined by the engaging stakeholder(s).

Stakeholders will assess declared patient engagement activities in accordance with their own policies and decide what constitutes a conflict of interest (or not). For an example, see Annex 1.

1. 2. Types of interests

In general, interests can be classified into:

- **Direct interests** arise when the person involved is likely to benefit from the activity. Examples include: employment, consultancy, strategic advisory role and financial interest
- **Indirect interests** may occur when the activity may cause a third party or someone closely related to the person in question to benefit. Examples include: close family member interests (e.g. spouse is an employee of a pharmaceutical company), being an investigator involved in a clinical trial, among others.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Alternatively they can also be considered as low, moderate or high impact which can restrict the involvement (fully or partially)[1,2,3,4]. See Annex 2 for examples.

These types of interest must be declared and then will be carefully assessed in accordance with the policies of the engaging stakeholder. They might lead to some restrictions in scope and activities that patients can be involved in both in the short term and long term. Declaring an interest does not necessarily imply the existence of any conflict, nor should it automatically disqualify a person from participating in the activities of the engaging stakeholder.

2. Patient engagement in a multi-stakeholder environment: impact for patients

The world of medicines development is a rich multi-stakeholder environment offering plenty of opportunities to create knowledge and learn from and contribute one's knowledge, experience and expertise to develop medicines that better address patients' unmet needs. However, it means that all stakeholders involved are exposed to potentially competing interests, as each stakeholder has their own roles and objectives. However, since medicines are developed for patients, they hold a central position to engage with every stakeholder along the medicines development process and beyond (Figure 1).

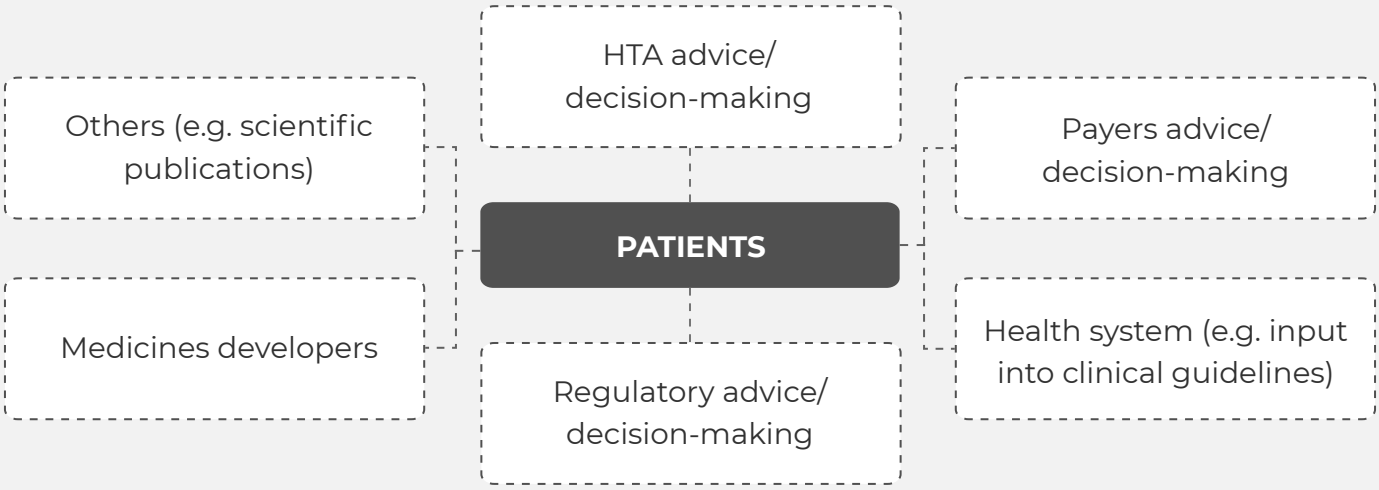


Figure 1. **Multi-stakeholder approach to patient engagement in medicines development**

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Nowadays patients are increasingly involved in medicines development as "experts by experience" and therefore may interact with several different stakeholders simultaneously and over time, which may lead to a potential situation of conflict of interest for them. Hence the importance to understand how the interaction with one stakeholder can impact the patient's ability to interact with other stakeholders, in order to anticipate and manage such situations appropriately.

Patients can contribute their expertise to different areas in the process of medicines development (see Annex 3, Table 2). Their level of involvement is subject to their capabilities and/or interest in a specific area and the activity in question. However, it may also be related to potential restrictions applied to a particular activity by the engaging stakeholder. For instance, a higher level of restriction might occur when the activity entails disclosure of commercially sensitive data (i.e. consultancy). See Annex 2.

Patients will be required to sign various documents according to the principles set out by the engaging stakeholder[5,6]. For example, regulators and HTA bodies commonly require a signed declaration of interest (DoI) and a confidentiality agreement (CA). Medicines developers need to ensure compliance with both internal and external regulations that result in specific and appropriate documentation being in place to justify the activity, ensuring protection for both parties. These documents usually focus on the areas of declaration of interests, confidentiality and also a written agreement outlining core expectations of each other (potentially including payment terms, etc).

Signing any of these documents as part of the commitment of the patient to be involved in activities with other stakeholders, places a heavy burden of responsibility on the patient: to fully understand the ethical and legal implications of these agreements to them (as patients); to keep accurate records of their interests or activities; and to disclose such interests and activities accurately and appropriately. Failure of patients (and the engaging stakeholder) to fully understand this dynamic might have personal, reputational and legal consequences to the patients.

In this regard, while there is a legitimate need by medicines developers to protect commercial information, this should be balanced with openness and transparency, essential for meaningful and informed trust-based PE. Similarly, confidentiality also applies to sensitive (non-public) information that exists within patient organisations, who may have legitimate reasons to protect what they consider confidential. Both parties must abide the pertinent agreements to enable open communication[5]. All patient engagement happening in the European Union and European Economic Area must also abide by the General Data Protection Regulation (GDPR).

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

3. Mitigation measures

Potential CoI situations should be identified as early as possible, and proactively managed to avoid or limit the extent of the conflict and the potential impact on the patient; their identification does not automatically cancel the engagement.

Ideally, both parties mutually agree on the mitigation strategies. Such strategies may vary from one stakeholder to another and should be documented. For example, patient organisations may diversify their workforce capabilities to be able to engage with regulators/HTA bodies/ payers and developers simultaneously.

On the other hand, regulators may grant special status to enable the participation of the right patient in particular activities where the pool of required patient expertise is very limited (e.g. EMA's expert witness status).

3. 1. Diversification of human resources in stakeholder organisations

One strategy followed by POs to overcome potential conflicts of interest of its members is by building firewalls between engagement and the advocacy activities. Patient representatives can also be assigned to different projects and activities within the same organisation. This ensures both the identification of the right capabilities for a given activity and equally important, that patients understand the consequences of their interaction with the different engaging stakeholders.

PO's organisational structure and patient representatives can be specialised in operational areas according to the engaging stakeholder, thus limiting potential conflict of interest scenarios. Such organisational structure may be more suitable to umbrella organisations given the scope of their activities, with disease-specific organisations having to develop alternative strategies. Very small organisations and individual non-affiliated patients may not have the capacity for such restructuring. Small disease-specific organisations would benefit from joining their respective umbrella organisations as a way to build capacity.

Lupus Europe (https://www.lupus-europe.org/), for example, has developed a model in which a patient representative signs the pertinent legal agreements with the developer and commits to gather the requested feedback from their constituency, thus limiting the impact of the interaction. Through this method it is only the signatory (individual patient) that may face potential restrictions when engaging with other stakeholders and not the entire community/ group they represent. Medicines developers follow similar risk mitigation strategies in their

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

own organisations. Best practices include having patient engagement functions sitting within medicines development and outside commercial departments to frame interactions with patients and their organisations as scientific exchange, hence avoiding the risk of being regarded as promotional.

3. 2. Granting experts special status

Under exceptional circumstances, an expert with an existing CoI can still be involved in some regulatory/health technology assessment (HTA) bodies' activities. European Medicines Agency (EMA) and European Network for Health Technology Assessment (EUnetHTA) provide for mitigating actions to help reach the best possible balance between limiting expert involvement and the need to have the right specialist expertise.

Participation as an 'expert witness', allows patients (and other experts) with a certain level of conflict to participate in some procedures under certain conditions[4] when justified, for example, where there is only a limited number of patient representatives available. An expert witness is an expert whose role is limited to testify and give specialist advice on a specific issue by providing information and replying to particular questions only. Expert witnesses can be invited to participate in scientific committees, working parties, scientific advisory groups or ad hoc expert group meetings[4]. Similarly, EUnetHTA may still seek the expert opinion of an individual with an existing CoI. However, in that case the expert shall not have access to any confidential document and would only give advice on a predefined set of questions[3].

4. Recommendations

Interactions between the patient community and medicines developers have to be done in a way that ensures respect, autonomy, independence and transparency in the process of engagement and related decision making[5]. The potential for patients to knowingly or unknowingly be precluded from engagement with other stakeholders can be particularly critical.

This is often the case in rare diseases as well as in underrepresented groups because of health-related stigma and geographical differences. Here we see that the pool of individuals with the necessary capabilities for engagement and specific disease-related expertise tends to be small. Therefore it is of paramount importance that barriers to their effective and continued engagement because of CoIs are examined and dealt with urgently. The following recommendations apply to all the relevant stakeholders involved in medicines development.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

4. 1. Follow established codes of conduct

Codes of conduct (also named Codes of Ethics or Codes of Practice) establish the rules of behaviour for the members of a group or organisation. Since PE occurs in a multi-stakeholder environment, all relevant stakeholder groups involved should have clear rules on how to interact with each other. Codes of conduct usually describe overarching ethical principles to be applied to those interactions, but they also contain provisions regarding PE in medicines development and on competing interests management. Both medicines developers and patient organisations should abide by respective codes of conduct to ensure ethical and meaningful interactions. Codes of conduct should be publicly available, reviewed periodically, and must be implemented and enforced. Some examples of existing codes of conduct (and their provisions regarding PE) are described in Annex 4.

PARADIGM has developed a code of conduct specific to PE and applicable to all stakeholders during the lifecycle of a medicine[9]. The PARADIGM code of conduct encourages comprehensive and consistent patient engagement in all aspects of medicines' research, development and access to treatment activities by protecting all involved stakeholders' interests and rights and ensuring reliable transparency in such collaboration.

4. 2. Establish a policy to manage competing interests and conflicts of interest

Patients and medicines developers should be able to effectively understand the implications and consequences of patient engagement. Therefore, it is essential that policies on conflict of interest are developed by the relevant stakeholder and are transparent, publicly available and easily accessible to all patient populations. Such policies may also consider the engagement with other stakeholders groups (e.g. healthcare professionals) and be kept on a high level. Additional specifications including the exclusion/inclusion criteria in activities expected to involve individual patients, as well as patient organisations and Community Advisory Boards (CABs)[10] may also be considered.

Policies should be clear about how a previous engagement with a developer (or any other stakeholder) could undermine the integrity of the patient's contribution and therefore, its impact and this is achieved by building these policies on these four principles[11]:

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

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

4. 3. Establish a breach of trust procedure

If agreements and/or policies are not followed by any of the involved parties, then a breach of trust can occur. It's therefore important to have effective mediation and dispute resolution procedures in place which would ascertain the integrity of the process. A breach of trust implies breaking a promise or confidence, but can also mean mean a breach of a contract or a contract clause[12]. Such a breach need not be intentional or with malice, but mere negligence. All stakeholders, including patients, should recognise this need and put in place the right procedures to deal with such circumstance should the breach arise.

Procedures should provide a detailed description of the steps and time frame to be followed from the moment a breach of trust is suspected until the final decision is taken (i.e. suspension or not of the expert's activities). Opportunities to clarify the situation and appeal the decision should be put in place. EMA has established a breach of trust procedure for competing interests and disclosure of confidential information by scientific committee's members and experts[13].

Alternatively, agreements of engagement and clauses therein may include provisions considering the immediate termination of the agreement if either party breaches trust or fails in their obligation. Examples of breach of trust may include failure to disclose interests by either party, disclosure of confidential information or to create false or wrong expectations both ways, among others.

5. Considerations when engaging with potentially vulnerable populations

Potentially vulnerable populations might be overlooked from patient engagement activities as their involvement may be considered challenging. The below recommendations may help to overcome these presumed difficulties:

- Provide and present information about competing interests (e.g. documents to raise awareness and existing policies and processes) in a format, language and structure that is accessible, tailored to the specific needs of that potentially vulnerable population.
- Design user-friendly declaration of interest procedure and forms which would allow patients with different conditions and disabilities to complete them independently; whenever necessary, provide support.
- Write inclusive definitions and policies related to CoI, which take into consideration the specific situation of groups of patients where, for different circumstances, the number of

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

patients involved in PE and advocacy work is limited.

- Find alternative ways to address CoI where these limit the participation of patients in a vulnerable group.

Below, we look at children and young patients and people living with dementia, as they are the selected vulnerable populations in PARADIGM, to highlight some specific considerations around this topic.

5. 1. People living with dementia

People living with dementia and their carers often face a number of issues in the context of medicines development and in other areas of research and policy. Some of these issues were identified as particularly relevant in the context of conflict of interest*:

- The involvement of people with dementia in PE activities in the context of medicines development is relatively new. Therefore, many people living with dementia may not be aware and fully understand the possible consequences, and concretely, the potential conflict of interests of their involvement with an organisation or developer.
- Many patients may find CoI and DoI challenging, stressful or both. This may be even more challenging for some people with dementia due to their cognitive impairment.
- In many European countries and due to different factors such as stigma, late diagnosis, lack of care and support services, very few people with dementia are involved in advocacy and/or PE activities. Very restrictive definitions of CoI and policies may be an issue in this context.

In the field of dementia, a number of Alzheimer associations in Europe have set up national Working Groups of people with dementia (and the EWGPWD at European level*) which are involved in PE activities and provide a safe and accessible approach for involving people with dementia in a meaningful way.

5. 2. Children and young patients

When engaging children and young patients, competing interests are measured against the same rules applied to adult patients, and age-appropriate explanation (with visuals if

---

* Summary of a face-to-face consultation with 11 members of the European Working Group of People with Dementia (EWGPWD) and their carers in February 2020. This consisted of an open discussion guided by some structured questions on the topic. Available at: http://imi-paradigm.eu/Paradigm-documents/Report-on-consultation-with-EWGPWD-2018_10-FINAL.pdf, [Accessed Day Mo. Year]

+From the focus group performed on September 2018 and an internal consultation done with the members of the Kids Barcelona Young Persons Advisory Group led by Fundació Sant Joan de Déu. Available at: https://imi-paradigm.eu/Paradigm-documents/Report-for-consultation-with-young-persons-FSJD-final.pdf, [Accessed Day Mo. Year]

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

appropriate) about the concept of conflict of interest before their involvement needs to be given. However, since children and young patients cannot enter into legal agreements, it would be the parents or their legal guardians who would have to agree to the terms of the DoI and sign the necessary documents.

When a minor is engaging with different stakeholders through Young Patient Advisory Groups (YPAGs), it is the facilitator responsible for the custody of the minor during their contribution in advocacy activities who signs the declaration of interest form. Even here, parents and legal guardians need to be informed about the activities being engaged in, their objectives and any potential CoI.

Established working groups with young patients usually include CoI-related information in the contract's general template. This general template would typically also include confidentiality clauses unless drafted in a separate agreement.

Having confidentiality and conflict of interest clauses in a standardised, single document facilitates and encourages the engagement of young patients.

6. Scope and limitations of the document

Since conflicts of interest may arise along the medicines development process, including the three main decision-making points relevant to PARADIGM, this document may also apply to other areas of engagement beyond these points.

Stakeholders are encouraged to engage with one another, and having clear rules on this interaction eliminates or minimises possible competing and/or conflicting interests.

Different stakeholders have their own rules and definitions which may be different from another stakeholder. Patient organisations, in their codes of conduct, for example, establish the limits of its members with medicines developers[14] but does not cover the interaction with regulators as these fall under the legal framework in which they operate. Therefore, a code of conduct or policy to handle competing interests will only cover the range of interactions defined for that particular stakeholder group.

The present document which is aligned with the PARADIGM Code of Conduct aims to describe the interactions between patients and stakeholders involved during medicines development; inform the reader about the potential consequences that such engagement might have; and provide recommendations on how to navigate this complex environment.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

However, we acknowledge that:

- the list of definitions of competing interest, conflict of interest and the types of interest we provide is not exhaustive; and
- the risk minimisation strategies we propose and recommendations we make are not exhaustive or applicable at all times. There are other potential solutions which are not presented in this document (e.g. public registries).

7. Tools to help manage competing interests and conflict of interests

7. 1. Log of activities

A declaration of interest (DoI) is commonly required when patients are engaged as experts in activities during medicines development. The potential conflict scenarios vary and may be differently assessed by one stakeholder to another.

Keeping a log of activities of one's participation and engagement would facilitate and ensure the proper completion of a DoI. This would be particularly helpful to patients who may not have the support and guidance of a PO.

Having an updated log of activities with the date, length and scope of each engagement to refer to when filling CoI forms saves time and makes the process less tedious. Remember that the burden of responsibility lies with the patient and not the engaging stakeholder.

As mentioned earlier, listing such activities does not automatically preclude the patient's involvement. After an assessment of the CoI, the patient engagement would be approved, restricted (as per the policy of the engaging stakeholder) or allowed under exceptional circumstances, see Section 3.2. (Involvement may be entirely restricted in specific scenarios, for relevant examples, see Annex 2)

Some activities would not generally result in a CoI, for example, in a research priority setting stage where the patient's input may not be targeted to a specific product (e.g. input on unmet medical needs in a particular disease area) or one specific developer (e.g. participation at a strategic meeting of EFPIA). An interaction that takes place in a pre-competitive environment (e.g. IMI project on developing a new methodology or research project on Patient-Reported Outcomes) would also not generally result in a CoI. In all these instances, even if it is assumed that a CoI would not arise, it is recommended that details are included in a log of activities.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

7. 2. Educational scenarios on competing interests and conflicts of interest

As conflicts of interest are defined by the engaging stakeholder, it may be difficult for patients to identify potential scenarios that may potentially result in a conflict of interest. Similarly, either engaging stakeholder may have a different perspective on what constitutes a conflict of interest. This tool has two objectives:

1. to support patients to take informed decisions before engaging with the relevant stakeholder and
2. to help the engaging stakeholder to understand the consequences that the act of engagement might have on patients during multi-stakeholder interactions.

7. 3. Short guidance on managing competing interests and conflicts of interest

This document helps clarify basic concepts and recommendations on how to manage competing interests and specific considerations for the different stakeholders involved.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Annex 1: **Definitions of competing interests and conflict of interest**

The terms 'conflict of interests' and 'competing interests' are often used interchangeably[15]. In the table below, we provide a non-exhaustive selection of definitions from various sources that help distinguish between the two.

TABLE 1: **Definitions of competing interests and conflict of interest.**

Field of work	**Competing interests**
Clinical practice	Competing interests occur when factors may fall short of constituting a conflict, but could influence an individual's judgement or her/his impartiality[16]
Clinical guidelines	Any declared interest that may affect or be perceived to affect objectivity and independence[1]
Legal	Competition by an Interested Person, either directly or indirectly, with the Corporation (Free Law Project) in the purchase or sale of property or property rights, interests, or services, or, in some instances, competition directly for the same donor or external resources[17]
Scientific publishing	Those of any kind that could undermine the objectivity, integrity or perceived value of a publication through their potential influence on behavior or content or from perception of such potential influence[18]
	Exists when professional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry)[19]
Field of work	**Conflict of interest**
Ethics	According to the National Research Ethics Advisory Panel (NREAP) of United Kingdom (UK) a conflict of interest has been defined as "a set of conditions in which professional judgment concerning a primary interest (such as patient welfare or the validity of research) can be influenced by a secondary interest (such as financial gain)" [20,21]
	It arises when two or more people (the parties) seek either: the same indivisible good or benefit, or part of a divisible good or benefit in an amount or in such a manner that there is insufficient in reserve to satisfy the needs or wishes of the other party or parties, or where the goods or benefits that each party seeks are of such a nature that they cannot be held by those parties without giving rise to some detriment to one party or the other[22]
Public sector	A conflict of interest involves a conflict between the public duty and the private interest of a public official, in which the official's private-capacity interest could improperly influence the performance of their official duties and responsibilities[23]
Clinical research	Set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest[24]
Clinical practice	Conflict of interest can occur in 4 main areas: financial, educational, relationships, or employment conflicts[16]

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Example: Competing interests vs conflicts of interest

A patient is first invited by the medicine developer, 'Company A'. Subsequently, the patient receives two invitations, one by Company B and by the European Medicines Agency (EMA). The activities the patient is being engaged for take place concurrently over a six months.

Below we look into these engagements and whether there are any competing or conflicting interests.

Conflicts of interest do not last forever; the engaging stakeholder's policy will specify the time frame in which a conflict of interest is active (e.g. for the next three years from the starting date of the engagement activity).

	Company A	Company B	EMA
Competing interests	Patient is invited to develop multiple sclerosis (MS) patient-reported outcome measures (PROs). Patient signs a non-disclosure agreement/ confidentiality agreement	Same patient offered to join a patient advisory board (PAB) to define MS unmet needs by company B	Same patient is contacted by the EMA to participate in a scientific advice (SA) procedure on a medicine development by company A
Declaration of interests and Assessment	Patient declares that they have no previous competing interests to declare.	Patient declares their activity with Company A to Company B	Patient declares current engagement with Company A and Company B
Conflict of interests	**NO:** Company A concludes that there is no CoI and the patient can be engaged	**NO:** Company B concludes that there is no CoI and decides to include the patient in the PAB	**YES:** EMA concludes that patient has a current **direct interest** with Company A according to EMA policy

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Annex 2: **Examples of levels of restriction**

EMA types of interest and level of restriction.
Adapted from EMA policy on handling competing interests [4]

Types of interest	EMA	Level of restriction in EMA activities
Direct (current or within the last 3 years)	Employed by a medicine developer	No involvement or severely restricted involvement
	Consultancy (regardless of financial compensation)	
	Strategic Advisory Role for a company	
	Financial (e.g. stocks, shares, etc.)	
Indirect current or within the last 3 years)	Principal Investigator	Involvement permitted but restrictions apply
	Investigator	
	Grant/funding to the patient organisation/ institution	
	Close family member interests	
No interest or interests over 3 years (except executive role or lead role)		Full, unrestricted involvement

EUnetHTA types of interest and level of restriction.
Adapted from EUnetHTA policy [3]

Types of interest	EUnetHTA	Level of restriction in EUnetHTA activities
Major	Employed by a medicine developer	No involvement
	Consultancy (regardless of financial compensation)	
	Strategic Advisory Role	
	Principal Investigator	
	Being a current member of an association (patient or HCP organisation) funded mainly by the industry (>40% of association budget)	
	Covering/subsidising travel costs or paying an honorarium for delivering a presentation or attending conferences/meetings sponsored by only one company producing either the technology under assessment, a comparator, or a relevant technology under development.	
	Receiving funds for research activities related specifically to the technology under assessment, a comparator, or a relevant technology under development.	Involvement can still occur if interests are no longer existing
	Financial (e.g. stocks, shares, etc.)	

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Annex 3: **Engaging stakeholder activities**

Table 2 provides a non-exhaustive list of patient engagement activities along the medicines' lifecycle adapted from the EUPATI roadmap[25].

TABLE 2: **Patient engagement activities along the medicines' lifecycle**

Phase of the medicine lifecycle	Types of activities	
Research priorities	**Setting research priorities**	Gap analysis
		Early horizon scanning
		Matching unmet needs with research
		Defining patient relevant added value and outcomes
Research priorities and Planning	**Protocol synopsis**	Design and target population
	Protocol design	Relevant endpoints
		Benefit/Risk balance
		Inclusion/exclusion criteria
		Diagnosis procedures
		Quality of life and patient reported outcomes
		Ethical issues
		Data protection
		Mobility issues/logistics
		Adherence measures
	Patient Information	Content, visual design, readability, language, dissemination
	Informed consent	Content, visual design, readability, language
	Ethical review	

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

TABLE 2: **Patient engagement activities along the medicines' lifecycle**

Phase of the medicine lifecycle	Types of activities	
Research conduct and operations	**Trial steering committee**	Protocol follow up
		Improving access and adherence
	Information to trial participants	Protocol amendments
		New safety information
	Investigators meeting	Trial design
		Recruitment
		Challenges and opportunities can trigger amendments
	Data & Safety Monitoring Committee	Benefit/risk; drop-out issues; amendments
	Study reporting	Summary of interim results and dissemination in patient community
Dissemination, communication, post-approval	**Regulatory Affairs**	For relevant activities see Table 3
	HTA	For relevant activities see Table 4
	Post-study communication	Contribution to publications; dissemination of research results to patient community/professionals

1. Engagement with regulatory authorities

1. 1. European Medicines Agency (EMA)

Since its establishment in 1995, EMA has seen a systematic increase in patient interactions, with patients currently involved in all aspects of the regulatory process from early dialogue to post-authorisation activities.

Patients acting as individuals have to declare their interests to participate in any medicine-related activity. EMA then assesses these depending on the particular activity in accordance with their policy[4]. This policy applies to all the Scientific Committee or Working Party chairs, members and experts involved in activities at the Agency in the context of the evaluation, authorisation and supervision of medicinal products for human and veterinary use. Patients can

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

be members of Scientific Committees (and alternates, where relevant) Management Board, or as patient experts (e.g. Scientific Advice, Protocol Assistance, Scientific advisory group (SAG)). Apart from being part of the regulatory process, patients and consumers can also represent their organisation as members of the Patient & Consumer Working Party (PCWP), for which a declaration of interest to safeguard transparency is required.

The involvement of patients, as is with any another expert, in EMA activities, may be restricted based on the assessment of the interests declared. The assessment looks into whether an interest is direct or indirect, the timeframe during which the activity took place and the type of activity, amongst other things.

Patients can also represent their organisation in workshops held by EMA or when they respond to consultations, in which case no declaration of interest is required. Participants in an engagement open to the public also do not need to sign a declaration of interest. However, all speakers are required to publicly declare any interactions with developers of the medicine(s) under discussion.

TABLE 3: **Types of EMA engagement activities[26] and DOI requirement**

Phase of the medicine lifecycle	Types of activities	DOI required
Pre-submission	Scientific Advice (SA) and Protocol Assistance (PA) (https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance)	Yes
	Parallel consultations with EMA and HTA bodies (https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance#parallel-consultations-from-regulators-and-hta-bodies-section)	
	Review of public documents (e.g. Public Summaries of Opinion on orphan designations https://www.ema.europa.eu/en/medicines/ema_group_types/ema_orphan)	
	Patients as members of the EMA Scientific Committees: Committee for Orphan Medicinal Products (COMP) (https://www.ema.europa.eu/en/committees/committee-orphan-medicinal-products-comp), Committee for Advanced Therapies (CAT) (https://www.ema.europa.eu/en/committees/committee-advanced-therapies-cat), and Paediatric Committee (PDCO) (https://www.ema.europa.eu/en/committees/paediatric-committee-pdco)	
	Patients can also be consulted in writing or invited to attend committees in person (e.g. disease-specific requests)	
	Patients can be consulted in writing or invited to attend committees in person (e.g. disease-specific requests)	

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

TABLE 3: **Types of EMA engagement activities[26] and DOI requirement**

Phase of the medicine lifecycle	Types of activities	DOI required
Evaluation	Scientific advisory group (SAG) (https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance)	Yes
	Patients can be consulted in writing or invited to attend Committees in person (e.g. disease-specific requests, benefit/risk assessment discussions at the Committee for Medicinal Products for Human Use https://www.ema.europa.eu/en/committees/committee-medicinal-products-human-use-chmp), and COMP for maintenance of orphan designation	
	Review of public documents, such as the Medicines Overviews, Herbal summaries and Package Leaflets, in order to review if the content is comprehensive and written in lay language	
Post authorisation	Scientific advisory group (SAG) or ad-hoc expert meetings convened by the Pharmacovigilance Risk Assessment Committee (PRAC) (https://www.ema.europa.eu/en/committees/pharmacovigilance-risk-assessment-committee-prac). These are meetings where experts are invited to discuss specific scientific questions to inform the Scientific Committees' decision-making process	Yes
	Patients can be consulted in writing or invited to attend Committees in person (e.g. disease-specific requests, PRAC referrals, etc.)	
	Review of public documents, such as the safety communications, in order to review if the content is comprehensive and written in lay language.	
	Public hearings (https://www.ema.europa.eu/en/about-us/how-we-work/publichearings)	No

1. 2. National regulatory agencies

In 2013, Guidelines on the prevention and management of conflicts of interest in EU decentralised agencies (https://europa.eu/european-union/sites/europaeu/files/docs/body/2013-12-10_guidelines_on_conflict_of_interests_en.pdf) were published. While these guidelines list EMA as the only regulatory authority, they may well be applicable to national regulatory authorities which should also have their own conflict of interest management policy.

1. 2. 1. Agenzia Italiana del Farmaco (AIFA)

The Italian Medicines Agency (AIFA) (http://www.agenziafarmaco.gov.it/en) launched the "Open-AIFA"[27] initiative that promotes direct contact and interaction between the Italian

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Drug Agency, patients, academics, and medicines developers with the aim of having an open and transparent dialogue and an active involvement of all the stakeholders in the regulatory process. In order to participate, one must fill a DoI which is assessed before the meeting against some of the EMA's policy criteria including the nature of the declared interest, the timeframe during which such interest occurred, as well as the type of activity.

In 2019, AIFA privileged the dialogue with representatives of patients organisations in the context of Open AIFA. Moreover, the Agency renewed a Memorandum of Understanding (MoU) with the Italian Patients Academy – EUPATI for the certification of the training materials disseminated to the alumni of the EUPATI Expert Patient courses with particular regard to the topics related to AIFA and the regulatory field.

AIFA is also considering how to establish a proper mechanism of patient engagement in the Agency's regulatory activities, starting with the definition of a legal framework of interaction. Most of these procedures take inspiration from the well-established process of PE at EMA.

2. Engagement with HTA bodies and payers

2. 1. European network for HTA bodies (EUnetHTA)

EUnetHTA is engaging with patients for the assessment and evaluation of health technologies in order to support the decision-making related to those. Patients as experts, can be invited to take part in scientific work of the EUnetHTA Joint Action, and as mentioned before within the parallel consultations with EMA and HTA bodies (e.g. EMA-HTA scientific advice).

Patients can participate in one-on-one conversations, group discussions or scoping e-meetings, and in order to do so, they have to complete and sign the EUnetHTA declaration of conflict of interest and confidentiality undertaking (DOICU) form. The level of involvement will be adjusted according to the degree of their conflict of interest[28].

Patient contributions to the HTA process can be incorporated directly via individual or group input. All patient organizations that contribute in the open call for patient input need to provide information regarding their funding[29], including the respective sources of their funding, the percentage of sponsoring by companies/institutions (separate as well as the overall funding), and the relevant time period.

For example, EUnetHTA considers as major conflicts some of the situations below which may lead to the exclusion of the expert from the task[3].

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

- Being a current member of an association funded mainly by the industry (>40 % of association budget)
- Currently receiving funds for research activities related specifically to the technology under assessment, a comparator, or a relevant technology under development.

EUnetHTA may still seek the expert opinion of an individual with an existing CoI, however, in that case the expert shall not have access to any document requiring confidentiality and would only give advice on a predefined set of questions.

The table below describes the types of contributions, compensation and confidentially issues of patient input.

TABLE 4: **Types of patient input at EUnetHTA.**[**]

Approach	Patient and/ or patient representative	Description of patient contribution & deliverables	Patient investment and compensation	Conflict of interest and confidentiality
Open call for patient input	Patient organisations (representatives) Patient will have access to information publicly available, no additional confidential data will be shared	General feedback from an organizational level; summarized view intended to be representative	Some investment for organizations; no compensation	Organizations provide information regarding funding and conflict of interest
One-on-one conversation	Individual patients (living with the condition) or caregivers providing general or specific feedback; patients or caregivers may also act as patient / caregiver representatives Patient will have access to information publicly available, no additional confidential data will be shared	Views are (mostly) individual Representatives may add a view that is intended to be representative	No travel costs if done via phone; compensation will be outlined in the SOP for compensation of external parties	Declaration of conflict of interest to be completed, any risk of conflict of interest will need to be assessed properly before patient engagement

[**] Adapted from reference 29, EUnetHTA Patient Input in Relative Effectiveness Assessments. Updated 29.05.2019. Available at: https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf, [Last accessed on 30 October 2019]

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

TABLE 4: **Types of patient input at EUnetHTA.****

Approach	Patient and/ or patient representative	Description of patient contribution & deliverables	Patient investment and compensation	Conflict of interest and confidentiality
Group discussion	Individual patients (living with the condition) or caregivers providing general or specific feedback Patient will have access to information publicly available, no additional confidential data will be shared	Views are (mostly) individual	Travel costs for individual patients or caregivers; compensation will be outlined in the SOP for compensation of external parties	Declaration of conflict of interest to be completed, any risk of conflict of interest will need to be assessed properly before patient engagement
Scoping e-meeting participation	Individual patients (living with the condition) or caregivers providing general or specific feedback; patients or caregivers may also act as patient / caregiver representative	Views are (mostly) individual Representatives may add a view that is intended to be representative	No travel costs; compensation will be outlined in the SOP for compensation of external parties	Declaration of conflict of interest to be completed, any risk of conflict of interest will need to be assessed properly before patient engagement

2. 2. National Institute for Health and Care Excellence (NICE UK)

Patients engage with NICE have to fill in a DoI which is assessed before engagement. The DoI makes a distinction between direct and indirect interests, and if potential conflicts of interest are detected restrictions may apply if potential conflicts of interest are detected.

NICE has involved patients in its work since its establishment in 1999. In 2009 it established Early Dialogues (Scientific Advice) which have taken a variety of forms including:

- The standard Scientific Advice process
- Combined scientific advice with the UK regulator (MHRA)
- Combined scientific advice with the European regulator (EMA)
- Early dialogues as part of the EUnetHTA joint HTA processes and pilots

** Adapted from reference 29, EUnetHTA Patient Input in Relative Effectiveness Assessments. Updated 29.05.2019. Available at: https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf, [Last accessed on 30 October 2019]

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

2. 3. Mechanisms of Coordinated Access to Orphan Medicinal Products (MoCA)

Patients can be also involved in early dialogues with payer organisation such as in the pilot, MoCA[32]. This initiative provides a mechanism for European countries to collaborate on coordinated access to orphan medicines in a voluntary and dialogue-based approach, intended to create a fluid set of interactions between key stakeholders across all aspects of a product[33].

Patients who participate in these pilots have to fill a DoI which will be assessed prior to the meeting, against EMA's criteria on direct and indirect interests. MoCA´s policy aims to protect patients' interests in their role of experts in medicine development, particularly in scientific, regulatory, and HTA activities at national or EU level.

It also ensures that patient representatives participating in the MoCA pilot projects have no competing interests with the medicine developer which could affect their impartiality during the engagement.

In MoCA, EURORDIS represents patients with rare diseases, and Medicine Evaluation Committee (MEDEV), a group of EU national competent authorities for pricing and reimbursement. Lastly, medicines developers with an orphan product or a rare disease therapy at any stage of pre or post authorisation phases of development are represented.

Experts from the EMA, EUnetHTA or other scientific committees/HTA bodies, as well as individual medical experts or selected representatives from the medicine developer, may also be invited and involved in specific pilots as appropriate and relevant, and upon the general agreement of all other regular participants.

2. 4. Canadian Agency for Drugs and Technologies in Health (CADTH)

The Canadian Agency for Drugs and Technologies in Health (CADTH) has developed a framework to include patient input in their Scientific Advice programme. In addition, the Canadian Institutes of Health Research Strategy for Patient-Oriented Research (SPOR) has also developed a framework for patient engagement in healthcare research.

CADTH has in place conflict of interest policies and guidelines for all employees, external experts, committee or panel members, and individuals contracted by CADTH. All experts, patient representatives, and CADTH staff members involved in the CADTH Scientific Advice Program are bound by the conflict of interest policies and guidelines.

In addition, the Canadian Institutes of Health Research Strategy for Patient-Oriented Research (SPOR) has also developed a framework for patient engagement in healthcare research.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

3. Simultaneous engagement with competitor developers

Patients can be involved with different medicines developers simultaneously or subsequently, and sometimes even competitor developers in numerous activities through different engagement instruments (Table 5). Simultaneous engagement with several medicines developers might result in a conflict of interest.

Transparency about any previous or current engagement with another stakeholder is required. The engaging stakeholder, according to their policy/rules, will ultimately decide if the engagement should take place.

Medicines developers have their own policies to engage with patients and other experts that require declaration of interests. If patients are engaged with several medicines developers, they may be required to sign a CA and/or a NDA and/or a non-compete clause (NCC)[5,6].

By signing such documents patients agree not to disclose any confidential information with any third party, or to exploit the confidential information to gain competitive advantage. However, as a general principle medicines developers should not request nor expect exclusivity from patients.

These legally binding agreements can be complex and sometimes may not be clear to patients what information can be disclosed or not. The legal ramifications of adhering to or not adhering to these agreements can also be unclear and difficult to grasp especially when engagement occurs with several different organisations.

Transparency, disclosure, compliance with signed agreements as a key element before starting any patient engagement activity. The above mentioned agreements can be signed by an individual patient, a CAB or a (industry-led) Patient Advisory Board. These documents should follow agreed principles between medicines developers and patients[5,6].

Medicines developers may require to patients, as well as to other experts (e.g. health-care professionals, etc.), disclosure of interests that could affect the company's business including but not exclusively:

- Employment in government organisations or public decision-making bodies
- Employment in private companies involved in the distribution, dispensation or commercialisation of medicinal products.

These interests may also apply to close family members.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

TABLE 5: **Types of engagement instruments**[#]

Focus group	A qualitative group discussion between participants, which is typically conducted in-person and moderated by a moderator with special expertise. Key considerations for focus groups may include research objectives, topic complexity, topic sensitivity, group size/number of participants per group, group diversity/heterogeneity, and number of focus groups needed.
Qualitative interviews	A semi-structured conversation between a subject and interviewer to collect rich, in-depth qualitative data related to the research question. This may include discussion about a patient's disease experiences, or their attitudes/perceptions towards treatment and its impact.
Online patient surveys	Completed by patients and can be used to collect quantitative data (discrete choices) or qualitative data (free-text answer boxes). Patients complete the survey independently, and do not interact with one another. Patient surveys are most valuable to assess stakeholder attitudes/perceptions and quantify disease burden/unmet needs; such surveys methods are indispensable when large datasets are required for quantitative analysis or when patient populations are geographically diverse.
Delphi panels	Multistage survey process with the intent to achieve consensus among experts, including patients, on a topic or issue. It can provide valuable data to help describe a patient experience or event[34]
Patient advisory panels/boards	Consists of patient experts (patients, patient advocates and/or caregivers) who are convened to bring unique knowledge to inform teams regarding the patient perspective. This tool places patients as strategic advisors rather than research participants.
Community advisory board (CAB)	Group of patients and patient representatives that serves as a link between a community and researchers/developers. Within clinical development, a CAB may review clinical trial protocols, monitor clinical trials, and help inform the community about them[35].
Public meetings	Offers the opportunity to tailor a meeting with patients, patient advocates, and a broader representative panel of decision-makers including clinicians, scientists, health authorities, and payers, to address specific objectives

[#] Types of patient engagement instruments table adapted from PARADIGM Recommendations on How to find the right match for the right patient engagement activity, Available at: http://imi-paradigm.eu/PEtoolbox/identification-of-patient-representatives

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

3. 1. Engagement through expert Working Groups

Engaging stakeholders assess the interests of the individual experts involved in their activities, and depending on the type of interest disclosed – direct or indirect – the patient's engagement may be partially or fully restricted for a particular activity.

Here we look at how engagement with stakeholders through established groups that operate through a well defined and transparent framework facilitates interaction with stakeholders compared to individual patient engagement.

We acknowledge that, according to current existing policies, the same rules and restrictions apply to individuals or to those involved in a standing expert group, and therefore this modality cannot be proposed as a mitigation strategy.

Below we describe the concept and functions of Community Advisory Board (CAB) but other examples include the European Working Groups of People With Dementia (EWGPWD) and the Young Patients' Advisory Groups (YPAGs) (see also Section 5). Together with CABs, EWGPWD and YPAGs, are examples of long-term meaningful collaborations between patients and engaging stakeholders following established engagement frameworks.

3. 1. 1. Community Advisory Board (CAB) concept

The CAB concept is comprehensively described in a separate PARADIGM deliverable[10].

A CAB is a group of patients and patient representatives that serves as a link between a community and researchers/developers. Within clinical development, a CAB may review clinical trial protocols, monitor clinical trials, and help inform the community about them.

The CAB model has also been implemented in areas such as policy making, HTA, and to discuss pricing and access to treatment issues in territories where access to treatment is limited. In some countries, they also act as a main advocacy platform for disadvantaged patient communities. They provide expert advice to all stakeholders/developers involved in the research, development and service provision of medical treatments.

Generally, CABs:

- are developed and driven by the patients/community;
- address issues that are largely driven by the community, reflecting some of the concerns and needs of that community;
- address questions medicines developers and regulatory bodies may want to address;
- contact different companies with whom they want to collaborate and then decides who will represent them from their community;

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

- allow for the patient community to receive feedback and follow up about the issues addressed at the meeting;
- work with several medicines developers simultaneously (hence involving potentially competing products from the same class, disease area);
- have continuous or long-term relationships between the company and the patients; and
- allow researchers to rapidly collect feedback from different people who are knowledgeable and ready to collaborate without the need to initiate the process at whatever moment it may be needed.

The collaboration between each CAB and different developer is covered by different documents which can include a Confidentiallity Agreement (CA), Memorandum of Understanding (MoU), or similar.

Individual members of the CAB can also be asked to sign a declaration of interest, non-disclosure agreement (NDA), statement on intellectual property, disclosure of financial contributions received from medicines developers for performing personal activities, and a document to prevent insider trading.

The CAB model involves a transfer of value from one or more medicines developers to a patient organisation, that may be perceived as having an impact on conflict of interest.

Existing CABs in Europe offer best practices of stable long-term meaningful collaboration between medicines developers and the patient community. CABs have established transparent governance, operations, legal and financial rules that provide a framework of interaction that would a priori reduce potential conflicts of interest (i.e. no exclusivity to one developer, transparent funding and communication).

4. Healthcare system

4. 1. Engagement with health care professionals to develop clinical guidelines

Patients, along with other experts, can be involved in the development of clinical guidelines. To safeguard the objectivity of the guidelines, all involved must disclose any competing or conflicting interests.

For example, the American College of Physicians (ACP) have developed a 3-tiered grading scheme to assess the seriousness of a CoI, as high-, moderate-, or low-level, and therefore the restriction or not in the activities[16] (Table 6)

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

TABLE 6: **Level of CoI and restriction.*****

Level of COI	Low	Moderate	High
Activities	Any inactive (past) high-level conflict Any intellectual interest partially related to the clinical topic area	Intellectual interest that may lead to cognitive bias Relationships with entities that may seek to profit by association with guidelines, but not vested in clinical conclusions of guidelines	Any active relationship with a high-risk entity (e.g. advisory board for pharmaceutical company
Level of restriction	No restrictions (discussion, voting or autorship)	Participation is partially restricted from voting and autorship, not discussions	Any active relationship with a high-risk entity (e.g. advisory board for pharmaceutical company

5. Publication of peer-reviewed articles or other types of communications

Patients can be also involved in authoring or reviewing articles, and before its publication, they must disclose and specify any competing interest during the submission process following each journal policy on CoI. Examples of two major scientific journals include:

- Nature publishing group has also a policy on competing interests for authors and reviewers. For peer reviewed contributions, authors' declarations are disclosed to peer reviewers in full[18].
- British Medical Journal (BMJ) encourages patients to publish articles. Patients as authors or reviewers are required to disclose any potential conflict of interest which will be assessed before publishing following its policy[19].

*** Adapted from Qaseem, A. and Wilt, T., 2019. Disclosure of Interests and Management of Conflicts of Interest in Clinical Guidelines and Guidance Statements: Methods From the Clinical Guidelines Committee of the American College of Physicians. Annals of Internal Medicine, 171(5), p.354. Available at: doi: 10.7326/M18-3279

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Annex 4: **Examples of code of conduct**

1. PARADIGM code of conduct

PARADIGM has developed a code of conduct (http://imi-paradigm.eu/PEtoolbox/code-of-conduct) specific to PE and applicable to all stakeholders during the lifecyle of a medicine[9].

The PARADIGM code of conduct encourages transparent, comprehensive and consistent patient engagement in all aspects of medicines' research, development and access to treatment activities by protecting all involved stakeholders' interests and rights.

2. Codes of conduct developed by medicine developers

We recommend that medicines developers ensure their processes include the necessary details about how they will work in a way that meets the standards set in their respective Code of Conduct. As an example, both the EFPIA[36] and the Association of the British Pharmaceutical Industry (ABPI) code of practice[37] include provisions on:

- the interaction between the developer and the PO. Written agreements on the type of activity or relationship with the PO including description of the activities and funding should be in place.
- the type of support and services provided to patient organisations. These activities must be disclosed on the company website either on a national or European level on an annual basis and must include:
  - the name of the PO
  - a description of the nature of the support or services provided
  - the monetary value of financial support and of invoiced costs or the non-monetary benefit (in kind services) that the PO receives when non-financial support cannot be assigned to a meaningful monetary value
  - the total amount paid per PO for contracted services
  - disclosures on the transfer of value to POs

Individual companies may also have their own code of conduct and conflict of interest policy[38, 39, 40].

As another example at national level, the German law on medicines distribution and marketing[41] includes a special section on Engagement with patient organisations, pointing at the following industry codes of conduct:

- FSA Code of Conduct on Patient Organisations
  https://www.ifpma.org/wp-content/uploads/2016/01/3_DE-EN-FSA-Code-Patients-20081.pdf

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

- AKG Code of Conduct on Patient Organisations https://www.ak-gesundheitswesen.de/wp-content/uploads/akg-verhaltenskodex-22-04-2015-en-ueberarbeitet.pdf

3. Codes of conduct developed by patient organisations

Patient organisations may also have specific rules by which they abide when engaging with different stakeholders such as the Code of Practice between patient organisations and the healthcare industry[14], a document developed by EURORDIS, EPF, EATG and the European Cancer Patient Coalition and endorsed by other organisations including Alzheimer Europe is one such example.

This document is intended as guidance to help and encourage patient organisations to develop their own Code of Practice along the following recommendations/guiding principles:

- Funding of patient organisation activities/events, core funding, project funding:
  - POs that receive funding from any source (including industry or governmental bodies) should remain open, honest and transparent concerning the amounts and sources of such funding. Funds should be balanced and diversified as much as possible to avoid conflicts of interest and guarantee independence.
  - POs should mention the names of the sponsors supporting their website or electronic materials (e.g. logo modest in size).
  - POs should not be funded for activities aimed at promoting the use of any specific product and/or service.
- Industry press releases: POs and their representatives must be vigilant and refuse to be quoted in industry press releases that relate to a marketed product or a product under development. If a PO feels the need to communicate to the media about a product, it should issue its own press release which is clearly independent of industry.
- Training or participation in conferences/seminars organised by medicine developers: PO should be aware that some programmes may influence the patient organisation or its representatives. Patients should consider public training resources[42].

The topic of conflict of interest from the specific perspective of the patients experts engaged across the medicines life-cycle is relatively new with very few published references mainly focusing on funding from for-profit sources received by patient organisations as a potential source of bias[43,44].

The recommendations provided in this document highlight the importance of abiding to codes of conduct and to develop clear procedures and policies to handle competing interests in a

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

transparent and fair manner.

While POs should remain as independent as possible, they must acknowledge that medicines developers are important stakeholders with whom they can address patients' unmet needs and provide knowledge that is essential to patients (e.g. conferences and symposia). Remaining conflict-free may prove difficult, and having mitigation mechanisms in place is both desirable and essential.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Annex 5: **Glossary**

Disclaimer

The terms used here have been defined or agreed upon within the context of this project. They should not be considered as exhaustive, finite or purposely exclusive of other considerations, but are representative of the specific focus of this project and its actions.

Code of conduct

Collection of rules and regulations that include what is and is not acceptable or expected behaviour (PARADIGM)

Community Advisory Board

Community Advisory Board (CAB) refers to a group of patients who offer their expertise to sponsors of clinical research and who advise several sponsors in their field. CABs are autonomous bodies, not related to the sponsor or chosen by them (EURORDIS).

Confidentiality Agreement (CA)/Non-disclosure agreement (NDA):

Legal contract between at least two parties that outlines confidential material, knowledge, or information that the parties wish to share with one another for certain purposes but wish to restrict access to.

(Wikipedia https://en.wikipedia.org/wiki/Non-disclosure_agreement)

Consultancy

Advice provided on company- or academia sponsored clinical trial protocols including related documents, regulatory documents or information about the products under discussion (e.g. medicinal products, biomarkers), strategic initiatives and other projects of commercial or academic relevance (PARADIGM)

Design of clinical trials

Designing protocols, discussing patient burden, discussing patient related outcomes (PARADIGM)

Early dialogues with regulators and Health Technology Assessment bodies

Early (multi-stakeholder) discussions between industry, HTA agencies and/or regulators (and

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

in some contexts with payers) to discuss developmental plans for a medicinal product and to ensure they meet the requirements.

** Early dialogue is not a decision-making time for any party. In practice it more closely resembles consultation with the chance for feedback and input (two-way communication).* (PARADIGM)

Health Technology Assessment (HTA)

Systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies. HTA is conducted by interdisciplinary groups that use explicit analytical frameworks drawing on a variety of methods.

(HTA glossary http://htaglossary.net/health+technology+assessment)

Health technology assessment (HTA) body

A body that undertakes or commissions health technology assessment to form recommendations or advice for healthcare funders and decision-makers on the use of health technologies (PARADIGM)

Healthcare professional (HCP)

This category of stakeholders is broad and heterogeneous as it encompasses general practitioners, nurses, clinical investigators/academics, pharmacologists, etc. (PARADIGM)

Medicine developer

Includes any organisation involved in the research, development, manufacture, marketing and/or distribution of medicinal products and/or any other health products such as medical devices or digital solutions. Clinical/contract research organisations (CROs) or consultancy companies providing advice or services relating to the above activities, fall under the definition of medicines developers.

Research organisations including universities and learned societies (i.e. an organisation that exists to promote an academic discipline, profession) are also included in the definition of medicines developers (PARADIGM)

Medicines development/medicines research and development (R&D)/ medicines lifecycle (in PARADIGM these terms are used interchangeably)

A medicines lifecycle comprises research and discovery, development (preclinical and clinical),

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

marketing authorisation, post-approval, HTA, pricing and reimbursement, commercialization, lifecycle management and Pharmacovigilance until deregistration.

(PARADIGM, adapted from: EUPATI: https://toolbox.eupati.eu/resources/making-a-medicine-step-7-phase-ii-proof-of-concept/ European Commission: https://ec.europa.eu/competition/sectors/pharmaceuticals/cycle.html EFPIA: https://www.efpia.eu/about-medicines/ Frontiers 'The Life Cycle of Health Technologies. Challenges and Ways Forward, Iñaki Gutiérrez-Ibarluzea et. al. 2017' https://www.frontiersin.org/articles/10.3389/fphar.2017.00014/full)

Memorandum of Understanding (MoU)

Type of agreement between two (bilateral) or more (multilateral) parties. It is not legally binding, but it expresses willingness between the parties to take forward a common line of action. (Investopedia https://www.investopedia.com/terms/m/mou.asp)

Participating organisation/engaging partner

An organisation which is organising and/or participating in a PE activity (PARADIGM)

Patient covers the following definitions:

- **"Individual Patients"** are persons with personal experience of living with a disease. They may or may not have technical knowledge in R&D or regulatory processes, but their main role is to contribute with their subjective disease and treatment experience.
- **"Carers"** are persons supporting individual patients such as family members as well as paid or volunteer helpers.
- **"Patient Advocates"** are persons who have the insight and experience in supporting a larger population of patients living with a specific disease. They may or may not be affiliated with an organization.
- **"Patient Organization Representatives"** are persons who are mandated to represent and express the collective views of a patient organization on a specific issue or disease area.
- **"Patient Experts",** in addition to disease-specific expertise, have the technical knowledge in R&D and/or regulatory affairs through training or experience, for example EUPATI Fellows who have been trained by EUPATI on the full spectrum of medicines R&D.

  (The European Patients' Academy on Therapeutic Innovation (EUPATI) https://www.frontiersin.org/articles/10.3389/fmed.2018.00270/full)

Patient community

Patients, patient representatives including their family and carers, patient advocates and patient organisations (PARADIGM)

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Patient engagement

the effective and active collaboration of patients, patient advocates, patient representatives and/or carers in the processes and decisions within the medicines lifecycle, along with all other relevant stakeholders when appropriate (PARADIGM)

Patient organisations

Patient organisations are defined as not-for profit organisations which are [patient-]focused, and whereby patients and/or carers (the latter when patients are unable to represent themselves) represent a majority of members in governing bodies (EMA 2018a)

Payer

Institution, organisation or individual paying for healthcare or health services (PARADIGM)

Pharmaceutical industry

The pharmaceutical industry is comprised of many public and private organizations that discover, develop, manufacture and market medicines for human and animal health. In short, the term "industry" is used to refer to the pharmaceutical industry (PARADIGM)

Policy-maker(s) (or policymaker(s)):

A member of a government department, legislature, or other organization who is responsible for making new rules, laws, etc.

https://dictionary.cambridge.org/dictionary/english/policymaker

Regulatory authority (or regulatory agency or in short 'regulators'):

A body that carries out regulatory activities relating to medicines, including the processing of marketing authorisations, the monitoring of side effects, inspections, quality testing and monitoring the use of medicines. (EMA)

Representative for pharmaceutical industry

An employee of the pharmaceutical industry designated to represent the company position in project/consortium/body (PARADIGM)

Research priority setting

Providing opinion, providing evidence and/or being part of a group that decides what is important to research. Design of clinical trials (PARADIGM)

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Three main decision-making points

The term, 'decision-making points' is defined as the key points in the development lifecycle of medicinal products. The three decision-making points relevant to PARADIGM are: research priority setting, design of clinical trials and early dialogues with regulators and Health Technology Assessment bodies (PARADIGM)

Vulnerable / underrepresented groups

Children and young patients, people living with dementia and their carers. This definition can also include underrepresented groups (e.g. migrant and non-settled populations, substance users, incarcerated people and people with mental health disorders other than dementia). (PARADIGM)

Terms related to conflict of interest/competing interest

Insider trading

It is the trading of a public company's stock or other securities (such as bonds or stock options) based on material, nonpublic information about the company.

(Wikipedia https://en.wikipedia.org/wiki/Insider_trading)

Intellectual property (IP)

Intellectual property (IP) refers to creations of the mind, such as inventions; literary and artistic works; designs; and symbols, names and images used in commerce.

IP is protected in law by, for example, patents, copyright and trademarks, which enable people to earn recognition or financial benefit from what they invent or create. By striking the right balance between the interests of innovators and the wider public interest, the IP system aims to foster an environment in which creativity and innovation can flourish.

(Wipo https://www.wipo.int/about-ip/en/)

Non-compete clause (NCC)

In contract law, a non-compete clause (often NCC), or covenant not to compete (CNC), is a clause under which one party (usually an employee) agrees not to enter into or start a similar profession or trade in competition against another party (usually the employer).

(Wikipedia https://en.wikipedia.org/wiki/Non-compete_clause).

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

Annex 6: **References**

1. Qaseem, A. and Wilt, T., 2019. Disclosure of Interests and Management of Conflicts of Interest in Clinical **Guidelines and Guidance Statements: Methods From the Clinical Guidelines Committee of the American College of Physicians. Annals of Internal Medicine**, 171(5), p.354. doi: 10.7326/M18-3279

2. **Policy on declaring and managing interests for NICE advisory committees**
https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf
Last accessed 19 May 2020

3. **EUnetHTA Procedure Guidance for handling Declaration of Interest and Confidentiality Undertaking (DOICU) Form**
https://www.eunethta.eu/wp-content/uploads/2019/04/EUnetHTA-DOICU-Procedure-Guidelines.pdf)
Last accessed 19 May 2020

4. **European Medicines Agency policy on the handling of competing interests of scientific committees' members and experts**
https://www.ema.europa.eu/en/documents/other/policy-44-european-medicines-agency-policy-handling-declarations-interests-scientific-committees_en.pdf
Last accessed 19 May 2020.

5. **Guiding Principles on Reasonable Agreements between Patient Advocates and Pharmaceutical Companies**
https://www.mpeurope.org/legal_agreements/wp-content/uploads/2019/03/Legal_Agreements_A5_3mm-bleed_PRINT_v2.pdf
Last accessed 19 May 2020**.**

6. **PARADIGM Legal toolkit**
http://imi-paradigm.eu/PEtoolbox/contract-templates

7. **PARADIGM Recommendations on the required capabilities for patient engagement**
http://imi-paradigm.eu/PEtoolbox/pe-capabilities/

8. **EURORDIS** framework of Patient Engagement Managers ensures that patient representatives acting at regulatory level are not involved in projects/activities with medicines developers.
https://www.eurordis.org/

9. **PARADIGM Code of Conduct document**
http://imi-paradigm.eu/PEtoolbox/code-of-conduct

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

10. **PARADIGM CAB Guidance document**
http://imi-paradigm.eu/PEtoolbox/community-advisory-boards

11. **Institute of Medicine (US) Committee on Conflict of Interest in Medical Research, Education, and Practice;** Lo B, Field MJ, editors. Conflict of Interest in Medical Research, Education, and Practice. Washington (DC): National Academies Press (US); 2009. 2, Principles for Identifying and Assessing Conflicts of Interest.
Available from: https://www.ncbi.nlm.nih.gov/books/NBK22937/

12. **Breach of trust.** (n.d.) Copyright © 1981-2005 by Gerald N. Hill and Kathleen T. Hill. All Right reserved. Retrieved December 19 2019 from
https://legal-dictionary.thefreedictionary.com/breach+of+trust

13. **European Medicines Agency breach of trust procedure for competing interests of and disclosure of confidential information by scientific committees' members and experts.** EMA/154320/2012, Rev. 2.
https://www.ema.europa.eu/en/documents/other/european-medicines-agency-breach-trust-procedure-competing-interests-disclosure-confidential_en.pdf
Last accessed 19 May 2020

14. **Code of Practice between patient organisations and the healthcare industry a document developed by EURORDIS, EPF, EATG and the European Cancer Patient Coalition and endorsed by other organisations including Alzheimer Europe.** Year of publication: 2009. Year of revision: 2011.
https://www.eurordis.org/sites/default/files/thumbnails/0904-PO-Code of practice.pdf

15. Ghooi, RB. **Conflict of interest in clinical research.** Perspect Clin Res. 2015; 6(1): 10–14.
doi: 10.4103/2229-3485.148794

16. **Standards of business conduct for NHS staff.** Oxford Deanery's policy on declaration of interests. Approved by the Oxford Deanery Executive Team: May 2011.
http://www.oxforddeanery.nhs.uk/pdf/Conflicts%20of%20Interest%20FV.pdf
Last accessed on 31 Jan 2019.

17. **Conflict of interest and ethics policy of Free Law project.** Free Law project is a California nonprofit public benefit corporation that provides free access to primary legal materials, develops legal research tools, and supports academic research on legal corpora.
https://free.law/pdf/policies/005-COI_and_Ethics_policy.pdf

18. **Nature Research journals' competing interests policy**
https://www.nature.com/nature-research/editorial-policies/competing-interests

19. **British Medical Journal Competing Interest Policy. BMJ uses competing interest and conflict of interest interchangeably.**
https://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

20. **National Research Ethics Advisory Panel of the United Kingdom. Guidance on Conflict of Inerests/Competing Interests.** NREAP/04 / 2012/02/13 v1.2

21. Thompson DF. **Understanding financial conflicts of interest.** N Engl J Med. 1993;329:573–6.

22. **The Ethics Centre. Understanding the nature of conflicts of interest**
https://ethics.org.au/understanding-the-nature-of-conflicts-of-interest/

23. **Managing conflict of interest in the public sector, a toolkit (2005). Organisation for Economic Co-operation and Development (OECD)**
https://www.oecd.org/publications/managing-conflict-of-interest-in-the-public-sector-9789264018242-en.htm

24. Lo B, Field MJ. **Washington (DC): National Academies Press; 2009. Conflict of Interest in Medical Research, Education, and Practice**

25. Geissler, J., Ryll, B., di Priolo, S. L., & Uhlenhopp, M. (2017). **Improving Patient Involvement in Medicines Research and Development: A Practical Roadmap.** Therapeutic Innovation & Regulatory Science, 51(5), 612–619.
https://doi.org/10.1177/2168479017706405

26. **Patient Involvement along the medicine lifecycle at EMA**
https://www.ema.europa.eu/en/partners-networks/patients-consumers/getting-involved

27. **Agenzia Italiana del Farmaco (AIFA), Open AIFA initiative.**
https://www.aifa.gov.it /open-aifa1
Last accessed on 30 October 2019

28. **EUnetHTA Stakeholder Involvement Policy EUnetHTA Joint Action 2010-2012.**
https://www.eunethta.eu/wp-content/uploads/2018/01/EUnetHTA-JA-Stakeholder-Involvement-Policy.pdf
Last accessed on 30 October 2019

29. **EUnetHTA Patient Input in Relative Effectiveness Assessments.** Updated 29.05.2019.
https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf
Last accessed on 30 October 2019

30. **The National Institute for Health and Care Excellence (NICE) Patient and Public Involvement Policy.**
https://www.nice.org.uk/media/default/About/NICE-Communities/Public-involvement/Patient-and-public-involvement-policy/Patient-and-public-involvement-policy-November-2013.pdf
Last accessed on 30 October 2019.

31. **Report of the PARADIGM WP1 HTA workshop on Early Dialogues, 19th October 2018, London**
http://imi-paradigm.eu/Paradigm-documents/Report-on-PARADIGM-HTA-Early-Dialogues-Workshop-FINAL.pdf

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

32. **Mechanism of Coordinated Access to Orphan Medicinal Products (MoCA) provides a mechanism for European countries to collaborate on coordinated access to Orphan Medicinal Products (OMPs) in a voluntary, dialogue-based approach, intended to create a fluid set of interactions between key stakeholders and across all aspects of an OMP.**
https://www.eurordis.org/content/moca

33. **MoCA Revised Terms of Reference, consolidated version adopted 25 January 2016**
http://download2.eurordis.org.s3.amazonaws.com/moca/today/MOCA%20Revised%20Terms%20of%20Reference%20endorsed%20Jan-2016.pdf

34. **Delphi methods described in Patient-Focused Drug Development: Methods to Identify What Is Important to Patients (USFDA)**
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-methods-identify-what-important-patients-guidance-industry-food-and

35. **EURORDIS Charter for Collaboration in Clinical Research in Rare Diseases**
http://download2.eurordis.org.s3-eu-west-1.amazonaws.com/clinical_trials/charter-for-collaboration-in-clinical-research.pdf

36. **European Federation of Pharmaceutical Industries and Associations (EFPIA) Code of practice (2019)**
https://efpia.eu/media/413022/efpia-code-2019.pdf

37. **Association of the British Pharmaceutical Industry (ABPI) Code of practice (2019)**
https://www.abpi.org.uk/media/6655/abpi-code-of-practice-2019.pdf

38. **Novartis code of conduct, 1 Februrary 2018.**
https://www.novartis.com/sites/www.novartis.com/files/code-of-conduct-english.pdf

39. **Novartis disclosure guidelines**
https://www.novartis.com/our-company/corporate-responsibility/reporting-disclosure/codes-policies-guidelines

40. **Novartis global conflict of interest policy, 1 January 2007**
https://www.novartis.com/sites/www.novartis.com/files/Conflict_of_Interest_Policy_Final_en.pdf

41. **Distribution and marketing of drugs in Germany: overview, Engagement with patient organisations.**
https://uk.practicallaw.thomsonreuters.com/5-618-6669?transitionType=Default&contextData=(sc.Default)&firstPage=true&bhcp=1

42. **Training programmes targeted to patients such as EUPATI, EURORDIS Open Academy, EMA training resources for patients and consumers, PARADIGM resources**
https://www.eupati.eu/

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

https://openacademy.eurordis.org/
https://www.ema.europa.eu/en/partners-networks/patients-consumers/training-resources-patients-consumers
https://imi-paradigm.eu/resources/

43. Mandeville, K. L., Barker, R., Packham, A., Sowerby, C., Yarrow, K., & Patrick, H. (2019). **Financial interests of patient organisations contributing to technology assessment at England's National Institute for Health and Care Excellence: policy review.** BMJ (Clinical research ed.),364, k5300.
doi:10.1136/bmj.k5300

44. Rose SL, Highland J, Karafa MT, Joffe S. **Patient Advocacy Organizations, Industry Funding, and Conflicts of Interest.** JAMA Intern Med. 2017;177(3):344–350.
doi:10.1001/jamainternmed.2016.8443

45. **We have adapted the definition of pharmaceutical company by the European Medicines Agency (EMA).** See EMA policy on handling competing interests
https://www.ema.europa.eu/en/documents/other/policy-44-european-medicines-agency-policy-handling-declarations-interests-scientific-committees_en.pdf
Last accessed 10 May 2020

46. **Health Technology Assessment international (HTAi) glossary**
http://htaglossary.net/health+technology
Last accessed 26 Jun 2020

47. O'Rourke, B., Oortwijn, W., & Schuller, T. (2020). **The new definition of health technology assessment: A milestone in international collaboration.** International Journal of Technology Assessment in Health Care, 1-4.
doi:10.1017/S0266462320000215

48. **Definition of regulatory authority by the European Medicines Agency, (EMA) (2017). Who we are.**
https://www.ema.europa.eu/en/about-us/who-we-are

49. **EUPATI glossary definition of national competent authority**
https://www.eupati.eu/glossary/national-competent-authority/

50. Haerry D, Landgraf C, Warner K, et al. **EUPATI and Patients in Medicines Research and Development: Guidance for Patient Involvement in Regulatory Processes.** Front Med (Lausanne). 2018;5: 230

51. Hunter A, Facey K, Thomas V, et al. **EUPATI Guidance for Patient Involvement in Medicines Research and Development: Health Technology Assessment.** Front Med (Lausanne). 2018;5: 231

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders

52. Klingmann I, Heckenberg A, Warner K, et al. **EUPATI and Patients in Medicines Research and Development: Guidance for Patient Involvement in Ethical Review of Clinical Trials.** Front Med (Lausanne). 2018; 5:251

53. Warner K, See W, Haerry D, Klingmann I, Hunter A, May M. **EUPATI Guidance for Patient Involvement in Medicines Research and Development (R&D); Guidance for Pharmaceutical Industry-Led Medicines R&D.** Front Med (Lausanne). 2018;5: 270

54. EATG is a patient-led advocacy NGO that defends the treatment-related interests of people living with or affected by HIV/ AIDS and related co-infections within Europe. http://www.eatg.org/

55. EURORDIS is a non-governmental patient-driven alliance of patient organisations representing over 800 rare disease patient organisations in more than 70 countries. https://www.eurordis.org/

56. Pangallo, A., Zibarras, L. and Patterson, F., 2016. **Measuring resilience in palliative care workers using the situational judgement test methodology.** Medical education, 50(11), pp.1131-1142.

57. Coles, C., Fenlon, D. and Morgan, A., 2010. **Questionnaire design.**

58. Ju, T.L., Chen, Y.Y., Sun, S.Y. and Wu, C.Y., 2006. **Rigor in MIS survey research: In search of ideal survey methodological attributes.** Journal of Computer Information Systems,47(2), pp.112-123.

59. Goss, B.D., Ryan, A.T., Waring, J., Judd, T., Chiavaroli, N.G., O'Brien, R.C., Trumble, S.C. and McColl, G.J., 2017. **Beyond selection: the use of situational judgement tests in the teaching and assessment of professionalism.** Academic Medicine, 92(6), pp.780-784.

Copyright 2020 PARADIGM – Raising awareness on managing competing interests in a multi-stakeholder environment: Guidance to patients and engaging stakeholders