European Reference Networks

MANAGING CONFLICTS OF INTEREST

Authors: members of the ERNs Working Group (WG) on Legal & Ethical issues & relations with stakeholders, the ERNs LES WG (see full list of WG (past and current) members at the end of this document)

(The document was originally drafted by the members of the Working Group of ERNs Coordinators dedicated to this issue and, in Summer 2018, the group was merged with the Working Group on Industry of the ERN Board of Member States. The new merged ERNs LES WG worked on this final version).

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I. Definitions

ERNs – *European Reference Networks*

HCPs – *Healthcare Providers*

COI – *Conflict of interest*

GDPR – *General Data Protection Regulation*

CPMS – *Clinical Patient Management System*

ERNs activity – *ERNs activities include the exchange of knowledge among health professionals to facilitate the diagnosis and treatment of patients with low and rare disease, the production of good practice guidelines, the implementation of outcome measures and quality control, as well as among others, the contribution to research activities*[1]

Affiliated partners - Associated National Centres, Collaborative National Centres and National Coordination Hubs [2]

Industry- *definition includes among others the pharmaceutical industry but also industry involved, for example, in the developing tools, software and methods for diagnostics, care and well-being of rare disease patients.*

ERNs Individuals – those are individuals involved within ERNs activities, including:

i. *Members of the ERNs Boards, committees or any other governing body in the ERNs,*
ii. *Professionals employed by the HCPs that are individual members of the ERN and are engaged with the activities of that ERN.*
iii. *All patient representatives who are active in the governance structure and activities of the ERNs.*
iv. *ERNs coordination officers (project management and ERNs support staff, such as IT staff to be hired for CPMS activities)*

[1] Based on Article 12 of Directive 2011/24/EU.

[2] The Commission Implementing Decision (EU) 2019/1269 of 26 July 2019 amending Implementing Decision 2014/287/EU and the Board Statement of 10 October 2017 defines Affiliated Partner. The legal act can be found in here https://ec.europa.eu/health/sites/health/files/ern/docs/boms_affiliated_partners_en.pdf.

v. *In certain cases, such as in the CPMS, individual external expert invited to contribute in panels members can be included within this definition.*
vi. *Affiliated Partners.*

II. Rationale

The European Reference Networks (ERNs) must comply with several "operational criteria", as formulated in the Assessment Manual developed for all ERNs. Several criteria are meant to fulfil the requirement set out in point (iii) of Article 12 (4) (a) of Directive 2011/24/EU: “offer a high level of expertise and have the capacity to produce good practice guidelines and to implement outcome measures and quality controls” (criteria for "6. Good practice, outcome measures, and quality control", see Annex 1).

The goal of this policy is to provide all ERNs with a general policy on managing conflicts of interests in such a way that they comply with operational criteria 6.3.2 (see Annex 2) as formulated in the Assessment Manual developed for all ERNs:

"The Network adheres to ethical criteria, is transparent, and avoids any conflict of interest when developing and implementing clinical guidelines, patient pathways, and other clinical decision-making tools."

A **conflict of interest** is **defined** as follows in this Assessment Manual relevant for all Networks:

"A conflict of interest is a set of circumstances that creates a risk that professional judgement or actions regarding a primary interest of the science or the patient will be unduly influenced by a secondary interest. Conflict of interest may distort the interpretation of results and evidence, the analysis of data, and the development of research methods."

The ERNs LES WG has developed this document to support the Boards of the Networks.

According to the Assessment Manual, for each Network, "*the Network Board should define specific rules and procedures to ensure transparency and adherence to ethics requirements. In particular, the Board should define a strong policy on the declaration and management of conflict of interest of the participants in the development of such tools given the high ethical standards and social responsibility required."* In addition, *"to ensure fairness, this policy should respect relevant National and European legislation and follow the recommendations and guidelines developed by independent organisations and recognised bodies."*

This policy also supports the Board of Member States Statement on ERNs and industry (the original statement adopted in November 2016 was updated and adopted by the ERN Board of Member States in June 2019[3]).

Engagement of the ERNs with industry (other stakeholders, private funders, third parties etc.) is crucial in developing and improving diagnosis and care for patients with rare or low prevalence complex diseases or conditions. However, collaboration with industry requires both a solid legal and ethical basis and a high level of transparency to ensure ERNs independency and integrity and to prevent and manage reputational risks and also to avoid any situation that could be interpreted as a conflict of interest. ERNs members, as healthcare providers (HCPs) following national legislations and regulations, must already respect and sign the existing national requirements and documents. The present policy document is not meant to replace such national framework, but to complement it with a framework common to all ERNs.

[3] You can find further information at this link https://ec.europa.eu/health/sites/health/files/ern/docs/statement_industry_conflictofinterest_en.pdf.

Statement of the ERN Board of Member States on European Reference Networks (ERNs) & industry

(Updated statement adopted on 25 June 2019)

In recognition of the importance of the role of industry in improving the knowledge of rare conditions and developing diagnostics tools and therapies, the Board of Member States agrees with the engagement of ERNs with industry where appropriate, for example on clinical trials and research projects. However, as there is no legal provision for the collaboration between ERNs and industry, the Board of Member States offers the following guidance:

1. ERNs may develop collaborations with industry stakeholders but these cannot have any role in the governance structure of an ERN.

2. Facilitating some aspects of research will be an integral task of ERNs that may require collaboration with industry. Any research involving a Network (1) or any of its Members must be organised and funded in an open and transparent manner with full declaration of existent or potential conflicts of interest.

3. ERNs are expected to gather patients' data to facilitate research. The legal and practical conditions for access to this data have to be carefully defined for each specific research project, be transparent and not provide preferential treatment to any researcher or any other actor. The access has to respect patients' consent and rights and relevant national and European legislation on data protection, safety and security such as the General Data Protection Regulation (GDPR).

4. ERNs should preferably seek public funding but, once exhausted, they could also look for solutions enabling shared funding from more than one industry partner. In case of financial support coming from multiple Industry partners or when activities in several ERNs are jointly funded, an independent external body could preferably be responsible for governance and reporting. All funding must be open and transparent with full declaration of existent or potential conflicts of interest.

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(1) Research in this context is defined as: "research activity involving at least two ERN members from two different Member States for conditions or diseases covered by the ERN and specifically naming the ERN" (as agreed within the ERN Research Working Group and the ERN Working Group on Monitoring),

2 To be developed by the ERN Working Group on Legal and Ethical issues and relations with Stakeholders and to be endorsed by the ERN Board of Member States (ERN BoMS).

5. There should be no funding from industry directly allocated for management and running of the Network nor for any type of activity relating to the development of diagnostic and clinical practice guidelines or any other clinical decision-supporting tools, development of outcome measures as well as establishing and maintaining patient registries.

6. Based on the ERN Code of Conduct (2), each ERN should adopt procedures to define conditions for partnerships and project selection, policies for disclosure of conflicts of interest as well as governance rules.

7. Conflict of interest policy must respect relevant national and European legislation and follow the recommendations and guidelines developed by relevant independent organisations and recognised bodies.

8. Each ERN member must respect and follow the national and local legislation relating to conflict of interest.

9. Follow-up of all collaborations with industry could become an integral part of the monitoring of ERNs. As part of the annual report of the ERN, each case should be reported to the ERN Board of Member States (BoMS) and also made publicly available, including the origin and amount of the funding and its (planned) use, the relationship between the private sponsor and the members of the ERN and any potential conflict of interest.

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The ultimate goal of the policy is to protect the interest of the ERNs, namely to ensure independency, integrity and credibility of all activities and results produced by the ERNs. Specifically, this policy is implemented in all ERNs in order to:

- Ensure that all the ERNs' activities remain free of commercial influence or other influences.
- Ensure that the ERNs materials remain clearly separated from promotional and commercial activities of commercial organisations, industry or partners,,
- Ensure that industry's content/materials are clearly identified and there is no suggestion of endorsement by the ERNs,
- Ensure that any agreement, collaboration or work with industry does not allow this commercial organisation to influence the activities of an ERN,
- Ensure that the best and long-term interests of the ERNs and their patients, of their members and of patient stakeholders are considered,
- Ensure that no influence is applied from industry on the choice of the activities and services of the network,
- Ensure that data management is in compliance with data protection rules and the General Data Protection Regulation (GDPR) and that no identifiable patient data is shared with industry i.e. out of the scope of privacy law and data sharing policies,
- Respect the national laws and guidelines of the country where the funded activity is considered to take place,
- Ensure that there is no conflict of interest when developing and implementing clinical practice guidelines, patient pathways, and other clinical decision-supporting tools as well as when developing of outcome measures and establishing and maintaining patient registries (as foreseen in point 5 of the 2019 Board statement on ERNs & Industry: "There should be no funding from industry directly allocated for management and running of the Network nor for any type of activity relating to the development of diagnostic and clinical practice guidelines or any other clinical decision-supporting tools, development of outcome measures as well as establishing and maintaining patient registries.").

III. Scope

Responsibilities

The nature of the ERNs and the high level of expertise of their members inevitably coincide with many personal interests and relations with third parties. If these interests are potentially in conflict with the interests of the ERNs, a strict and transparent policy of disclosure of these interests is needed to counterbalance them to preserve the interests of the ERNs which are meant to facilitate discussion on complex or rare diseases and conditions that may require highly specialised treatments.This can guarantee credibility in an independent way and preserve the interests of the ERNs, which are to facilitate the European collaboration on rare or low prevalence complex diseases and conditions that can require highly specialised treatments, and allow patients across Europe access highly specialised diagnosis and care.

This policy provides a simple, yet strict way of disclosing relevant personal interest and managing conflicts of interests in the operation of the ERNs. All those participating in and collectively guiding ERNs activities (Members, Boards, Coordinators, and Affiliated Partners) are expected to:

a) adhere to the Code of Conduct (template under development) and
b) fully disclose personal and professional interests in detail and report any conflict of interest (COI), as identified in Section V, if and when this arises in relation to their duties in the ERNs.

Given the nature of collaboration in the ERNs and the individual responsibility, the management of COI is based on a disclosure and peer review model rather than a prohibition model[4]. Full disclosure of all relevant interests, either personal, collective and professional, as well as an initial assessment whether any of these interests might be in conflict with the interest of the ERNs is the responsibility of the ERNs members (and/or affiliated partners): the relevant healthcare provider has to check that each individual representative involved in an ERN activity

[4] https://www.nap.edu/read/1821/chapter/7#63

declares all possible COIs. Likewise the coordinator of a specific ERN should monitor and check that each member has done its duty in this.

This policy must be read in conjunction with the applicable legal, regulatory or statutory provisions and any other rules that apply to individuals involved within the ERNs with regards to conflict of interest. This policy shall have an additional effect on these provisions and does not replace any of the other obligations the ERN individual has in disclosing interests and reporting of conflict of interest.

Target groups

In the ERNs operational structure, we distinguish the following target groups for this policy:

i. Members of the ERNs Boards, committees or any other governing body in the ERNs,
ii. Professionals employed by the HCPs that are individual members of an ERN and are engaged with the activities of that ERN.
iii. All patient representatives who are active in the governance structure and activities of the ERNs.
iv. ERNs coordination officers (project management and ERNs support staff, such as IT staff to be hired for CPMS activities).
v. In certain cases, such as in the CPMS, individual external experts invited to contribute in panels members can be included within this definition.
vi. Associated National Centres, National Coordination Hubs and Collaborative National Centres chosen by Member States with no member of a given Network, particularly if the objectives of the Network are among those listed under Article 12(2)(f) and (h) of Directive 2011/24/EU (Affiliated Partners).

Target activities

This conflict of interest policy covers all activities undertaken by an ERN that involve decisions (policy, management or implementing decisions) related to the ERN and the results stemming from the activities of that ERN.

These activities and results include, but are not limited to the following: ERNs meetings; patient care; patient pathways; development of diagnostic and clinical practice guidelines or any other clinical decision-supporting tools; ERNs specific indicators; ERNs specific training materials or courses; registries and data management; any other activity or result defined by the ERNs to be subject to this policy.

This policy specifies, as examples, a number of activities and results that are subject to disclosure of interests and reporting of COI by the ERNs individuals involved. Each ERN should list for each of these categories what activities and results are subject of disclosure of personal interests and reporting of COI, and define any other activity or result to be subject to this policy.

I. ERNs meetings

During ERNs meetings that include decision making (e.g. development and approval of a guideline, choice of service provider, strategic decisions), the ERN needs to be aware of any COI of the attending individuals. All attending ERNs members will complete or update *the ERN disclosure form of interests*, or state that the form on file is still valid (see section 3 for timing and frequency of reporting).

If ERNs individuals identify a COI situation during a meeting, they should verbally declare the COI to the chair of the meeting, and this should be recorded in the minutes of the meeting. They should then withdraw from all related discussions and not participate in any decision making associated with the identified COI.

Subsequent to the meeting, should an ERN individual identify that the COI situation is ongoing and not a one-off matter, the general procedure described in Section 4 for reporting a COI should be followed.

II. Patient care

III. With respect to patient care provided by the ERNs, only the provision of virtual expert advice as panel member in the Clinical Patient Management System (CPMS) is covered by this policy. Panel members will be asked to tick a check box in the CPMS declaring that they have no conflict of interest related to the advice they provide for the specific panel in the CPMS. ERNs individuals that do have a COI with regard to this advice should decline as panel member or, if their expert advice is necessary, should disclose their interests and inform other panel members so that other panel members can decide taking this into account.

IV. Patient pathways
V. Clinical guidelines and general clinical recommendations
VI. ERNs specific indicators
VII. ERNs specific training materials or educational course
VIII. Data management and Registries
IX. Other activities or results as defined by the ERN

Any individual engaged in the development, implementation or execution of the named ERNs activities or results listed under III to VIII should disclose their interests and any conflict of interest with the specific ERN activity or result in the *ERN disclosure form of interests*.
ERNs individuals need to disclose any information that indicates or may suggest a bias to any part of the ERNs results under development. This includes, but is not limited to research they perform(ed), sponsorships, membership of professional boards or advisory boards, holding financial interests. This policy applies to everyone involved in any decision in the ERN context, within or in partnership with ERNs.

IV. Reporting of personal interests

All ERNs individuals (including the ERNs Coordinators, and Affiliated Partners) need to report their personal interests as soon and as long as they are engaged in an ERN activity that requires the disclosure of their personal interests. The type of interests that need to be reported are identical for all ERNs individuals and are not dependent on the ERN activity or result they are engaged with. However, the *ERN disclosure form of personal interests* should include a list of

ERNs activities that the ERN individual is engaged in. A conflict of interest is reported and reviewed in relation to a specific ERN activity or result.

The timing and frequency of reporting depends on the activities and results the ERN individual is engaged in. The first time the ERN individual engages in an ERN activity, the individual completes the form. Any time the individual engages in an additional activity, the individual is asked to update the form. Completed *ERN disclosure form of personal interests* have a validity of 1 year, provided there are no changes to the statement. In case a not-previously-declared COI occurs, the general procedure described in Section 4 for reporting a COI should be followed.

For activities that take place over a period of time, the *ERN disclosure form of personal interests* is completed before starting the activity and at completion of the activity, provided there are no changes to the statement. In case a not-previously-declared COI occurs, the general procedure described in Section 4 for reporting a COI should be followed.

For one-time activities, such as an annual Board meeting, the attending ERNs individuals will complete or update *ERN disclosure form of personal interests*.

V. Identification of a Conflict of Interest

A conflict of interest (COI) is a set of circumstances that creates a risk that professional judgement or actions regarding a primary interest of the science or the patient will be unduly influenced by a secondary interest (ERNs operational criteria 6.3.2, see Annex 2).

A COI can exist at the following levels:

- actual – it currently exists,
- potential – it may arise, given specific circumstances,
- perceived – members of the public could reasonably form the view that a conflict exists (or could arise) that may improperly influence the individuals' performance of his or her duty to the ERNs.

Identification of a COI (actual, potential or perceived) is done in relation to a specific ERN activity or results and is the prime responsibility of the ERN individual.

The *ERN disclosure form of personal interests* includes a question whether the reported personal interest is in conflict (actual, potential or perceived) with any of the ERNs activities (s)he is engaged with.

If this question is answered affirmatively, the ERN individual is asked to indicate to what ERN activity or result the COI relates to and to provide more details about the COI in Part B of the form (under development).

A COI needs to be reported as soon as the ERN individual is aware of the fact that any of his or her personal interests is (possibly, actually or perceived to be) in conflict with the interest of the ERNs and if this conflict has not been reported already.

VI. Evaluation of conflicts of interest

Following identification of a COI, the Approval Procedure outlined below should be followed:

(1) As soon as the ERN individual is aware of the COI, he/she must abstain from any decision or act that may be related to the COI until the Approval Procedure is completed.

(2) The COI faced by the ERN individual must be reported to the Board of the Network (via the ERNs Coordinator or following a procedure agreed within the ERN) - or another designated ERNs body responsible for handling COI - as soon as reasonably possible, either when the conflict manifests itself or even earlier when one recognises that a possible COI could arise.

(3) Reporting of the conflict must be made through the *ERN disclosure form of personal interests* and must contain all the elements that will allow for a proper assessment of the content of the (potential) COI. The ERN individual may include suggestions for mitigating or neutralising the conflict.

(4) Measures to mitigate or neutralize the COI will be discussed between ERNs individuals and ERNs coordinators or designated body and the solution or conclusion will be recorded in Part B of the *ERN disclosure form of personal interests*.

(5) In exceptional circumstances when no satisfactory solution can be found by the ERNs individuals and the ERNs Coordinators or designated body, or in case the ERNs Coordinators or designated body wish to abstain from discussing the COI

with the ERNs individuals, the ERNs Coordinators seek assistance from the Board of the Network and/or the ERNs Coordinators' Group, the ERN Board of Member States or DG SANTE.

(6) In case of COI by the ERNs Coordinators, the COI will directly be discussed between the ERNs Coordinators and the ERN Board of Member States and/or DG SANTE.

VII. Recording personal interests and COIs

The ERN keeps records of which ERN individuals are required to disclose their personal interests for what activities and results and archives all information in the ERN records for reporting and future reference.

The format for reporting by the ERNs will need to be defined and reporting requirements will possibly be incorporated in the ERNs monitoring system.

In order to facilitate the completion of the forms by the ERNs individuals, the tracking, processing and follow-up of the forms by the ERNs Coordinators and reporting by the ERNs, a web-based questionnaire and database will need to be developed. The form should allow for easy updating or approval of previously reported information by the ERNs individuals.

Disclosure information about the ERNs individuals will be included in all public ERNs results.

Annexes

Annex 1: Full list of past and current members of the ERNs LES WG (ERNs Working Group on Legal & Ethical issues & relations with Stakeholders) who contributed to this document

1) On the side of European Reference Networks (ERNs):	
ERN GENTURIS	ERN for Genetic Tumour Risk Syndromes
Nicoline Hoogerbrugge	ERN Coordinator, chair of the WG until Sept. 2018, before merge with ERN BoMS industry WG
Lisette Giepmans	
Joan Brunet Vidal	
ERN RITA	ERN for Rare Immunodeficiency, Auto-inflammatory and Auto-Immune Diseases
Nico Wulffraat	ERN Coordinator, co-chair of the WG since Sept. 2019
MetabERN	ERN on Rare Metabolic Disorders
Maurizio Scarpa	ERN Coordinator, co-chair of the WG, Oct. 2018-Sept. 2019
Viktor Kozich	
Christina Lampe	
ERN-EYE	ERN for Rare Eye Diseases
Hélène Dollfus	ERN Coordinator
ERN ITHACA	ERN for Rare Congenital Malformations and Rare Intellectual Disability
Jill Clayton-Smith	First ERN Coordinator
VASCERN	ERN for Rare Multisystemic Vascular Diseases
Romain Alderweireldt	
Bruno Fonteyn	
2) On the side of the ERN Board of Member States (ERN BoMS):	
Finland	
co-chair of the WG	Helena Kääriänen
France	Anne-Sophie Lapointe
	Jérôme Weinbach

Ireland	Eileen Treacy
Italy	Lucia Guidotti
Spain	Laura Chamorro Gonzalez
	Inés Palanca
	Carmen Perez
	Laura Marin
United Kingdom	Monika Preuss
3) On the side of the European Commission, DG SANTE, Unit B3, ERN team:	
Hélène Le Borgne Anna Mirandola	Supporting this WG from May 2018 to Dec. 2019 Supporting this WG from Jan 2020 until now (May 2020)
Adam Day	Blue-Book Trainee (Oct. 2019 – Feb. 2020)

Annex 2: criteria for "6. Good practice, outcome measures, and quality control" of the Assessment Manual developed for all ERNs (page 27 of the Manual)

6.GOOD PRACTICE, OUTCOME MEASURES, AND QUALITY CONTROL		
6 To fulfil the requirement set out in point (iii) of Article 12 (4) (a) of Directive 2011/24/EU ("offer a high level of expertise and have the capacity to produce good practice guidelines and to implement outcome measures and quality control"), the Network must:		
Criteria		
6.1 The Network offers specialised clinical expertise and produces good practice guidelines for rare or low prevalence complex diseases or conditions.		
Legislated Requirement	**No.**	**Measure(s)**
6 (a) exchange, gather and disseminate knowledge, evidence and expertise within and outside the Network, in particular on the different alternatives, therapeutic options and best practices with regard to the provision of services and the treatments available for each particular disease or condition;	6.1.1	The Network gathers, exchanges, and disseminates knowledge, best practice evidence, and clinical expertise within and outside of the Network.
	6.1.2	Representatives from each Member meet periodically to review and share best practices, and discuss new evidence-based treatments, therapies, and health care technologies.
Criteria		
6.2 The Network collaborates with its Members and other relevant partners to bring healthcare within its area of expertise closer to its patients.		
Legislated Requirement	**No.**	**Measure(s)**
6 (b) promote expertise and support healthcare providers in order to bring local, regional and national provision of healthcare closer to patients;	6.2.1	The Network shares expertise and supports healthcare providers in order to bring local, regional and national provision of care to patients closer to home.
Criteria		
6.3 The Network develops and/or implements clinical guidelines and cross border patient pathways.		
Legislated Requirement	**No.**	**Measure(s)**
6 (c) develop and implement clinical guidelines and cross-border patient pathways;	6.3.1	The Network has a formal process for developing or selecting and disseminating clinical guidelines.
	6.3.2	The Network adheres to ethical criteria, is transparent, and avoids any conflict of interest when developing and implementing clinical guidelines, patient pathways, and other clinical decision making tools.
	6.3.3	The Network develops cross border pathways in collaboration with its Members.
	6.3.4	The Network monitors implementation of established clinical guidelines and patient pathways to encourage consistent use across its Members and monitor their appropriateness. Information is used to make ongoing quality improvements.
Criteria		
6.4 The Network implements quality controls and monitors clinical outcome measures of care for rare or low prevalence complex diseases or conditions.		
Legislated Requirement	**No.**	**Measure(s)**
6 (d) design and implement outcome and performance indicators;	6.4.1	The Network develops and regularly monitors performance and outcome indicators. The information is used to support ongoing quality improvement.
6.(e) develop and maintain a quality, patient safety and evaluation framework.	6.4.2	The Network develops and maintains a quality, patient safety, and evaluation framework.