Working Group 2: Independence and Transparency

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Independence and transparency
Chair: Laura Yates
Code of Conduct
• Assess the need to supplement the Code of Conduct with additional tools to support good governance of pharmacoepidemiological research.
• Further elaborate some of the provisions already included in the Code of Conduct, e.g. by developing specific guidance, policies or sample/template contracts.
• Explore ways to better monitor implementation of the Code of Conduct for ENCePP Seal studies.
• Support the use of the Code of Conduct.
• Support registration of studies in the EU PAS Register.
EU PAS Register and ENCePP databases
• Support EMA in the further development of the EU PAS Register and ENCePP databases.
• Provide recommendations for business requirements to ENCePP Steering Group and EMA.

Code of Conduct version 4

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance

15 March 2018
EMA/929209/2011

The ENCePP Code of Conduct

For Scientific Independence and Transparency in the Conduct of Pharmacoepidemiological and Pharmacovigilance Studies

The ENCePP Code of Conduct was adopted on 7 May 2010 by the Steering Group of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). The terms of the Code of Conduct are reviewed by the ENCePP Steering Group periodically after its adoption.

Steps taken	Date
Adoption	7 May 2010
Revision 1	12 September 2010
Revision 2	21 November 2011
Revision 3	21 February 2014
Revision 3 editorial amendment	14 July 2016
Revision 4	15 March 2018

Main provisions of the Code of Conduct

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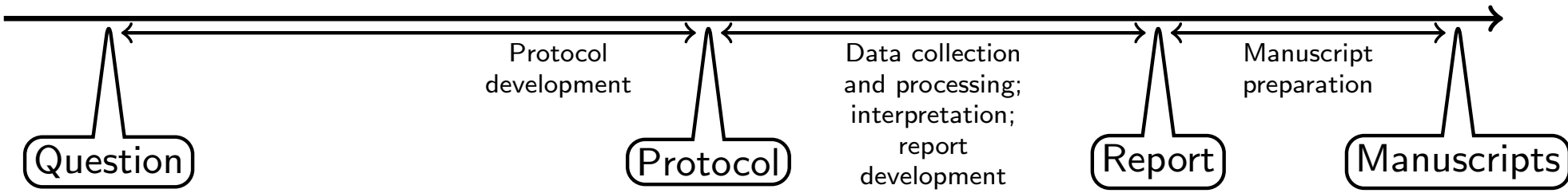

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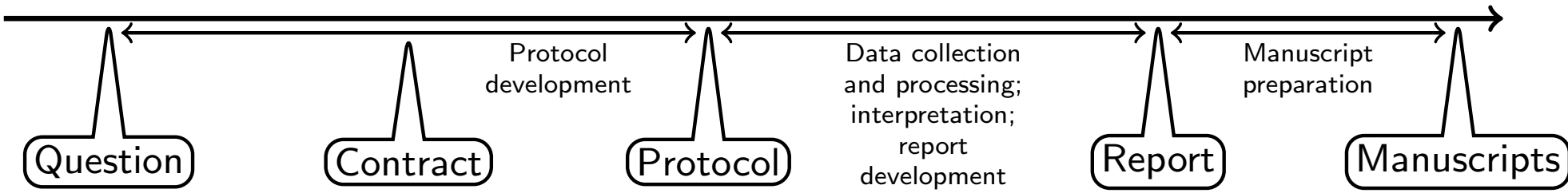

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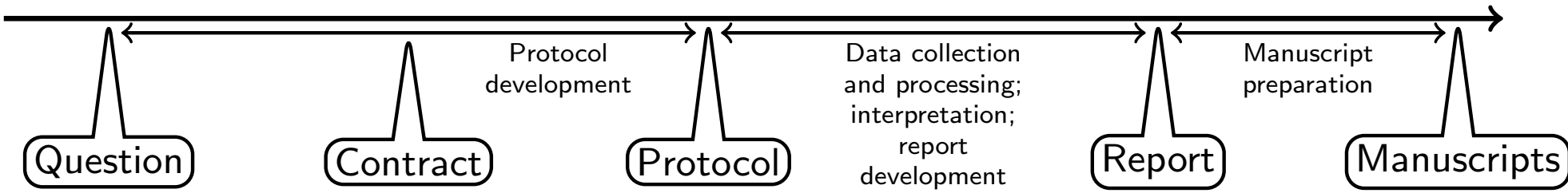

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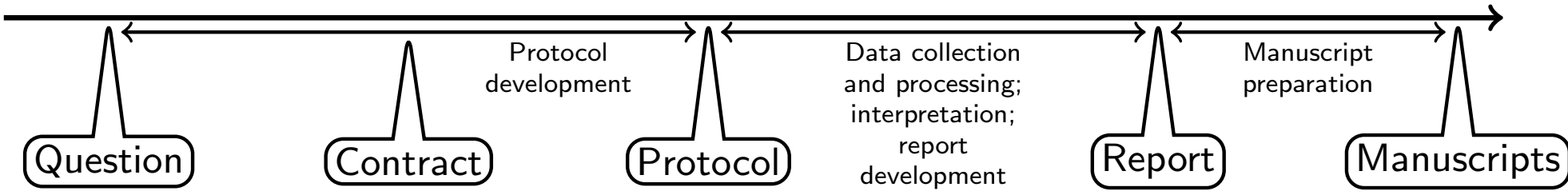

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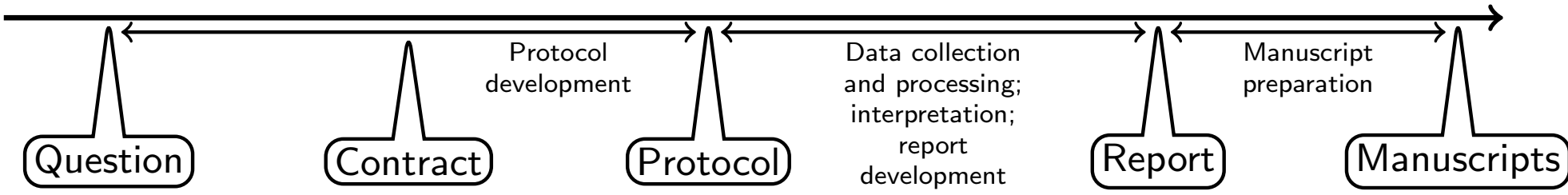

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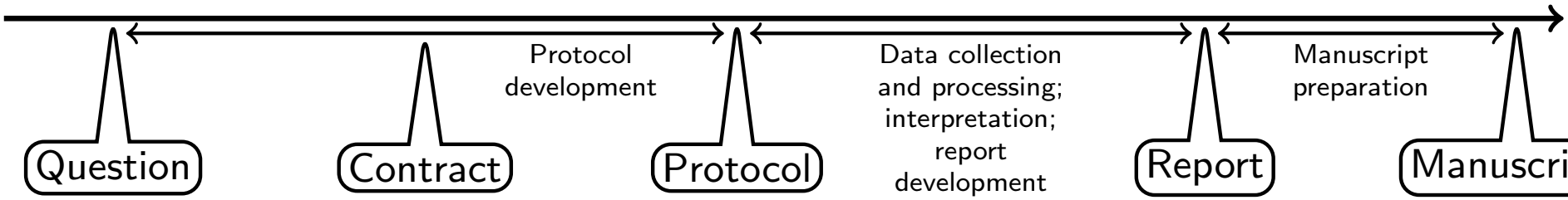

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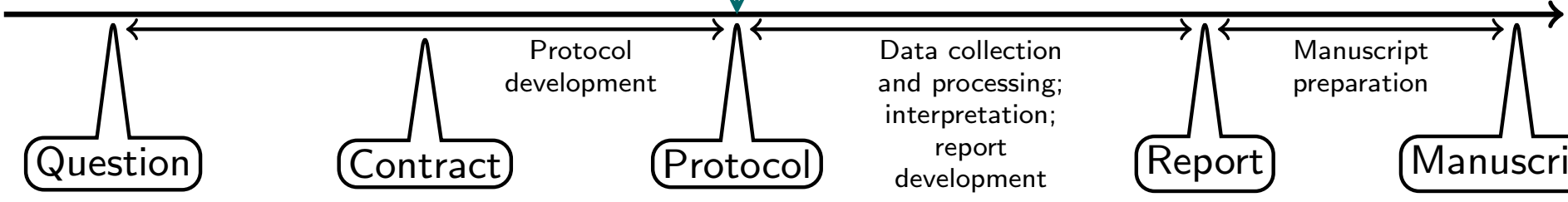

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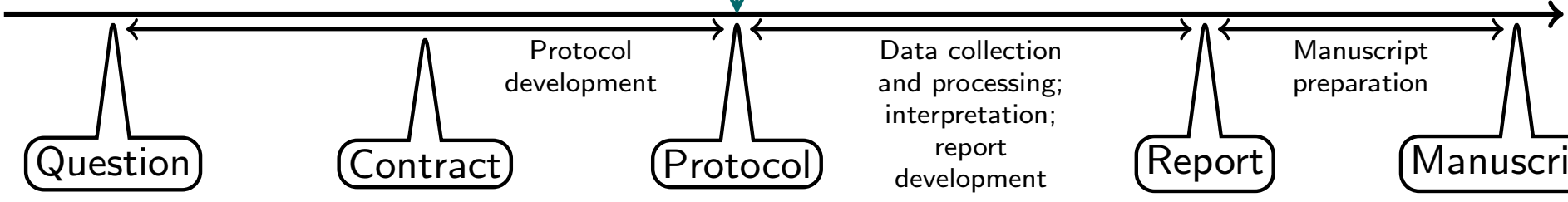

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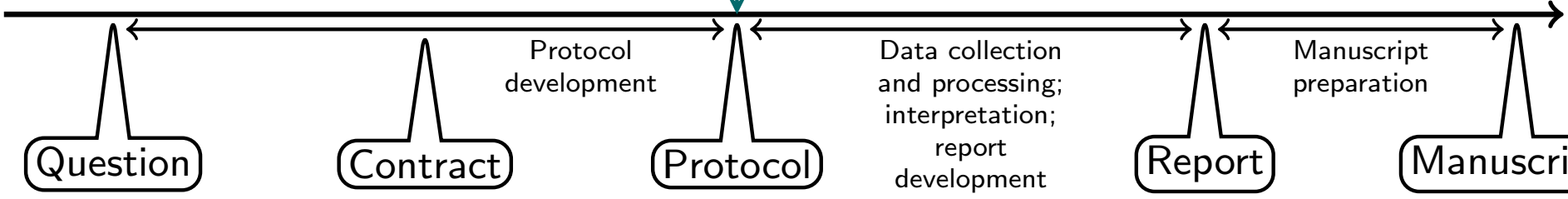
An abstract of the study findings (. . .) shall be provided through the EU PAS Register within three months following the final study report (. . .) If the final report is not published together with the abstract, the timelines for its publication should be specified in the abstract.



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Information on all parties involved in the writing and adoption of the protocol (. . .) shall be made publicly available in the abstract

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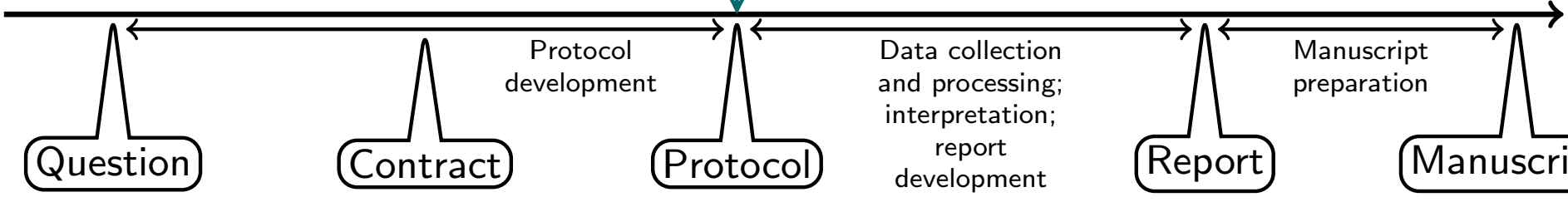

Classification of interests

Commercial
legitimate interest of an organisation selling a medicinal product involved in the study

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legitimate interest of an organisation in the costs of a medicinal product involved in the study, or whose corporate financial value can be impacted by the activity of selling/buying the medicinal product

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legitimate interest of an organisation with a responsibility for health policies (e.g. vaccination policies)

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Other legitimate interests (e.g. willingness to publish, or that universal healthcare services remain sustainable)

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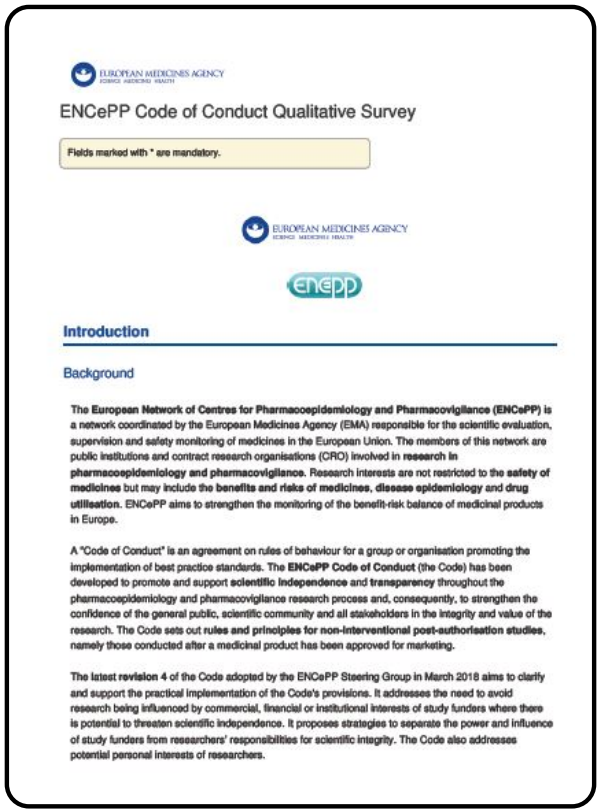
Survey on Code of Conduct



EUROPEAN MEDICINES AGENCY

ENCePP Code of Conduct Qualitative Survey

Fields marked with * are mandatory.

EUROPEAN MEDICINES AGENCY

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Introduction

Background

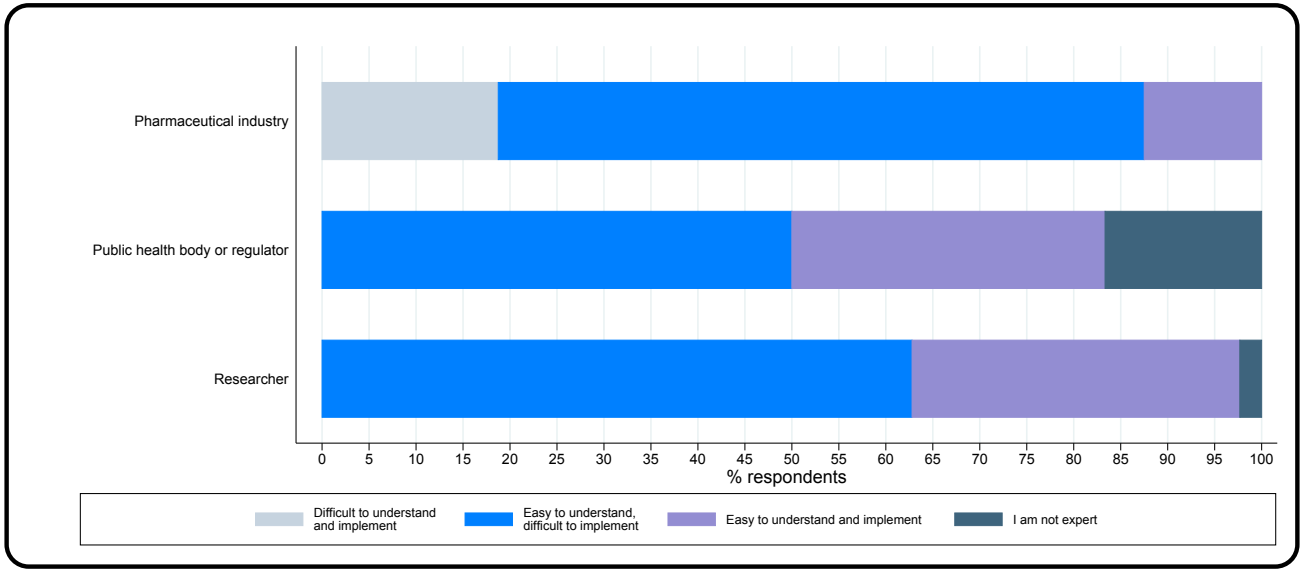
The **European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)** is a network coordinated by the European Medicines Agency (EMA) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the European Union. The members of this network are public institutions and contract research organisations (CRO) involved in **research in pharmacoepidemiology and pharmacovigilance.** Research interests are not restricted to the **safety of medicines** but may include the **benefits and risks of medicines, disease epidemiology** and **drug utilisation.** ENCePP aims to strengthen the monitoring of the benefit-risk balance of medicinal products in Europe.

A "Code of Conduct" is an agreement on rules of behaviour for a group or organisation promoting the implementation of best practice standards. The **ENCePP Code of Conduct** (the Code) has been developed to promote and support **scientific independence** and **transparency** throughout the pharmacoepidemiology and pharmacovigilance research process and, consequently, to strengthen the confidence of the general public, scientific community and all stakeholders in the integrity and value of the research. The Code sets out **rules and principles for non-interventional post-authorisation studies,** namely those conducted after a medicinal product has been approved for marketing.

The latest revision 4 of the Code adopted by the ENCePP Steering Group in March 2018 **aims** to clarify and support the practical implementation of the Code's provisions. It addresses the need to avoid research being influenced by commercial, financial or institutional interests of study funders where there is potential to threaten scientific independence. It proposes strategies to separate the power and influence of study funders from researchers' responsibilities for scientific integrity. The Code also addresses potential personal interests of researchers.

Survey on Code of Conduct

The principles and rules of the Code (as further explained in the summary of revision 4) seem to me



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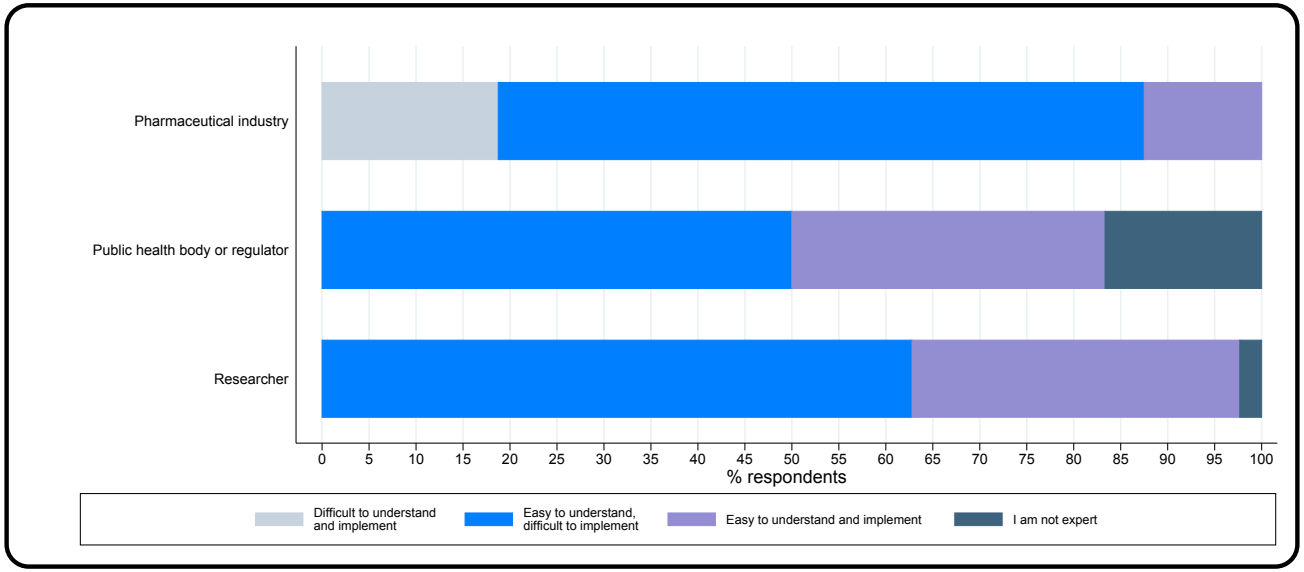
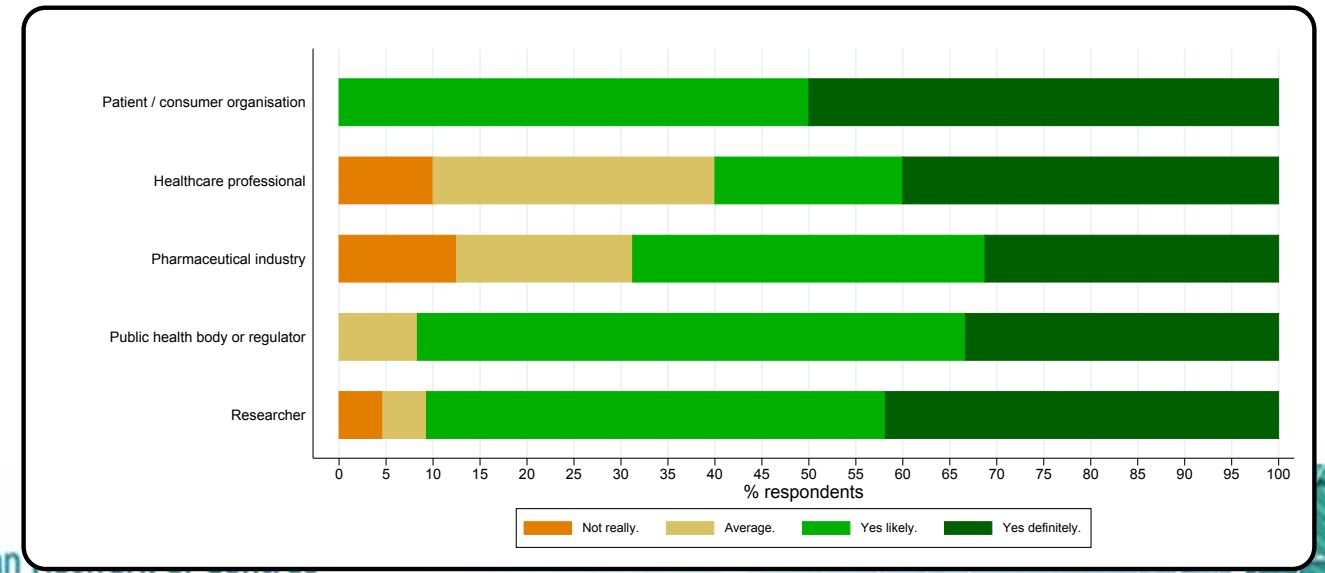


Studies applying the Code would reinforce my trust in the study results



Paper on Code of Conduct

Received: 15 January 2019 | Revised: 8 February 2019 | Accepted: 12 February 2019
DOI: 10.1002/pds.4763

REVIEW

WILEY

The ENCePP Code of Conduct: A best practise for scientific independence and transparency in noninterventional postauthorisation studies

Rosa Gini[1] | Xavier Fournie[2] | Helen Dolk[3] | Xavier Kurz[4] | Patrice Verpillat[5] | François Simondon[6] | Valerie Strassmann[7] | Kathi Apostolidis[8] | Thomas Goedecke[4]

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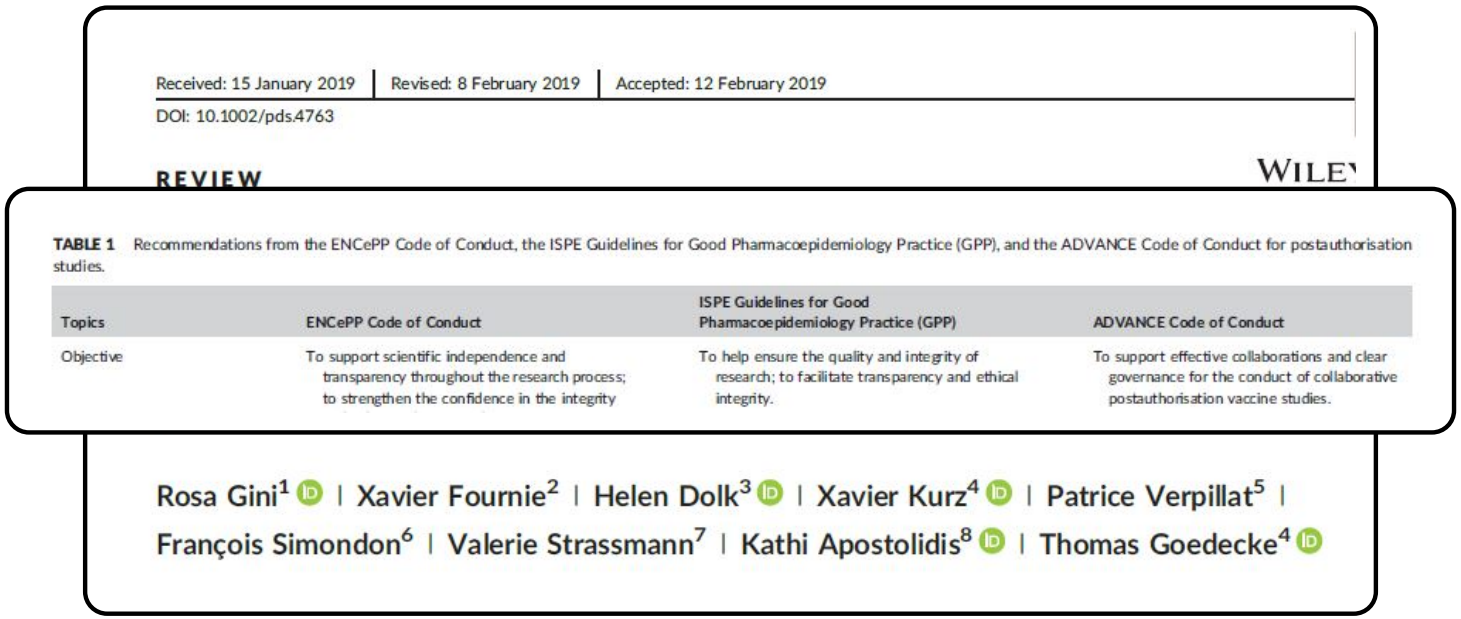

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Topics	ENCePP Code of Conduct	ISPE Guidelines for Good Pharmacoepidemiology Practice (GPP)	ADVANCE Code of Conduct
Objective	To support scientific independence and transparency throughout the research process; to strengthen the confidence in the integrity	To help ensure the quality and integrity of research; to facilitate transparency and ethical integrity.	To support effective collaborations and clear governance for the conduct of collaborative postauthorisation vaccine studies.

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Paper on Code of Conduct

3.2 | ENCePP stakeholders' perspective

The following section provides the perspective of the different stakeholder groups of ENCePP based on the individual experience of the co-authors: H.D. is a senior member of ENCePP Working Group 2 and one of the coauthors of the initial Code; X.F. is a member of the Board of the European CRO Federation; P.V. and K.A. are representatives of their respective stakeholder groups in the ENCePP Steering Group; V.S. is an appointed expert and former alternate member of the Pharmacovigilance Risk Assessment Committee (PRAC).

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4.1 | Limitations of the Code

The expression "commercial interest in an outcome of the study" is clarified in the Code to refer to the legitimate interest of those organisations marketing drugs. However, it may be perceived that research institutes that rely on funding from pharmaceutical companies to thrive (if public or private not-for-profit) or to pursue their legitimate profit (if for-profit), may be subject to indirect, possibly unwanted, influence from their funders. Even though compliance with the Code does protect researchers and funders from this risk within the realm of a single study, it cannot avoid a more subtle influence, because of a perception that funders may select the institution, which will conduct the next study based on the result of previous studies, instead of professional reputation. A related risk is that investigators and researchers may be tempted to interpret evidence of negative results as need for further research, with the objective of attracting new funding. In Europe, according to the current legislation, the funders for pharmacoepidemiology studies requested by regulators are mostly manufacturers themselves, which are therefore the most common funders for European research institutions in pharmacoepidemiology. This makes the risk of indirect influence higher than in the United States, where public funding is substantial. The ADVANCE project attempted to address the indirect influence of study funders, by producing guidance on the selection of research institutions. Three models of selection were proposed, in increasing order of perceived independence: led by the study funder, led by a selection committee, led by an external body.[25]

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4.2 | The way forward

The Code is perceived as useful but, at the same time, has to date been seen as potentially difficult to apply in practise. As discussed above, this is partly due to the inherent complexity of the relationships between study funders and investigators. It is hoped that the current major revision will help in clarifying and disseminating the provisions of the Code to support understanding of its advantages and promote its adoption. Examples of translation of principles of the Code into concrete actions should be made available that could also support training activities.[13] To reinforce trust in the actual application of the Code's provisions funders and investigators may decide to enter in the EU PAS Register together with the final study report, a final self-assessment of compliance with the Code, signed by all involved parties. Alternatively, an independent scientific committee overseeing the study conduct could also take the responsibility to review compliance with the Code. A periodic, independent review of a random sample of EU PAS Register records would also be useful. Finally, to address the limitations of the Code and building on previous work, ENCePP could develop specific guidance on the selection of research institutions.

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Conclusion