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## The ENCePP Code of Conduct

FOR SCIENTIFIC INDEPENDENCE AND TRANSPARENCY IN THE CONDUCT OF  
PHARMACOEPIDEMIOLOGICAL & PHARMACOVIGILANCE STUDIES

Draft for public Consultation

The ENCePP Code of Conduct was adopted on --/--/---- by the European Medicines Agency (EMA) and the participants of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCEPP). The terms of the Code of Conduct will be reviewed periodically after its adoption.

### Steps taken

<b>Key elements of the Code of Conduct</b> agreed by the ENCePP Working Group on <i>Independence and Transparency</i>	21 November 2008
<b>1<sup>st</sup> draft Code of Conduct</b> agreed by Drafting Group of the ENCePP Code of Conduct	8 May 2009
<b>2<sup>nd</sup> draft Code of Conduct</b> agreed by ENCePP Working Group on <i>Independence and Transparency</i>	17 June 2009
<b>Final draft Code of Conduct</b> approved by ENCePP Implementation Advisory Group	27 October 2009
<b>Public consultation</b>	16 November 2009 – 5 January 2010
<b>Adoption of the Code</b>	--/--/----

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## 53 1. Background

54 In recent years, the EMEA has concentrated on developing a more proactive approach to  
55 Pharmacovigilance as part of the European Risk Management Strategy<sup>1</sup>. ENCePP originates  
56 from the EMEA's endeavour to enhance the scientific and operational expertise and capacity  
57 in the fields of Pharmacoepidemiology and Pharmacovigilance across Europe and to improve  
58 pharmacoepidemiological research and post-authorisation safety surveillance of medicines  
59 by offering access to a robust network of resources.

60  
61 The ENCePP Code of Conduct, referred to subsequently as the "Code" has been primarily  
62 developed by the ENCePP Working Group on *Independence & Transparency* and has been  
63 subsequently adopted by the ENCePP Plenary.

## 64 2. Rationale and Scope

### 65 **Rationale**

66 The aim of the Code is to maximise Transparency and to promote scientific independence  
67 throughout the research process of Pharmacoepidemiology and Pharmacovigilance studies.  
68 By applying the principles of Transparency and scientific independence, the Code aims to  
69 strengthen the confidence of the general public, researchers and regulators in the integrity  
70 and value of Pharmacoepidemiology and Pharmacovigilance research. This is in line with the  
71 EMEA's undertaking to increase and uphold Transparency in the Agency's activities.

### 72 **Scope**

73 The Code of Conduct sets out rules and principles for Pharmacoepidemiology and  
74 Pharmacovigilance studies, with an emphasis on non-interventional Post-Authorisation  
75 Studies (see also definitions of Post-Authorisation Study and Non-interventional Study in  
76 Annex 1). This includes - but is not restricted to - active surveillance studies, registries, drug-  
77 utilisation studies, and any other type of observational research. However, the definition of  
78 Pharmacoepidemiology and Pharmacovigilance studies may also include Clinical Trials (see  
79 Annex 1).

80 The Code does not include rules or guidance on methodological aspects or scientific  
81 standards to be used for specific studies or study types. Adherence to the rules will not  
82 guarantee validity or integrity of study data. However, knowledge of these rules and a  
83 documented commitment of applying them to a study will help regulators and other  
84 stakeholders in the assessment of the reliability of study findings.

85  
86 The use of this Code is a requirement in order for a study to be presented as "ENCePP  
87 study" or to claim to be a "study performed in accordance with the ENCePP Code of Conduct  
88 for scientific independence and transparency" (see also Chapter 3 and 5 for further details).

### 89 **Main principles**

90 The Code has been conceived after consultation of both academic and commercial  
91 Investigators also taking into account regulatory requirements in Europe, and lays down rules  
92 and recommendations as regards:

- 93 - **scientific independence**, by ensuring best practice in the relationship between  
94 Investigators and Study Funders, including protocol agreement and publication of  
95 results;

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<sup>1</sup> The European Risk Management Strategy (ERMS) is a joint effort between the EMEA and the Heads of Medicines Agencies (HMA) started in July 2002 aiming at strengthening the safety-monitoring in the EU/EEA of medicinal products for human use. More information is available at <http://www.hma.eu/43.html>.

96 - and **Transparency** throughout the research process.

### 97 3. Implementation of the Code in the context of “ENCePP Studies”

98 Adherence to the Code is one of the prerequisites for studies to qualify for the title “ENCePP  
99 Study” (see also Chapter 5). In short, all Pharmacoepidemiological and Pharmacovigilance  
100 studies can qualify as an “ENCePP study” provided that the (Primary) Lead Investigator  
101 belongs to an entity that is included in the ENCePP Inventory of resources and that the  
102 “CoRe requirements” are met as detailed below.

#### 103 CoRe requirements

104

- 106 • Code of Conduct: Signed declaration and checklist

- 107 • Methodological Research Standards: Signed checklist<sup>2</sup>

108 *The signed declaration and checklists and the Study Protocol must be provided to the ENCePP*  
109 *Secretariat before the study commences and will be made publicly available.*

- 110 • e-Register of Post-Authorisation Studies<sup>3</sup>

111 *The study needs to be included in the electronic ENCePP Register of Post-Authorisation Studies*  
112 *before it commences.*

### 114 4. Legal framework & approved guidelines

115 In addition to the rules and principles laid down in the ENCePP Code of Conduct, studies  
116 performed in line with the Code need to comply with relevant legislation, as applicable.  
117 Specifically, the Declaration of Helsinki<sup>4</sup> and the provisions on processing of personal data  
118 and the protection of privacy as outlined in of Directive 95/46/EC and Regulation 45/2001 of  
119 the European Parliament and of the Council need to be followed.

120

121 In case of interventional research, the Clinical Trials’ Directive (Directive 2001/20/EC)  
122 applies.

123

124 As Post-Authorisation Studies are carried out with authorised medicinal products, relevant  
125 European and national legislation applies. Specifically, Marketing Authorisation Holders will  
126 need to comply with Directive 2001/83/EC and Regulation (EC) No 726/2004 of the  
127 European Parliament and of the Council.

128

129 This Code should not be considered as a stand-alone document but should be read in  
130 conjunction to other relevant guidance. Notably, this Code takes into account the ISPE’s  
131 Guidelines for Good Pharmacoepidemiology Practices (ISPE GPP, Revision 2, 2007) and  
132 refers to relevant parts thereof, as appropriate. Other relevant guidance including Volume 9A  
133 of the Rules Governing Medicinal Products in the European Union - Pharmacovigilance for  
134 Medicinal Products for Human Use, the STROBE Statement (Guidelines for Reporting  
135 Observational Studies), the Guidelines for Good Clinical Practice (Commission Directive  
136 2005/28/EC) and the International Guidelines for Ethical Review of Epidemiological Studies  
137 of the Council for International Organizations of Medical Sciences (CIOMS) should be taken  
138 into account when conducting pharmacoepidemiological studies.

<sup>2</sup> The Checklist for Methodological Research Standards is currently released for public consultation at  
<http://www.encepp.eu>.

<sup>3</sup> The electronic ENCePP Register of Post-Authorisation Studies is currently under development.

<sup>4</sup> World Medical Association declaration of Helsinki (see also chapter 15)

## 139 **5. Application of the Code and Compliance**

140 Studies performed in accordance with the rules laid down in this document shall be eligible to  
141 be considered as “studies performed in accordance with the ENCePP Code of Conduct for  
142 scientific independence and transparency”. In publications, the section ‘conflicts of interests’  
143 should make reference to the Code. In addition, adherence to the Code is one of the  
144 prerequisites for studies to qualify for the title “ENCePP Study” (for details on the  
145 requirements of “ENCePP studies” see Chapter 3).

146  
147 The (Primary) Lead Investigator of the study must complete the checklist (Annex 2) and sign  
148 the declaration that he will comply with the provisions of the Code (Annex 3). Originals of the  
149 signed checklist and declaration together with a copy of the agreed full Study Protocol shall  
150 be provided to the ENCePP Secretariat, who will archive them for no less than five years  
151 after the termination of the study, check the documentation for completeness and confirm the  
152 *a priori* eligibility of the study to be considered as “study performed in accordance with the  
153 ENCePP Code of Conduct for scientific independence and transparency”. The declaration,  
154 the checklist and the Study Protocol will be made publicly available on the ENCePP  
155 webpage.

156  
157 At the same time, the (Primary) Lead Investigator should ensure that the funding contract  
158 makes appropriate reference to the Code. By signing the funding contract the Funder  
159 commits to abide by the rules of the Code (see also Chapter 8).

160  
161 Investigators and Funders who, for a particular study, make use of the claim “ENCePP  
162 Study” or “studies performed in accordance with the ENCePP Code of Conduct for scientific  
163 independence and transparency” commit to adhere to the rules of this Code throughout the  
164 research process including the publication of the research results.

### 165 ***Withdrawal and Breach***

166 In case the (Primary) Lead Investigator decides to deviate and/or no longer follow the rules of  
167 the Code, he should inform the ENCePP Secretariat without delay. The ENCePP Secretariat  
168 may subsequently request the (Primary) Lead Investigator to cease using the title “ENCePP  
169 Study” or making reference to the study as “study performed in accordance with the ENCePP  
170 Code of Conduct for scientific independence and transparency”. If the ENCePP Secretariat is  
171 not informed before the implementation of such a decision, the deviation from the provisions  
172 of the Code may be considered as a breach of the declaration (Annex 3).

173  
174 In the event of a breach of the declaration, the concerned study shall be deprived of the title  
175 “ENCePP study” or “study performed in accordance with the ENCePP Code of Conduct for  
176 scientific independence and transparency”.

177  
178 In case of either a voluntary withdrawal or a deprivation for breach, the ENCePP Secretariat  
179 may identify the respective studies in the annual reports and on the ENCePP website.

## 180 **6. General Provisions**

181 ENCePP Studies should comply with the highest possible standards for independent and  
182 transparent research. By agreeing to follow the Code, Investigators and Study Funders  
183 commit to adhere to the following general principles:

- 184  
185
- 186 ▪ The primary purpose of a study shall be to generate data of potential scientific or public  
health importance and not to promote the sale of a medicinal product;
  - 187 ▪ The design of the research shall not be aimed towards producing a pre-specified result;

- 188     ▪ A contract shall be concluded between the Investigator and the Funder clearly defining  
189     the assignment and addressing in sufficient detail critical areas of their interaction,  
190     remuneration, protocol agreement, analysis of results and publication of results;
- 191     ▪ Remuneration shall only be granted as specified in the contract and shall not depend on  
192     the study results;
- 193     ▪ The results of a study shall always be published or made available to public scrutiny  
194     within an acceptable time frame, regardless of the (positive or negative) results and the  
195     statistical significance;
- 196     ▪ Relevant information on the research contract, process and results as specified in this  
197     Code shall be publicly available.

## 198     **7. Ensuring Transparency**

199     A maximum level of Transparency with regard to any information pertaining to the research  
200     process - including the disclosure of the Study Protocol and any revisions thereof - and the  
201     publication of study findings should be ensured. Open access to this information should be  
202     provided to regulators, health care professionals and the scientific community, as well as,  
203     patients and the general public.

204     The following means to ensure transparent research are addressed by the Code:

- 205
- 206     • Registration of the study in the ENCePP Register of Post-Authorisation Studies prior  
207     to the study start, and thereby making publicly available information on the study  
208     including the Study Protocol, the expected timelines and the results on study  
209     completion;
  - 210     • Accurate and detailed documentation of all steps throughout the research process,  
211     especially any changes to/deviations from the original Study Protocol and the  
212     justification thereof;
  - 213     • Agreement to make available on request any information including the content of the  
214     funding contract, reports from independent reviewers, non-identifiable study data, all  
215     interim and final study findings irrespective of positive or negative results; this  
216     includes the publication of the results aiming at the highest possible level of scrutiny;
  - 217     • State in advance and in publications the affiliations of the Investigators and any  
218     potential Conflicts of Interest.

## 219     **8. Funding Contract**

220     The contractual arrangement between the (Primary) Lead Investigator or the Coordinating  
221     Study Entity and the Funder should be signed in a legally binding manner prior to the first  
222     step in the research process subject to the assignment.

223

224     The funding contract shall specifically refer to the ENCePP Code of Conduct and shall  
225     include the statement “The parties to this agreement and individuals acting on their behalf  
226     hereby commit to adhere to the rules of the ENCePP Code of Conduct in their entirety”. The  
227     relevant version of the Code at the time of the signature of the funding contract should be  
228     annexed to the contract for reference.

229

230     The following aspects should be addressed in the funding contract:

- 231     ▪ The main objectives and a brief description of the intended methods of the research  
232     which is subject to the contract. The name of the study and a clear assignment of  
233     tasks and responsibilities should be stated.

- 234       ▪ The amount of the financial support and the payment scheme.
- 235       ▪ Ownership of and access to the data produced during the study. The provisions on
- 236       data ownership addressed in Chapter 11 shall apply.
- 237       ▪ A communication strategy for the interim and final results should be included. Plans
- 238       for publication should be stated. The contract should provide for the rights and
- 239       obligations as detailed in Chapters 9 and 13.
- 240

241 In case of complaints from Third Parties questioning the compliance of a particular ENCePP

242 Study or a study claiming to be a “study performed in accordance with the ENCePP Code of

243 Conduct for scientific independence and transparency” with the provisions of this Code, the

244 ENCePP Secretariat may request to see the funding contract to verify it is not in breach of

245 the Code.

## 246 **9. Rights & Obligations of the Investigator and the Study Funder**

247 The (Primary) Lead Investigator shall be responsible for the content of the assigned research

248 project including the design of the protocol, the conduct of the study, the analysis and

249 interpretation of the study results and the preparation and publication of the study outcome.

250 All those contributing to the development of the Study Protocol and their roles in doing so

251 should be specified in the Study Protocol. Any Conflict of Interest among the Investigators

252 should be declared and be made publicly available. The (Primary) Lead Investigator shall

253 keep the Funder informed about the study progress in terms of recruitment, where relevant,

254 and data collection, any modification of the protocol and the reasons for it, but should not

255 communicate preliminary results. The final study results and interpretations of the findings in

256 advance of publication could be provided for comment within a time limit specified in the

257 contract.

258

259 Detailed provisions on the reporting and publication of the study results can be found in

260 Chapter 13.

### 261 **Registration of Studies**

262 The (Primary) Lead Investigator on behalf of the Coordinating Study Entity undertakes to

263 register the study before it commences in the electronic ENCePP Register of Post-

264 Authorisation Studies<sup>5</sup>. Information on the study including the Study Protocol and information

265 on the researchers, the (Primary) Lead Investigator and the team of Investigators if

266 applicable, their affiliations, the Coordinating Study Entity and all research institutes and

267 study sites involved as well as the Funder, will be made publicly available through the

268 ENCePP webpage.

269 The Register should be regularly updated as appropriate.

## 270 **10. Development of the Study Protocol**

271 The protocol shall be developed before the study commences by individuals with appropriate

272 scientific background and experience. The funding contract should refer to a clear protocol

273 taking into account the elements of the *Checklist of Methodological Research Standards*

274 (also see Chapter 4). Any amendments or updates from study start need to be duly justified

275 and should be documented in a traceable and auditable way. Changes for reasons such as

276 marketing and/or advertising strategies shall not be acceptable.

277

278 The protocol must be designed to ensure scientifically valid and sound results are generated

279 independently from any potential conflicting interest of the Funder or the researcher. To

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<sup>5</sup> The electronic ENCePP Register of Post-Authorisation Studies is currently under development.

280 achieve this aim, the protocol needs to pre-define certain information before the study starts  
281 as outlined in the *Checklist of Methodological Research Standards* including a timetable for  
282 the study progress and completion of the study describing milestones (e.g. interim reports)  
283 and deadlines.

284  
285 Any deviation from the initial protocol should be duly justified and documented including the  
286 date of the change. Particularly, any changes after the start of data collection, especially after  
287 the first results have become available, shall be identifiable and reported as such in  
288 publications and the ENCePP Register of Post-Authorisation Studies and this should be  
289 considered for the purpose of the interpretation of the findings. This includes objectives or  
290 endpoints added or amended after the study start that are based on (initial) findings.

### 291 **Protocol Agreement**

292 The funding contract between (Primary) Lead Investigator or Coordinating Study Entity and  
293 the Study Funder shall specify the negotiation procedure to achieve agreement on the Study  
294 Protocol. If the development of the Protocol is part of the assignment, the Investigator shall  
295 write the Protocol within the remits of the assignment. Involvement of the Funder in the  
296 design of the protocol is permitted but any involvement shall be specified in the contract and  
297 information on the degree of the Funder's involvement shall be made publicly available  
298 together with information on all parties involved in the writing and adoption of the Protocol.  
299

300 Irrespective of the origin of the Study Protocol, the (Primary) Lead Investigator shall have  
301 final responsibility for its content. It is recommended to subject the Protocol to an impartial  
302 peer-review before its final adoption.

### 303 **Availability of the Study Protocol**

304 The full Study Protocol<sup>6</sup> shall be made publicly available through the ENCePP Register of  
305 Post-Authorisation Studies. In case of amendments to the Protocol, the former version or the  
306 information on the concerned elements should be replaced without delay by the new  
307 version/information including the date of the amendment and a summary of the main  
308 changes should be provided.

## 309 **11. Data Ownership and Access to Data**

310 The (Primary) Lead Investigator and Study Funder shall agree on data ownership in the  
311 funding contract (see Chapter 7). Intellectual ownership by the parties directly involved in the  
312 planning and conduct of the study as well as the analysis and interpretation of the study data  
313 should be taken into account and should be provided for in the contract. As regards the  
314 relation between data ownership and publication of results please refer to Chapter 13.  
315

316 Both the Study Protocol and the funding contract should address rules for access to raw  
317 data, processed data and final results generated under the study. Any identifiable data  
318 should be maintained under secure conditions in line with data protection legislation (see  
319 also Chapter 4).  
320

321 The (Primary) Lead Investigator should ensure that all data collected and generated in a  
322 study are recorded in an accurate way that allows access e.g. for the purpose of verifying the  
323 published results at all times whilst ensuring personal data protection.

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<sup>6</sup> For the purpose of the Code, a *full* Study Protocol is a version of the Protocol which includes enough detail in order to answer all questions in the Checklist of Methodological Standards (also see Chapter 4).



## 324 **12. Study Conduct**

325 Any step in the research process shall follow the agreed procedures laid down in the Study  
326 Protocol and shall be directed towards the generation of sound and valid findings. The  
327 Investigator shall be responsible for the conduct of the study within the remits of his  
328 assignment, including the data collection and analysis, the interpretation of the study results  
329 and the preparation and publication of the study outcome.

330  
331 All parties to be involved in the conduct of a study shall declare existing direct or indirect  
332 interests of a commercial, financial or personal nature. Any party with a financial interest in  
333 the results of a study should not actively participate in the conduct of the study except for  
334 providing expert advice on requests of the (Primary) Lead Investigator.

### 335 **Data Analysis**

336 A detailed statistical analysis plan shall be described in the Study Protocol. Any deviations  
337 from the analysis plan should be clearly documented and a reasonable scientific justification  
338 should be provided (also see chapter 10.).  
339

340 Outcomes resulting from changes to the analysis plan after data analysis has begun, e.g.  
341 formation of new sub-groups based on knowledge of (initial) study results may not be used  
342 for the purpose of verifying or rejecting a hypothesis of a causal association. In any case, all  
343 changes need to be documented and shall also be indicated in communications on the study  
344 results.  
345

### 346 **Study Steering Group**

347 If a steering group or a scientific oversight committee is foreseen for the purpose of providing  
348 scientific advice and guidance and/or to oversee the conduct of the study, the members of  
349 this steering group shall declare existing direct or indirect interests of a commercial, financial  
350 or personal nature and should only be appointed if no Conflict of Interest exists.  
351

352 Other parties and stakeholders including the Study Funder, if they have a Conflict of Interest,  
353 may only participate in meetings of the steering group as invited observers. Observers may  
354 be consulted by the members of the steering group on specific questions; however, any  
355 decision-making steps should take place in the absence of observers. The Study Funder  
356 may only be represented by a person with proven expertise and scientific knowledge in the  
357 area of the research.  
358

359 The composition of the steering group including observers participating in its meetings  
360 should be made publicly available.

## 361 **13. Publication/Reporting of Study Results**

362 A dissemination and communication strategy should be pre-defined as part of the funding  
363 contract. Any deviation should be duly justified.  
364

365 A clear summary of the main results of a study including results from pre-maturely terminated  
366 studies, whether positive or negative, should always be made available to the public  
367 according to the timetable agreed in the Study Protocol. In addition, an abstract of the study  
368 findings shall be provided to the ENCePP Secretariat for publication on the ENCePP  
369 webpage within 3 months after the final study report. The (Primary) Lead Investigator may  
370 ask the ENCePP Secretariat to delay the publication of this abstract for a limited period  
371 based on ongoing response to peer-review comments.  
372

373 A full report of all results with a scientific or public health impact must be made publicly  
374 available without unjustified delay. In case of a (suspected) public health impact, relevant  
375 legal provisions shall be followed and the respective regulatory authority(ies) shall be  
376 informed forthwith and in advance of publication.

377  
378 The outcome of a study shall always be presented in an objective and truthful manner  
379 providing a comprehensive and accurate description of the findings. In no way shall the  
380 interpretation and presentation of the results be aimed towards any commercial, financial or  
381 personal interests. As for the content of the report(s), it is recommended to follow the ISPE  
382 GPP and the STROBE statement.

383  
384 If necessary, the published results shall be updated, e.g. in case of re-analyses or additional  
385 analyses, including an explanation for the update. Presentations to a limited audience at  
386 meetings will not suffice as the only or main means of communication.

387  
388 The (Primary) Lead Investigator should have the right to independently prepare publications  
389 of the study results irrespective of data ownership (see also Chapter 11). The Study Funder  
390 shall be entitled to view the final results prior to the publication and to comment on the results  
391 and interpretations of the findings in advance of publication within a reasonable time limit,  
392 e.g. one month, as agreed in the funding contract and without unjustifiably delaying the  
393 publication. Requests that interpretation of the results or their presentation be changed must  
394 be based on sound scientific reasons. The Investigator is free not to take the comments of  
395 the Funder into account and the Funder may only require that the presentation of the results  
396 be changed to delete Confidential Information (see also Chapter 14). Any comments of the  
397 Funder should be made publicly available.

398  
399 In line with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by  
400 the International Committee of Medical Journal Editors (2009), the authors of the study  
401 should be those individuals who have made substantial intellectual contributions to the  
402 research. As is usually demanded by respected peer-reviewed journals, information on the  
403 actual role of all authors and the Study Funder should be provided. In addition, affiliations  
404 and Conflicts of Interest should be disclosed. The responsible author shall accept  
405 responsibility for the overall conduct of the study and the accuracy and integrity of the data  
406 presented (even if medical writers have been involved) as well as for any conclusions drawn  
407 from the data.

#### 408 **Scientific Review**

409 The study results and any publications and/or communications thereof should be peer-  
410 reviewed by independent experts regardless of whether a steering group has been  
411 established.

412  
413 The report(s) of the reviewer(s) should be documented. If the reviewer(s) recommend(s)  
414 changes, the (Primary) Lead Investigator should either revise the results and publications  
415 thereof or provide a rationale why the original version should be retained. The reports and  
416 related information e.g. regarding the implementation of the reviewers' recommendations  
417 should be made available upon request.

### 418 **14. Confidentiality**

419 A maximum level of Transparency with respect to regulators and health care professionals  
420 as well as patients and the general public should be strived for regarding any information  
421 pertaining to the research process, including the disclosure of the Study Protocol, and any  
422 revisions thereof, and the publication of study findings.

423 As information which constitutes Confidential Information depends on the actual research  
424 topic as well as the nature and relationship of the parties who contribute to a study, the exact

425 definition should be agreed on a case-by-case basis but in any event in advance before the  
426 study commences, in the funding contract or a separate agreement between the relevant  
427 parties. In any event, any data produced during the study shall not be regarded as  
428 Confidential Information. To this end, it is recommended that Investigators and Funders enter  
429 into appropriate confidentiality agreements.

## 430 15. References

- 431  
432 **Checklist of Methodological Research Standards for ENCePP Studies**, currently a draft is released for public  
433 consultation at <http://encepp.eu>.
- 434 **Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good  
435 clinical practice as regards investigational medicinal products for human use, as well as the requirements  
436 for authorisation of the manufacturing or importation of such products** (Official Journal L 91, 9/4/2005 p.13-  
437 19 ), available at <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:091:0013:0019:en:PDF>.
- 438 **Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation  
439 of the laws, regulations and administrative provisions of the Member States relating to the  
440 implementation of good clinical practice in the conduct of clinical trials on medicinal products for human  
441 use** (Official Journal L 121, 1/5/2001 p. 34 - 44), available at  
442 [http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1\\_en.htm](http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm).
- 443  
444 **Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the  
445 Community code relating to medicinal products for human use** (Consolidated version: 30/12/2008), available  
446 at [http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1\\_en.htm](http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm).
- 447  
448 **Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of  
449 individuals with regard to the processing of personal data and on the free movement of such data**,  
450 available at [http://ec.europa.eu/justice\\_home/fsj/privacy/law/index\\_en.htm](http://ec.europa.eu/justice_home/fsj/privacy/law/index_en.htm).
- 451  
452 **Guidelines for Good Pharmacoepidemiology Practices (GPP)**, International Society for  
453 Pharmacoepidemiology, (Revision 2: April 2007), available at  
454 [https://www.pharmacoepi.org/resources/guidelines\\_08027.cfm](https://www.pharmacoepi.org/resources/guidelines_08027.cfm).
- 455  
456 **International Ethical Guidelines for Epidemiological Studies**, The Council for International Organizations of  
457 Medical Sciences (CIOMS), 2009, ISBN 92 9036 081 X, superseding the 1991 International Guidelines for Ethical  
458 Review of Epidemiological Studies which are available at  
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478 **Volume 9A of the rules governing medicinal products in the European Union: Guidelines on  
479 Pharmacovigilance for Medicinal Products for Human Use** (September 2008), available at  
480 [http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol9\\_en.htm](http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol9_en.htm).
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483 Human Subjects**, 1964, last amended 2008, available at  
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## 485 **Annex 1 (Definitions)**

### 486 **Definitions**

#### 487 **ENCePP Study**

488 Pharmacoepidemiological and Pharmacovigilance studies performed taking into account  
489 relevant methodological research standards as agreed by ENCePP and in line with the rules  
490 and requirements for the independent and transparent conduct of pharmacoepidemiological  
491 and Pharmacovigilance research laid down in the ENCePP Code of Conduct, and whose  
492 (Primary) Lead Investigator belongs to an entity that is included in the ENCePP Inventory of  
493 resources.

#### 494 **ENCePP Code of Conduct**

495 A set of rules and principles laying down the responsibilities and good practices to guide the  
496 interaction between research centres, pharmaceutical industry and regulators, as well as  
497 rules and principles for the conduct of pharmacoepidemiological and pharmacovigilance  
498 studies to be followed throughout the research process in order to maximise Transparency  
499 and scientific independence.

#### 500 **Post-Authorisation Study**

501 Any study conducted with an authorised medicinal product.

#### 502 **Non-interventional Study**

503 Based on Directive 2001/20/EC, in a non-interventional study the assignment of the patient  
504 to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within  
505 current practice and the prescription of the medicine is clearly separated from the decision to  
506 include the patient in the study. No additional diagnostic or monitoring procedures shall be  
507 applied to the patients and epidemiological methods shall be used for the analysis of  
508 collected data.

#### 509 **Study Protocol**

510 A document that describes the objective(s), design, methodology, statistical considerations  
511 and organisation of a study. The term protocol refers to the initial protocol, successive  
512 versions of the protocol and protocol amendments.

#### 513 **Lead Investigator**

514 A person with the scientific background and experience required for the conduct of a  
515 particular pharmacoepidemiological or Pharmacovigilance study. The Investigator is  
516 responsible for the conduct of a study at a study site.

#### 517 **Primary Lead Investigator**

518 If a study is conducted at several study sites by a team of Investigators, the (Primary) Lead  
519 Investigator is the Investigator who has overall responsibility for the study across all sites.

#### 520 **Coordinating Study Entity**

521 A legal person, company, institution or organisation which takes responsibility for the  
522 initiation and/or the management of a study. The Coordinating Study Entity can be a Contract  
523 or an Academic Research Organisation and can be identical with the Study Funder. The

524 (Primary) Lead Investigator is the person authorised to represent the Coordinating Study  
525 Entity.

526 **Study Funder**

527 A legal person who provides the financing for a study. The Funder can be the originator of  
528 the research question and is identical with the client in Contract Research.

529 **Contract Research**

530 Outsourced research, including either the complete research process or specific steps  
531 therein, such as the design of a protocol, data collection that is conducted by an independent  
532 contractor on behalf of a Funder.

533 **Pharmacoepidemiology**

534 The study of the utilisation and effects of drugs in large numbers of people. To accomplish  
535 this study, Pharmacoepidemiology borrows from both pharmacology and epidemiology.

536 **Pharmacovigilance**

537 The science and activities relating to the detection, assessment, understanding and  
538 prevention of adverse effects or any other possible drug-related problems.

539 **Clinical Trial**

540 Any investigation in human subjects intended to discover or verify the clinical,  
541 pharmacological and/or other pharmacodynamic effects of one or more investigational  
542 medicinal product(s), and/or to identify any adverse reactions to one or more investigational  
543 medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of  
544 one or more investigational medicinal product(s) with the object of ascertaining its (their)  
545 safety and/or efficacy.

546 **Transparency**

547 Transparency is based on openness, communication and disclosure of or making available  
548 information whilst respecting the protection of both personal data as well as commercially  
549 confidential information. Research may be labeled as (partly) transparent if some or all  
550 relevant aspects of the research are open in the sense of open access to information on the  
551 research process and data thereby facilitating an objective assessment of the quality and  
552 independence of the research and validity of the research results.

553 **Conflict of Interest**

554 In the context of this document, Conflicts of Interest include any direct or indirect interests of  
555 a commercial, financial or personal nature other than purely scientific motivation which might  
556 compromise the impartiality of the persons contributing to a study and may have an effect on  
557 relevant decisions including the choice of the study design, interpretation of data, and  
558 publication of results etc.

559 **Confidential Information**

560 Confidential Information means all information, facts, data and any other matters  
561 communicated between the Investigator(s), the Coordinating Study Entity and the Study  
562 Funder in the framework of the study undertaken which are clearly identified or marked as  
563 being confidential at the moment of their disclosure.

564  
565 For the purpose of this document, Confidential Information shall be understood as  
566 information which may not be disseminated without the direct or indirect approval of the  
567 owner of such information as agreed between the above mentioned parties. This especially

568 includes commercial or financial information other than information on the identity of the  
569 Study Funder or information related to patents or copyrights. Data derived from a study shall  
570 reasonably be treated confidentially only in relation to data privacy law.

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571 **Annex 2 (Checklist)**

572

573

574

575 **Checklist of the ENCePP Code of Conduct**

576 (To be developed once the Code has been finalised)

577

578 *The Checklist will capture the key elements of the Code and require applicants to respond to*

579 *questions regarding the compliance with the rules of the Code. All questions must be answered.*

580 *In certain cases it might also be necessary to provide supporting documents in support of the answers*

581 *given. The Checklist should be signed by the (Primary) Lead Investigator thereby declaring upon*

582 *honour the answers in relation to the company or organisation that he/she represents.*

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583 **Annex 3 (Declaration)**

584

585 **Declaration**

586

587 The (Primary) Lead Investigator and a person authorised to sign on behalf of the  
588 Coordinating Study Entity hereby declare for the purpose of conducting the study <include  
589 study name and identifier/registration no.>

590 - to follow the rules and principles for the independent and transparent conduct of  
591 pharmacoepidemiological and Pharmacovigilance research of the ENCePP Code of  
592 Conduct of --/--/---- <include revisions>;

593 - to inform the ENCePP Secretariat, without delay, of any change or decision to change  
594 which constitutes a deviation from the provisions of this Code.

595

596 It is of note that the (Primary) Lead Investigator and the person authorised to sign on behalf  
597 of the Coordinating Study Entity may be identical.

598

599

600 Name of (Primary) Lead Investigator :

601 \_\_\_\_\_

602 Date: xx/yy/yyyy

603 Stamp and signature:

604

605

606

607 Name of the Coordinating Study Entity:

608 \_\_\_\_\_

609 Address:

610 \_\_\_\_\_

611 \_\_\_\_\_

612

613 Name of person authorised to sign on behalf of the Coordinating Study Entity [if different  
614 from (Primary) Lead Investigator]:

615 \_\_\_\_\_

616 Date: xx/yy/yyyy

617 Stamp and signature:

618

619

620

621

622

623 **Mandatory supporting documentation to be provided in support of the above declaration:**

624

625 - **Identification of the (Primary) Lead Investigator**

626 - **Identification of the Coordinating Study Entity**

627 - **Identification of the Study Funder**

628



629 Of note, in order to comply with this obligation it might be sufficient to submit the Study Protocol provided that the  
630 above mentioned persons and entities are clearly identified.

631 Applicants are requested to note that supporting documents provided must relate to legal persons and/or natural  
632 persons including, where considered necessary by EMEA, directors or any person with powers of representation,  
633 decision-making or control in relation to the candidate.

634 If there is any doubt about the mandatory documentation required, it is strongly recommended that the ENCePP  
635 Secretariat is contacted for clarification since failure to provide the correct documents may lead to elimination  
636 from the procedure.

637 The (Primary) Lead Investigator should also sign and date the Checklist (Annex 2). EMEA is unable to accept  
638 electronic signatures and will not accept photocopies of the completed declaration.

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