EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 January 2016

Submission of comments on draft Scientific guidance on post-authorisation efficacy studies (EMA/PDCO/CAT/CMDh/PRAC/CHMP/261500/2015)

Comments from:

Name of organisation or individual
ACRO (Association of Clinical Research Organizations)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 110,000 employees engaged in research activities around the world (including 30,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 9,000 clinical trials involving nearly two million research participants in 142 countries. On average, each of our member companies works with more than 500 research sponsors annually. ACRO welcomes and supports the draft guidance. In particular, ACRO appreciates the flexibility that the guidance allows in choosing the most appropriate study design to achieve the scientific objectives of a proposed post-authorisation efficacy study (PAES), and the emphasis placed on incorporating measures to improve the quality of data and the validity of studies.	

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	Throughout the draft guidance document, the words “trial” or “trials” are used in the context of clinical studies that may or may not meet the definition of a clinical trial in Directive 2001/20/EC. To avoid confusion with regard to the regulatory status of different types of PAES, ACRO recommends that the terminology in the draft guidance is revised so that any reference to a “trial” or “trials” means a clinical trial as defined by the Directive, and the term “study” or “studies” is used in other cases. This approach is consistent with the definitions in the new Clinical Trial Regulation (EU) No, 536/2014.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
64 - 68		Comment: ACRO welcomes and supports the flexibility that allows for an imposed PAES to included additional investigational arms for other purposes (e.g., health technology assessment) provided this does not impact on study integrity and the primary objectives of the study. Proposed change (if any):	
69 - 72		Comment: In ACRO's view, this statement lacks clarity and may lead to confusion. ACRO recognises the distinction between a scientific guideline and a regulatory guideline but, as the current guidance will be issued by a regulatory agency (the EMA) and used by marketing authorisation holders and third parties for regulatory purposes, ACRO is of the opinion that the definition of terms used within the guideline should be consistent with that of the associated legislation and regulatory guidance. Proposed change (if any): Delete the sentence that states "Note, as this is a scientific guidance, terms such as randomised, non-randomised and observational are used without prejudice to the definitions pertaining to clinical trials that may be applied in European Union and national legislation, and related regulatory guidance."	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
79 - 81		Comment: ACRO welcomes and supports the flexibility that allows a PAES, when appropriate, to be of non-randomised design provided that measures are included to minimise limitations/biases. Proposed change (if any):	
112 - 118		Comment: ACRO welcomes and supports the flexibility that will allow for some elements of explanatory trial design to be made more pragmatic, when appropriate, without relaxing all of the design parameters associated with explanatory type trials. Proposed change (if any):	
199 - 215		Comment: ACRO agrees with the comment that using electronic routinely collected healthcare record databases to facilitate the conduct of clinical studies is relatively new and raises some challenges if the results of such studies are to be used to support regulatory decision making. This is not an issue that is specific to PAES and applies equally to PASS and, to some extent, to clinical trials regulated by Directive 2001/20/EC, where it may be possible to auto-populate some, if not all, electronic case record form data elements directly from electronic healthcare record databases. ACRO supports the recommendation in the present draft guideline for regulatory dialogue in such cases and, additionally, recommends the Agency to develop a guidance document of	

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		more general applicability that addresses the issues associated with the use of electronic healthcare record databases in clinical research studies. Proposed change (if any):	
216 - 217		Comment: ACRO recommends that the statement “The use of primary and secondary data collection sources for observational studies are well described elsewhere” is accompanied by relevant references. Proposed change (if any): Add the appropriate references.	
		ACRO thanks the EMA for the opportunity to submit comments on the “Draft Scientific Guidance on Post-Authorisation Efficacy Studies.” Please do not hesitate to contact us if we can provide additional information (knoonan@acrohealth.org or +1 202 464 9340).	

Please add more rows if needed.