29 August 2018

Submission of comments on Draft Guideline on the responsibilities of the sponsor with regard to handling and shipping of investigational medicinal products for human use in accordance with Good Clinical Practice and Good Manufacturing Practice (EMA/202679/2018)

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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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 130,000 employees engaged in research activities around the world (including 57,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 7,000 clinical trials involving 1.3 million research participants in over 100 countries. On average, each of our member companies works with more than 700 research sponsors annually. ACRO welcomes and supports the draft guideline on the responsibilities of the sponsor with regard to handling and shipping of investigational medicinal products (IMPs) for human use in accordance with Good Clinical Practice and Good Manufacturing Practice, which ACRO recognizes as addressing current best practice on this topic.	

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	However, ACRO notes that the title of the draft guideline shows that it is focused specifically on the responsibilities of the sponsor with regard to handling and shipping of IMPs. The experience of ACRO member companies is that investigational sites performing clinical trials, following receipt of an IMP from the sponsor, show considerable variability in their handling of IMPs. Consequently, ACRO recommends that either the scope and content of the current draft guideline are expanded to include site responsibilities for handling IMPs or a separate guideline is developed on this topic.	

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)*
Lines 28-30, 71		Comment: For clarity and completeness, ACRO recommends adding the following sentence at the end of this paragraph. Proposed change (if any): Add: “The term “sponsor” as used in this guideline also includes any third party to whom the sponsor has contracted relevant activities related to the handling and shipping of an IMP.” And remove “(or representative)” from line 71	
Line 35		Comment: The words “until after” in the first sentence of this paragraph is confusing, as IMP should stay under the sponsor responsibility until arrival at site. Proposed change (if any): Replace the sentence, “Investigational medicinal product should remain under control of the sponsor until after completion of the two-step procedure,…” with “Investigational medicinal product should only be shipped after completion of the two-step procedure,…”	
Line 58		Comment: The regulatory release by the sponsor is required before shipment of the IMP from the manufacturer. It would be helpful to include examples of the form the regulatory release can take, e.g. a shipping order.	

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)*
		Proposed change (if any): Add examples to clarify in what form the manufacturer, who is typically responsible for shipping the IMP to the clinical site, should receive notification from the sponsor of the regulatory release.	
Line 63		Comment: The statement “the applicable elements of guidelines on Good Distribution Practices” requires clarification. GDP guidelines are focused on the wholesale distribution of commercial medicinal products. IMPs are not typically distributed via wholesalers. Therefore, it is not clear what specific elements of the GDP guidance are expected for the distribution of IMPs. Consequently, it would be helpful for the proposed guideline to describe the “applicable elements” that apply to IMPs. Proposed change (if any): Describe the specific elements of the GDP guidance expected to be applied to the distribution of IMPs.	
Lines 70-72		Comment: As this sentence describes that the sponsor’s responsibility is until receipt & acceptance of the shipment at the clinical investigator site or pharmacy, it would be good to point out the any product complaint or product quality issues (such as temperature excursions at clinical investigator site or pharmacy, missing, partially missing or damaged IMP) should be processed by the sponsor, even after the IMP arrived at the clinical investigator site or pharmacy.	

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)*
		Proposed change (if any): Add sentence after above mentioned sentence: “Product quality issues, like product complaint and temperature excursions after arrival at the clinical investigator site or pharmacy should still be processed and investigated under the sponsor (or representative) responsibility.”	
Lines 75-76		Comment: Transfers of IMPs happen as well when a clinical investigator site or pharmacy moves to a different facility, but remains the same trial site for the clinical trials. Proposed change (if any): Change the sentence, “Such transfers should be covered by standard operating procedures.” to add the wording, “Such transfers, including the move of a clinical investigator site or pharmacy to a new facility, should be covered by standard operating procedures.”	
Line 79		Comment: For a transfer of IMP between sites in different countries, there’s a risk the batch might not have been certified by a QP for the country of arrival, hence needing the advice of the certifying QP in case it’s not. Proposed change (if any): Add “, especially when the country of arrival is different from the original trial site’s country.” at the end of the sentence “… and the advice of the certifying QP should be sought”	
Lines 79-81		Comment: The sentence “The product should be returned to the manufacturer, or another authorised manufacturer, for re-	

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)*
		labelling, if necessary, and certification by a QP" is confusing. The circumstances in which this would be considered necessary are not defined, and the statement does not appear to take account of the fact that transfer of IMP between investigational sites is usually undertaken only when there is an urgent need and, therefore, to avoid disrupting provision of IMP to trial subjects, there may not be sufficient time available to return the product to a manufacturer for relabelling. ACRO therefore recommends that the sentence is modified as follows. Proposed change (if any): Add "Where time permits," at the start of the sentence.	
Lines 81-82		Comment: As the aim of the guideline is to cover the handling of IMP under sponsor responsibility under GCP requirements (shipping and presence at clinical investigator site or pharmacy), there are 2 activities that can happen during IMP storage at site that are not covered: recall and relabelling at clinical investigator site or pharmacy. Proposal change (if any): add a paragraph covering the sponsor responsibilities for recalls and one for relabelling at clinical investigator site or pharmacy. Sponsor to provide at the start of a project process and guidelines to sites how to handle IP which underwent any deviations i.e. allowed temperatures threshold, timelines for QA evaluation, etc.	

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)*
		ACRO thanks the Agency for the opportunity to comment on this “Draft Guideline on the responsibilities of the sponsor with regard to handling and shipping of investigational medicinal products for human use in accordance with Good Clinical Practice and Good Manufacturing Practice (EMA/202679/2018).” Please contact ACRO (knoonan@acrohealth.org) if we can provide additional details or answer any questions.	