EUROPEAN MEDICINES AGENCY (EMA) CONSULTATION

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)

In August 2018, the UKCRC Registered CTU Network submitted the following comments on the draft guideline on behalf of its members.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31st August 2018

Submission of comments on '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
UKCRC Registered Clinical Trials Unit Network

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)*
	Thank you for the opportunity to comment on this document. We consider the guideline in general to be clear and concise. It is useful to have these requirements summarised in one document. UKCRC Registered Clinical Trials Units (CTUs) are academic CTUs conducting national and international clinical trials predominantly on behalf of non-commercial sponsors. Non-commercial sponsors are rarely the manufacturer of the IMP, and this has influenced the majority of our comments and suggestions.	

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)*
Line 35		Comment: '*under control of the Sponsor*' might imply that the Sponsor has physical custody and/or direct involvement in distribution of batches to sites, which is not usually the case in non-commercially sponsored (e.g. NHS/HEI-sponsored) CTIMPs. In addition, some marketed products used as IMPs are not supplied to the clinical investigator sites for a trial, and so would be already available to/under the control of the clinical investigator site. Proposed change (if any): "Where supplied to clinical investigator sites for a clinical trial, the i~~I~~nvestigational medicinal products should not be shipped to the sites or pharmacies ~~remain under the control of the sponsor~~ until after completion of the two-step procedure."	
Line 36-37		Comment: Clarification of the two-step procedure proposed, one being technical and one being regulatory. Proposed change (if any): ".. The two-step procedure consist~~s~~~~ing~~ of a technical release in the form of the batch certification by the Qualified Person (QP) and the regulatory release by the sponsor for use in a clinical	

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		trial."	
Lines 58 - 60		Comment: Please could this paragraph be adapted to allow for situations where a sponsor's regulatory release procedure includes shipment of IMP to clinical investigator sites prior to activation of the site in a trial. For example following a risk-based approach where the sponsor has a two-step approach to the regulatory release itself, firstly allowing for IMP release to the site (with appropriate mitigations e.g. the IMP would be quarantined at the site) and then followed by later full activation which allows the site to actively recruit. Proposed change (if any):	
Line 66-67		Comment: Please could the sentence: "*Records including timing to support the supply chain should be maintained*" be clarified. It is unclear what '*timing*' is referring to – for instance is it "intended and actual timelines" or "required timeframes" etc? Proposed change (if any):	
Lines 78-79		Comment: As written, the implication is that the QP should always be consulted in relation to site-to-site transfer of IMPs. We suggest there are situations where this is not required.	

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		Proposed change (if any): "..and the advice of the certifying QP should be sought if applicable."	
Lines 79-81		Comment: Clarification requested, as there may be situations where re-labelling could be undertaken at the trial site by appropriately trained personnel. Proposed change (if any):	
Lines 83-90		Comment: Some clarification would be helpful to explain the reference to '*written agreement*' in line 84 and '*technical agreement*' in line 90, and their complementary/alternative use/s. Proposed change (if any):	
Line 90		Comment: Clarification proposed to link previous sentence (line 88-90) with the list that follows. Proposed change (if any): "Examples of such areas for which responsibilities need to be defined include:"	

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Lines 91 - 117		Comment: If the proposed change above at line 90 is agreed, the wording of some of the items in the subsequent list may need to be adapted. The list could also be made more concise. Proposed change (if any): For example – line 91: • ~~Ensure that~~ re-labelling ~~responsibilities are defined~~ etc	
Lines 91 - 117		Comment: '*If applicable'* and '*where applicable'* are used a few times and as this is a list of 'examples' we suggest this is implicit. Otherwise, a suggestion is that '*where applicable'* is added once at start of the list. Proposed change (if any): At line 90 - "Examples of such areas for which responsibilities need to be defined, where applicable, include:"	
Lines 91 - 93		Comment: Suggest re-order list for clarity of processes, e.g. following order of events in a trial. Unclear why the first two items appear at the top of the list. Proposed change (if any): Suggest move bullet points at line 91 & 92 further down the list.	

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Line 92		Comment: Add commas (unless removing/changing '*where applicable'* as per earlier comment) Proposed change (if any): • Ensure that, where applicable, comparators are sourced from an authorized vendor and that arrangements for recall are in place.	
Line 109		Comment: Additional wording proposed to clarify nature of 'samples' and the information to be documented. Proposed change (if any): Define the conditions for storage and the period of required retention, for 'reference' and 'retention' ~~of~~ samples, where required.	
Line 109		Comment: This would not apply to clinical trials involving Advanced Therapies (ATIMPs), which may need to be retrospectively released by the QP. It would be helpful to include reference to this, or to have similar guidance for ATIMPs. Proposed change (if any):	

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Line 111		Comment: Regulatory release should always fall under Sponsor responsibility. What situations is this line intended to cover? Proposed change (if any):	
Line 111		Comment: Missing word. Proposed change (if any): "If applicable, clarify with the manufacturer responsibility for the regulatory release."	
Line 116		Comment: We would suggest it is not always necessary for a manufacturer to agree to a site-to-site transfer as the requirement often occurs due to an emergency situation and therefore any potential delays need to be avoided. Wording clarification proposed below. Proposed change (if any): "Define ~~T~~the process ~~of~~ for authorisation and management of transfer~~ring~~ of IMPs from one investigator site to another when applicable. ~~should also be addressed~~."	

Please add more rows if needed.