EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 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
The Alliance for Regenerative Medicine (ARM) is the preeminent global advocate for regenerative and advanced therapies. ARM fosters research, development, investment and commercialization of transformational treatments and cures for patients worldwide. By leveraging the expertise of its membership, ARM empowers multiple stakeholders to promote legislative, regulatory and public understanding of, and support for, this expanding field. ARM convenes all stakeholders with an interest in regenerative and advanced therapies to provide a unified voice for our 300+ member organizations, including companies – especially small- to medium-sized enterprises (SMEs); academic/research institutions; non-profit organizations; patients, and other members of the advanced therapies community. Our aim is to connect all parts of the innovation lifecycle to address the unmet needs of patients, particularly through supporting commercialization objectives via legislative and policy frameworks that enable next generation therapies to reach those who need them. To learn more about ARM, visit http://www.alliancerm.org. Transparency register number ID: 244710319190-73

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)*
	ARM welcomes the opportunity to comment this draft guideline. This response is based on ARM members experience in handling and shipping investigational medicinal products which are Advanced Therapy Medicinal Products (ATMPs). Some of the comments may more specifically relate to ATMPs but other, more general, comments are also included for your consideration.	
	<u>ATMP complexity should be addressed:</u> It would be helpful to clarify whether this guideline is also applicable to ATiMPs and if so, to consider adding some specific considerations applicable to them. ATMPs are complex products that often involve manufacturing steps at the clinical site and remote release. Specific aspects that should be considered include the following: - ATiMPs may need to be shipped to a cell laboratory rather than to the pharmacy prior to use by investigators. - ATiMPS may need to fulfill GMO requirements and be granted authorization by the relevant EU national GMO authorities.	
	<u>Consistency with other ATMP specific guidelines</u> : Consistency of the newly proposed guideline with the	

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	existing guideline on Good Manufacturing Practices for ATMPs guideline and the new guideline on Good Clinical Practices for ATMPs should to be ensured and the text adapted, where relevant.	

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 32-34		Comment: ATMPs such as gene therapies consist of or contain Genetically Modified Organisms (GMOs). In such case, a clinical trial in the EU can only start after an authorisation has been granted by the relevant GMO competent authorities in addition to the clinical trial authorisation by health authorities in the EU Member States.	
Lines 43-44		Comment: Regulatory release of IMP often occurs at different time points for individual sites rather than by country, so it is suggested to revise for either option Proposed change: It should be noted that regulatory release of the IMP can be given for individual sites/~~some~~ countries at ~~one~~ different time points.~~, and for others at a later stage.~~	
Lines 45-46		Comment: Further clarification of the two-step release procedure would be welcomed. Batch certification by QP is well supported by other regulatory documents, such as Annex 1, section 8. However, the regulatory release lacks concise language and is open to possible misinterpretation, e.g. whether regulatory release is confirmed at trial initiation, or every time a batch is	

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)*
		released to a site. The current Annex 13 clarifies that IMPs should remain "under control of a sponsor until after completion of a two-step procedure: certification by the Qualified Person; and release by the sponsor for use in a clinical trial following fulfillment of the requirements of Article 9 (Commencement of a clinical trial) of Directive 2001/20/EC." This clarifies that the regulatory release is for the commencement of a clinical trial. [Note: Regulation 536/2014 does not include this clarification]. Proposed change: The regulatory release by the sponsor ~~will also~~ needs to verify at commencement of the study that any aspects required for compliance with the Regulation are in place before IMPs are shipped to the clinical investigator sites.	
Lines 47-51		Comment: It would be useful to provide a checklist of the minimum requirements needed for regulatory release for any study, and then provide examples of other requirements that may be needed dependent on the study. The point on authorisation subject to conditions may cause confusion as many conditions of clinical trial approvals are quality based and would be considered under QP release. ARM suggests to delete it from here. Clinical conditions within clinical trial approvals often relate to required changes to protocol/ICF, etc. so it is	

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)*
		suggested to stipulate there is an approved protocol/ICF as part of the mandatory checks required for regulatory release. Proposed change: Checks required for regulatory release include: - Regulatory agency approval - IRB/EC approval - Approved protocol - Approved ICF - Contracts with investigators and applicable service providers ~~These~~ Additional checks may be required ~~will vary~~ depending on the trial, but may cover for example: ~~• Contracts with investigators and applicable service providers.~~ ~~• If the authorisation of the clinical trial is subject to conditions, that these conditions are met.~~ ~~• Any local/national approvals.~~ • Where applicable, de-coding arrangements are in place.	
Line 59		Comment: Situations where an ATiMP needs to be sent to a cell laboratory rather than the pharmacy before use by the investigator should be considered and addressed in the text.	
Lines 62-64		Comment: The requirement to ensure shipping minimises risk whilst	

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)*
		ensuring quality doesn't indicate how this could be achieved. It is suggested to add an example that this could be by qualification, leveraging vendor documentation. Proposed change: It should be ensured, e.g. through qualification, that the shipping of the IMPs minimises any risk while ensuring that the quality of the product is maintained and the applicable elements of guidelines on Good Distribution Practice (GDP) of medicinal products for human use are taken into consideration.	
Line 65		Comment: Situations where an ATiMP needs to be sent to a cell laboratory rather than the pharmacy before use by the investigator should be considered and addressed in the text.	

Please add more rows if needed.