Submission of comments on Targeted stakeholder consultation on the draft Guidelines on Good Clinical Practice for Advanced Therapy Medicinal Products

Comments from:

Name of organisation or individual
NHS ATMP Working Party (subgroup of the NHS Pharmaceutical QA Committee)

Please find attached comments prepared and consolidated by the above group which represents all hospitals NHS participating in the delivery of ATMP clinical trials (both non-commercial and commercial Clinical Trials).

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General Comments

The national group above welcome this document and the clarification that it provides for this novel group of medicinal products. As these in many cases have been innovated via academia and are manufactured often in small to medium enterprise manufacturers or by non-commercial manufacturers, the above named groups would recommend that it is made explicitly clear that the role of pharmacy in an ATMP trial site is to:

- Facilitate an organisational feasibility assessment to incorporate appropriate local organisational governance requirements for ATIMPs (many sites will appropriately require more than routine Research and Development Committee approvals in view of the novel nature of the products)
- Provide oversight of the IMP whilst acknowledging that optimal storage and handling may not involve pharmacy staff and facilities directly.
- Approve local receipt, storage, preparation, issue and accountability arrangements for the ATIMP and ensure compliance with handling instructions / pharmacy manual.
- Ensure that the pharmacy trial file is appropriate, even where this is being operationally delivered by expert colleagues other than pharmacy e.g. via stem cell laboratories

The ATMP Working Party believes that systems for ATMP trial delivery and patients benefit if Pharmacy is integral in the delivery of ATMP clinical trials and that this should be made clear in the document.

Specific Comments

Line	Comment
121	"Unreasonable" requires further definition. The regulator should be the arbitrator.
134 – 136	This may require further detail as grant funding usually requires trials to be 'powered' statistically.
144 – 147	Agree. Pharmacy should play a key role in ensuring that traceability and accountability systems are optimal.
154	It would be better to state that release specification should be defined and justified in the IMPD and to identify whether a simplified IMPD would ever be acceptable.
162-164	The dose should be related to the product specification, otherwise the trial data will not be robust.
172	A section on Preparation/Reconstitution is required which should reference the requirement for a pharmacy manual. It can reference the GMP for ATMP definition of reconstitution and acknowledge that pharmacy oversight will be acceptable if the operationally optimal staff are not from pharmacy.
185	… with **Pharmacy** clinical …
186	to ensure appropriate use of the recall procedure and serious breach procedures
199 – 200	Non Specification products which are released as unlicensed medicines should be mentioned also in relation to follow up requirements.
217	Consider the inclusion of / making reference to the EMA guidance on preclinical studies for gene therapy first in human trials.
247	Reconstitution arrangements should be referenced at line 172 under the "protocol " section.
249	"instructions" should read "pharmacy manual / handling instructions"
253 - 254	Addition of: Decisions regarding the optimal location and staff for complex reconstitution of these medicines should involve pharmacy. Where an annex 13 compliant label is required to be applied after reconstitution activity- clarification regarding the applicability of the requirement for pharmacist supervision should be included (Reg 37 exemption).
264	Pharmacy oversight of dosing is appropriate.
271	As at Line 186 – recall and serious breach procedures should be referenced.
284	The addition of a requirement to document local storage and handling arrangements in a technical agreement is recommended as sites may need to make arrangements

with departments who are not used to handling IMP.

287 Receipt should be by a pharmacy or pharmacy risk assessed location.

290 Trained pharmacy or trained pharmacy approved staff should make this confirmation.

304 Where administration is complex and novel the clinicians may appreciate a sponsor representative to be present.

313 “Investigator” should read “site” as receipt should be by a pharmacy or pharmacy approved location.

315 Pharmacy Clinical Trials staff should oversee accountability arrangements.

364 The benefits of a registry should be emphasised. It would be better to state that a justification for exclusion of a registry is required as it is the routine expectation.

409 “Investigator is received” – This needs corresponding entries at Line 199 and Line 154. Pharmacy governance is required as the product will be an unlicensed medicine, not IMP. Patient is withdrawn from the trial and the investigator’s organisation has responsibility rather than the sponsor.

413 It should be emphasised that any out of specification administration is not eligible to be included in the study data and that as it is actually the administration of an unlicensed medicine, that any local governance required should be undertaken.

437 Clarify reporting requirements for out of specification ATIMPs which are administered as unlicensed medicines.