Line(s)	Current text	Comments/Proposed text
78-79	"(*e.g.* regarding retention of samples)"	(*e.g.* regarding retention of samples of ATMPs to reconfirm specifications)
121-122	"The risk posed by the procedure should be duly explained in the protocol."	The risk posed by the procedure should be duly explained in the protocol and informed consent.
167-172	*(iii) Upstream interventions on subjects*: In an autologous setting, the subject must undergo a medical intervention to extract cells/tissues prior to the manufacture and administration of the product. The process of taking biopsies/extracting cells may entail risks to the subject and may also have an impact on the quality and safety of the product. Therefore, it is important that such processes are clearly explained The level of documentation should be adapted to the complexity and the novelty of the procedure.	We feel that this section should either include the allogeneic setting or the guidance needs to make clear that the donation would not be considered part of the trial process in this setting. *(iii) Upstream interventions on subjects and/or donors*: In an autologous or allogeneic setting, The subject and/or donor must undergo a medical intervention to extract cells/tissues prior to the manufacture and administration of the product. The process of taking biopsies/extracting cells may entail risks to the subject and/or donor and may also have an impact on the quality and safety of the product. Therefore, it is important that such processes are clearly explained in the protocol and informed consent. The level of documentation should be adapted to the complexity and the novelty of the procedure.
193		*PROPOSED NEW SECTION* Although other guidance (e.g. CT-1) mentions that arrangements for care following trial participation should be included in the protocol this is often not present or lacks sufficient detail for adequate preparation. Consideration for continued access is of particular relevance for ATMP trials as the treatment options for the patients are likely to be more limited and the national pathways to provide such treatment are likely to be more complex. (viii) Treatment of subjects after end of trial: A description of the arrangements for the provision of care of the subjects once their participation in the trial has ended should be described in the protocol and informed consent. Continued access to trial treatment needs to considered, particularly when: • It is reasonable to expect that it will be possible to give the ATMP safely after the trial;

		• It is reasonable to expect a clinically important benefit; • The intervention is not otherwise available; and • Treatment options are limited. Reference: CARE AFTER RESEARCH: A FRAMEWORK FOR NHS RECs https://www.hra.nhs.uk/documents/321/hra-care-after-research.pdf
240-254	(iii) *Reconstitution*	We suggest this is moved from section 3.2 'Specific considerations regarding the Investigator's Brochure (IB)' to section 3.1. 'Specific considerations concerning the protocol'.
255-260	(iv) *Administration procedure*	We suggest this is moved from section 3.2 'Specific considerations regarding the Investigator's Brochure (IB)' to section 3.1. 'Specific considerations concerning the protocol'.
305-307	"If the presence of the administration is envisaged before the start of the clinical trial, this should be explained in the informed consent."	If the presence of the Sponsor (or representative thereof) during the administration is envisaged before the start of the clinical trial, this should be explained in the informed consent.
312-314	"The individual product should be traceable from delivery to the investigator up to the administration to the clinical trial subject."	The individual product should be traceable from sourcing up to the administration to the clinical trial subject. Based on MHRA grey guide A.3.1 that states "The ATIMP must be traceable from sourcing through to administration to the subject" ref. Section 4 (1) of SI 2010/1882.
334	"7. Retention of samples"	7. Retention of samples of ATMPs
351-353	"Subjects that participate in a clinical trial with ATMPs should receive adequate information on the risk of the product, including risk of treatment failure and effects of the treatment on future therapies typical for the diagnosis or treatment of the disease."	Subjects that participate in a clinical trial with ATMPs should receive adequate information on the risk of the product and trial processes, including risk to offspring and close contacts, risk of treatment failure and effects of the treatment on future therapies typical for the diagnosis or treatment of the disease.
379-383	"In accordance with applicable requirements, the sponsor should ensure that approval of a clinical trial protocol is obtained in the country where the long term follow-up takes place. In EU/EEA such follow-up of a clinical trial in a different Member State /EEA country compared to where the	Is this still required if the original investigating site is performing the follow up remotely via phone call/access to medical records?

	treatment was given requires an application for an additional Member State concerned to be added."	
409-411	"him/her" "his/her"	them or the investigator their or the investigator's We strongly suggest the use of gender neutral pronouns to aid gender inclusivity.
414-436	Safety Reporting	Can this section please include the reporting expectations for events/issues that are related to ATMP application, lack of efficacy or required concomitant medication? If one of these was serious, related and unexpected would this be considered a SUSAR?