MANCHESTER 1824
The University of Manchester

31 October 2018

TSC 01/2018 on GCP for ATMPs

Please find attached feedback on behalf of the University of Manchester, UK, as a stakeholder to the Consultation Document Good Clinical Practice for Advanced Therapy Medicinal Products - https://ec.europa.eu/health/human-use/consultations/2018_gcp_atmp_en.

We look forward to the European Commission finalising the Guidelines on Good Clinical Practice specific to Advanced Therapy Medicinal Products in light of the feedback received from the stakeholders in this consultation.

Regards,

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http://www.staffnet.manchester.ac.uk/services/rbess/governance/clinicaltrials/

2. (i) on staggering trials for paediatric populations and providing evidence of efficacy in adults where feasible	Disagree. For most gene therapy and cell therapy applications the genetic disease affects mainly children, and children of younger ages often benefit more from treatments as they have been treated earlier in disease progression. If safety is not a significant concern – ie where an ATMP is no longer first in class and has a suitable safety record in at least one or two diseases – I feel this section should be disregarded in favour of treating the population that is most likely to benefit the most from the treatment – be the 3 months old or 15 years old.
2 (v)	The requirement for dose escalation studies should be limited to first in class products or where there is a specific concern over the potential toxicity of the delivered product from the preclinical work package. I have seen several current examples of trials where patients are being dosed with increasing doses of AAV9 (that already has a significant safety record), using genes that are very unlikely to have high dose effects (with no evidence of this in the preclinical package). Those on the low doses are not receiving clinical benefit as a result. Given that in some cases they could have been on a different clinical trial – this is an unethical approach in my opinion. Companies tend to follow guidance of this kind to the letter rather than adapting to the needs of patients and arguing the case.
2(vii)	(Cohort size number suitable to meet study objectives) is very hard to meet in the orphan disease space where most of these ATMPs fall.
3.1 (viii)	Is a 15 year follow up too onerous on small SMEs? Previously this was 10 years.
4 – section 4 – quality of the ATMP	Largely in agreement with the points made here but isn't about time that we addressed the issues of the fact that QC requirements for ATMPs are not fit for purpose and should be redefined to be a) less onerous, and b) more relevant – eg pH measurement. – this can be somewhat irrelevant for a live product.