OxfordBioMedica

25th September 2016

To: SANTE-D5-ADVANCED-THERAPIES@ec.europa.eu

Dear Sir / Madam

REF: European Commission's Public Consultation Paper on Good Manufacturing Practice for Advanced Therapy Medicinal Products persuant to Article 5 of Regulation 1394/2007 (DEADLINE: 25 SEPT 2016)

We are writing to you in our capacities as senior representatives of ATMP Manufacturing and ATMP Quality at Oxford BioMedica (UK) Ltd, and hereby provide our feedback on the proposed changes to the way GMP will be applied within the EU specifically for Advanced Therapy Medicinal Products (ATMPs). By way of reference, Oxford BioMedica is a gene and cell therapy company based in Oxford, UK, that has been actively developing and pioneering ATMPs and platform technologies to support ATMPs for the past 20 years. In this time, Oxford BioMedica has accumulated through its own internal product programs and in close collaboration with multiple large pharma partners (e.g. Novartis, Sanofi), an in-depth understanding, knowledge and experience in ATMP product lifecycle development from R&D to First In Man clinical trials up to preparing ATMP commercial license applications with partners to treat diseases with either limited or no alternative treatment options.

The following paragraphs outline significant concerns we have, should the proposed changes be implemented.

It is our opinion that the consultation document fails to clearly indicate that it is the EC's intention for a stand-alone guidance for GMP, which would be independent from the existing guidance in EudraLex Volume 4. It is our opinion that such an approach to set aside the ATMPs as somehow different in terms of the way GMP should be applied to other types of medicinal products (or IMPs) is unwarranted and could lead to a number of significant issues. All other sectors in the manufacture of medicines obtain guidance from Volume 4, either directly through Parts I, II and III, or through specific guidance provided in Annexes to the Volume. It is our firm opinion that applying the same approach for ATMPs would be preferable, thereby ensuring that the wealth of relevant and directly applicable guidance already available for GMP would be applied in a consistent manner by all ATMP developers. As a consequence of the stand-alone nature currently presented in the consultation document, it is our opinion that the proposed approach provides inadequate guidance for all stages of ATMP manufacture and at all scales of production, and lacks critical details including but not limited to qualification, clean room set up and operation, aseptic manufacture, change control etc. An alternative approach, wherein ATMP-specific guidance could be managed by an ATMP-specific Annex to the established GMP regulations and guidances would, in our opinion, more clearly facilitate direct and important reference to existing GMP regulations and guidances and thereby facilitate the development of novel and potent ATMPs whist maintaining a consistent approach to GMP wherever possible. It is also our view that independent guidances for non-ATMPs (i.e. all other types of medicine in development) and ATMPs will cause operational and regulatory problems and contradictions for the sector which would make it extremely challenging for; i) a licensed site to comply with both approaches simultaneously, ii) sites and developers to tackle complex and unwarranted licensing challenges (in that it would lead specific subsets of GMP certificates and MIA or MIA (IMP) licences).

In addition to the fundamental concerns we have in relation to the intended stand-alone nature of the ATMP guidance as proposed, in order to illustrate the disadvantages in the intended approach, and to provide examples of unclear regulations or guidance that would result from the proposed changes to ATMP regulation, we list below a number of key cross-references to existing Annex 13 GMP that are omitted as the document is currently drafted (*please note that this is not intended to be an exhaustive list, merely a means of illustrating the point we are trying to make in this letter*):

- Guidance related to ensuring that the entire supply chain is documented and available to the QP
- All audits of sites involved in the manufacture and testing for the product have been carried out and that the audit reports are available to the QP prior to certification
- Sites of manufacture and testing are compliant with the terms of the MA (or CTA) for the intended territory

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- All manufacturing testing activities are compliant with the terms of the MA (or CTA) for the intended territory
- Active substances have been manufactured and distributed in compliance with GMP and GDP for active substances (Eudralex Vol 4 Part II)
- Manufacturing and testing remain in a validated state and that personnel are trained and qualified
- All ongoing complaints investigations or recalls do not negate the conditions for certification of the batch in question
- Technical agreements are in place

It is our opinion that the aforementioned inadequacies of the draft guidance, and in particular the proposed approach to manage GMP for ATMPs 'differently' to other medicines in development, would inevitably lead to poor quality ATMPs, hinder or prevent life changing medicines getting to patients and potentially risk both patient health and the reputation of what is currently a rapidly growing sector. We ask that the EC reconsiders its approach to GMP for the ATMP sector to be much more closely aligned with all other sectors of pharmaceutical development and production, through the maintenance of a single standard for GMP. This should be achieved by providing any ATMP-specific guidance where necessary within an annex to EudraLex Volume 4.

Yours faithfully,

James Miskin PhD
Chief Technical Officer

Matthew Ryan
Head of Quality & Qualified Person (QP)