Below are comments on the proposed regulation:

- A two tier authorisation procedure does raise questions on suitability / effectiveness of the reviewers. If a national approach as opposed to a centralised approach was sought by the sponsoring manufacturer, the same level of skill and guidance available to a centralised approach would be expected on a national level for the HTEP review. If at the national level approval was given to market a HTEP, and this proposed regulation was used in reviewing and approving the HTEP, which would be expected if the regulation was adopted, then the national approval should have no reason to **not** be accepted throughout the European Union allowing the sponsor to market openly in the EU. Consistency in review and requirements is required.

- Regulation on Human Clinical Trials with HTEP's should be detailed in the regulation (similar to the Medical Device Directive) to avoid confusion in industry.

- It is important to have an Ombudsman set up (similar to FDA) to assist in classifying these more complex products, especially in view of this industry being relatively new and technology rapidly changing - this has a risk of making regulation inadequate / obsolete.

- Xenogenic material is used in the manufacture of some cell therapy products for example. It is common for there to be residual Xenogenic material in the final product which by definition essentially excludes some of these products from this proposed regulation according to section (b) of the scope. This should be reconsidered as the primary aim of such products may have nothing to do with the small percentage of residual Xenogenic material however having the residual would exclude the product from the proposed regulation. thought should go into the safety requirements of such Xenogenic materials when being used in the manufacturing process, rather than focusing on their elimination from final product in isolation.

- It is important to consider the manufacture of HTEP's outside of the EU and how this proposed regulation will handle such products. If for example a sponsor from Australia wanted to market a HTEP in the EU and have it manufactured in Australia, how would this scenario fit into the regulation proposed?

- It would be useful to have a set of GMP's that are specific to HTEP's developed as opposed to defaulting to pharmaceutical GMP's. Other countries, for example, have successfully done this previously such as the Therapeutic Goods Administration who developed a code of GMP's for Human Blood and Tissue in 2002, which despite its relevance being questioned at the moment with the changes in technology, was a huge step forward for industry and provided great guidance on the key idiosyncrasies of HTEP's as opposed to classic pharma products.

- I believe that Grandfathering is important at this stage. However if the HTEP was only accepted in some member states then this may create difficulties. Maybe grandfathering is reasonable for states where the HTEP is already on

the market, but if sponsors are seeking additional markets then either the centralised approach or the member state approach would be required.

- Thr regulation needs to detail review times. For example if a sponsor puts in an application for a new HTEP it is reasonable to expect that a review time of 90 days. Industry needs to have some indication of time when bringing products to market.

Hope these comments are useful. Thanks for allowing us the opportunity to comment.

Regards,

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