COMMENTS FOR THE EUROPEAN COMMISSION WEBSITE

Comments from Professor Robert A Brown University College London (UCL) and European Tissue Engineering Society, on proposed harmonised regulatory framework for human tissue engineering products: Stakeholders Consultation.

RAB Background:

I. Director UCL Tissue Repair and Engineering Centre.
II. Director of British Tissue Engineering Network.
III. Secretary UK Tissue and Cell Engineering Society [retiring]
IV. Secretary European Tissue Engineering Society.
V. Director London Tissue Bioreactor Consortium.

COMMENTS:

1. There seems to be a serious anomaly with xenogeneic devices with respect to the use of non-cellular materials as opposed to viable cells in such devices. Numerous xenogeneic proteins, polysaccharides etc., [i.e. cell products] are used in tissue engineering devices including serum, collagen, protein inhibitors (aprotinin). Many such devices need not contain cells at all.

Suggest that reference to xenogeneic elements is restricted to viable cells only. This will circumvent many of the complications.

2. Considerable amount of discussion focused on the operation of tissue engineering products for local use in local hospitals. My experience is that this will be a disappearing issue. Those hospitals in the UK, which do carry out autologous cell culture, have to raise local laboratory and personal standards to good practice, at considerable cost. The result is a tendency for such activities to serve larger and larger communities (normally complete regions) and many are becoming neo-business enterprises. It seems likely that this sector will evolve into preparation businesses or pseudo-companies with wide catchments, which will be suitable to regulate in a conventional manner.
3. It is recommended that a definition based on “substantial modification” to give “altered physiology” will prove difficult to sustain as both of these elements are subject to subjective interpretation.
4. This stakeholder strongly suggests that a solution to the long discussion around autologous allogeneic applications lies in a small shift in logic and nomenclature. The quantitative difference between the risk of single cell donation and the use of pooled cells from multiple donors was clearly not understood by many of those present.. The risk from a single donation of cells to a single recipient clearly needs to be regulated BUT involves only the single recipient (with its limited downstream infective consequences). On the other hand the risk from pooled cell preparations (i.e., to many recipients) represents one of **population** infection with exponentially greater risks for loss of control to the wider community. This difference is well understood in the blood products field. Consequently, it is the terms allogeneic and autologous

which are misleading. If these are replaced by single donor and pooled donor cell sources then these terms could be used much more effectively to distinguish between different regulation procedures. The system is then more logical, links more closely to the real risk (quantifiable) and ceases to have the emotive connotations seen in the discussion.

5. On the basis of this distinction (4) it would be logical to make the regulation criteria and follow up requirements simpler and less demanding for single donation cell pooled donor products. This may or may not imply local or central regulation.

I hope that these positive suggestions provide a way forward and a route to simpler regulation with maximum flexibility focused onto the most pressing risk area.