When considering whether biological material that has undergone processing has been substantially manipulated, it is useful to consider the purpose of the processing and how it affects the original biological material. Some examples are as follows :

A tissue sample is plated to allow its constituent cells to undergo culture-expansion, resulting in a new generation of cells, and the creation of a cell line.	This would be considered substantial manipulation. The resulting culture-expanded cells and new cell lines would not be considered human tissue.
A tissue sample is subjected to a biological or chemical agent, resulting in the cells being genetically modified and/or irreversibly altered at the cellular level (e.g. immunolabelling, formalin-fixed paraffin-embedded tissue, tissue maintained in animal serum).	This would be considered substantial manipulation. The modified/altered cells would not be considered human tissue.
A tissue sample is subjected to enzymatic treatment to dissociate cell-cell contact and release the cells from the extracellular matrix.	This would be considered substantial manipulation. The cell suspension would not be considered human tissue.
A tissue sample is subjected to a buffer or chemical agent, to break open the cells and recover the subcellular components (e.g. tissue lysate, DNA, RNA, proteins, metabolites, organelles)	This would be considered substantial manipulation. The subcellular components would not be considered human tissue.
A tissue sample is subjected to high heat and fluid rinse, to destroy the constituent cells and recover the decellularised extracellular matrix.	This would be considered substantial manipulation. The extracellular matrix would not be considered human tissue.
A tissue sample undergoes freezing/ cryopreservation, to help preserve and prolong the viability of the tissue in its original state.	This would not be considered substantial manipulation. The frozen sample would continue to be human tissue.
A tissue sample is cut into several roughly equal segments, to allow the sample to be distributed and used by several different researchers.	This would not be considered substantial manipulation. The cut samples would continue to be human tissue.