



Comparability for Regen-Med Products



When is comparability required

Minimally processed products. Eg: Bone-marrow transplants

Autologous processed products- Eg: ADSC

Allogenic Minimally processed products- eg: Cord Blood, Adult stem cell

Allogeneic large scale-
replacement of MCB
site to site manufacture
lot to lot manufacture
major change in manufacturing process
Change in cell line used



Historically FDA has addressed this by asking to demonstrate comparability

Actual clinical studies- eg Bone Marrow

In vivo preclinical studies. Eg: AAstrom

Historical data eg; Cord blood

In vitro data

- Comparability of MCB


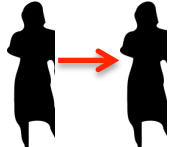
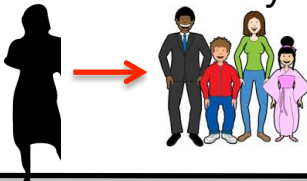
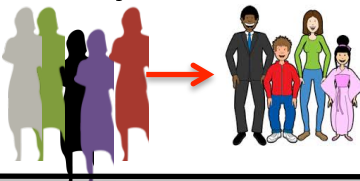
- Matching release criteria



What we are asking is for clarity and proposed comparability criteria

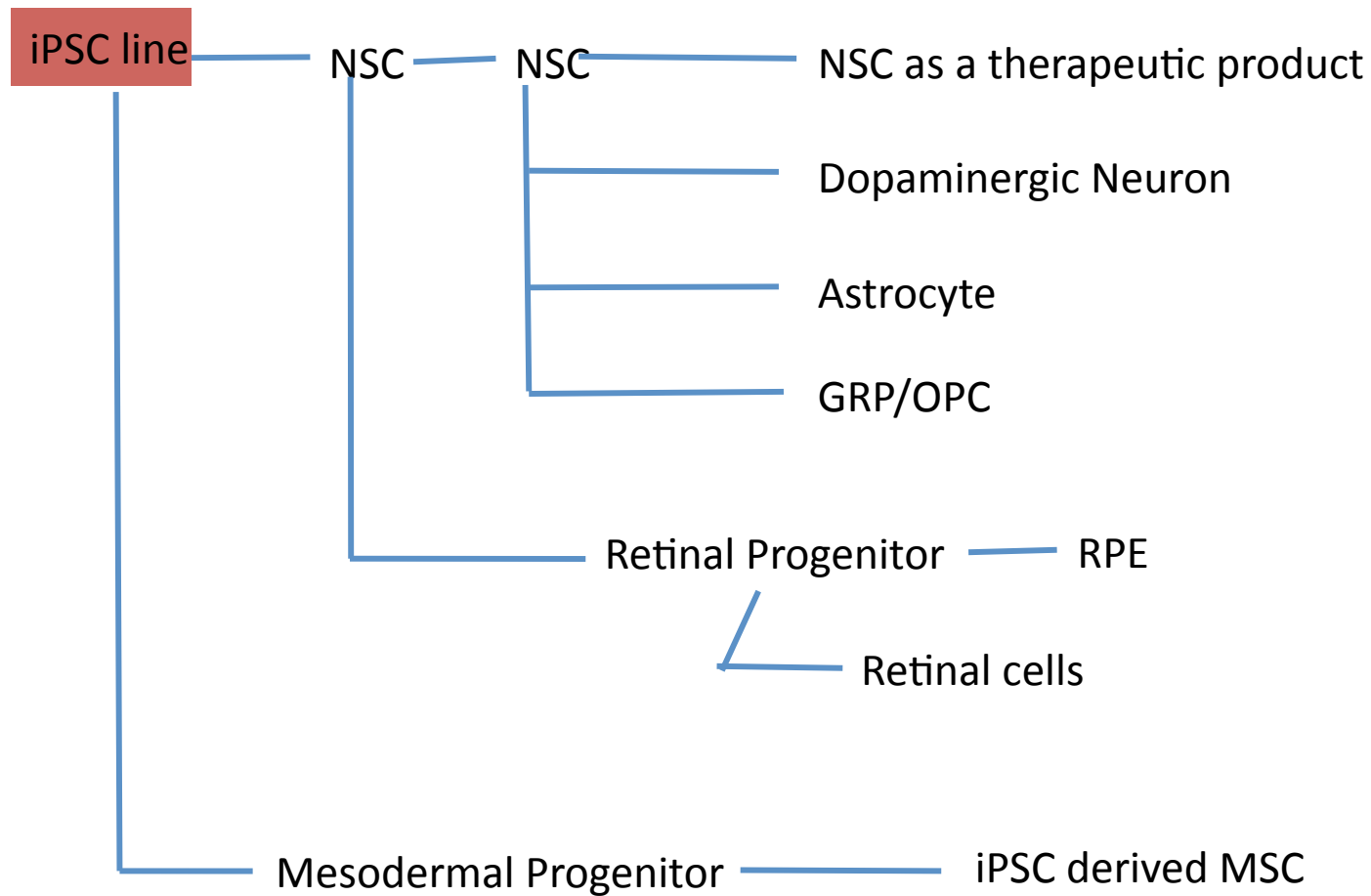


Current Model of therapy using iPSC as an example

 iPSC Therapy models	One to One 	One to Many 	Many to Many 
Autologous Donor No of lines Regulated as BLA Multiple products Fewer tests and tracking issues Longer time to therapeutic product May be GLP HE exemption Consent straightforward Immune suppression Cost	Yes Self 1-3 clones Yes Yes Yes Yes Possibly Possible Yes Unnecessary High/patient	No Healthy 5-10 lines Yes Yes More Much shorter Unlikely Unlikely Burdensome High per patient Lowest	No HLA matched >100lines Yes Yes Even More Shorter Unlikely Unlikely Burdensome Intermediate Intermediate Mahendra Rao LLC



One Line many products





Our suggestion for the FDA to consider

Use the cell bank for biological product manufacture as a model

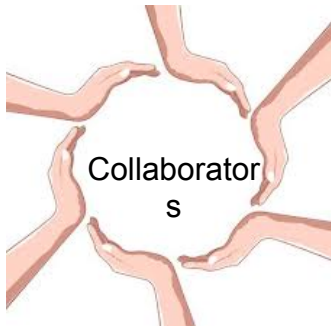
Cells are an important input material that should have a defined process for replacement at the MCB stage

New MCB should meet same specs as the old and the final product should meet the same release criteria

This should be released as a white paper or guidance for the industry

- This should allow the current models of therapy to be implemented with clarity and would integrate well with previously approved products.
- It would be of particular important to adult stem cells and allogenic small scale manufacture where intermediate working banks are made

Summary



- Its possible
- It is worthwhile
- Problems are solvable
- But it will take coordination