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

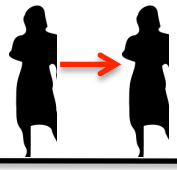
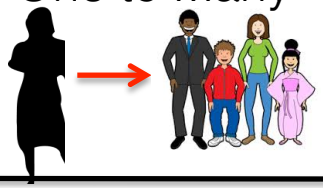
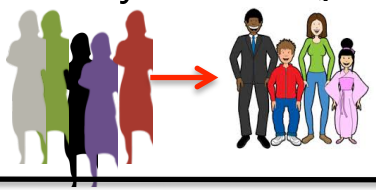
In vitro data

Comparability of MCB

Matching release criteria

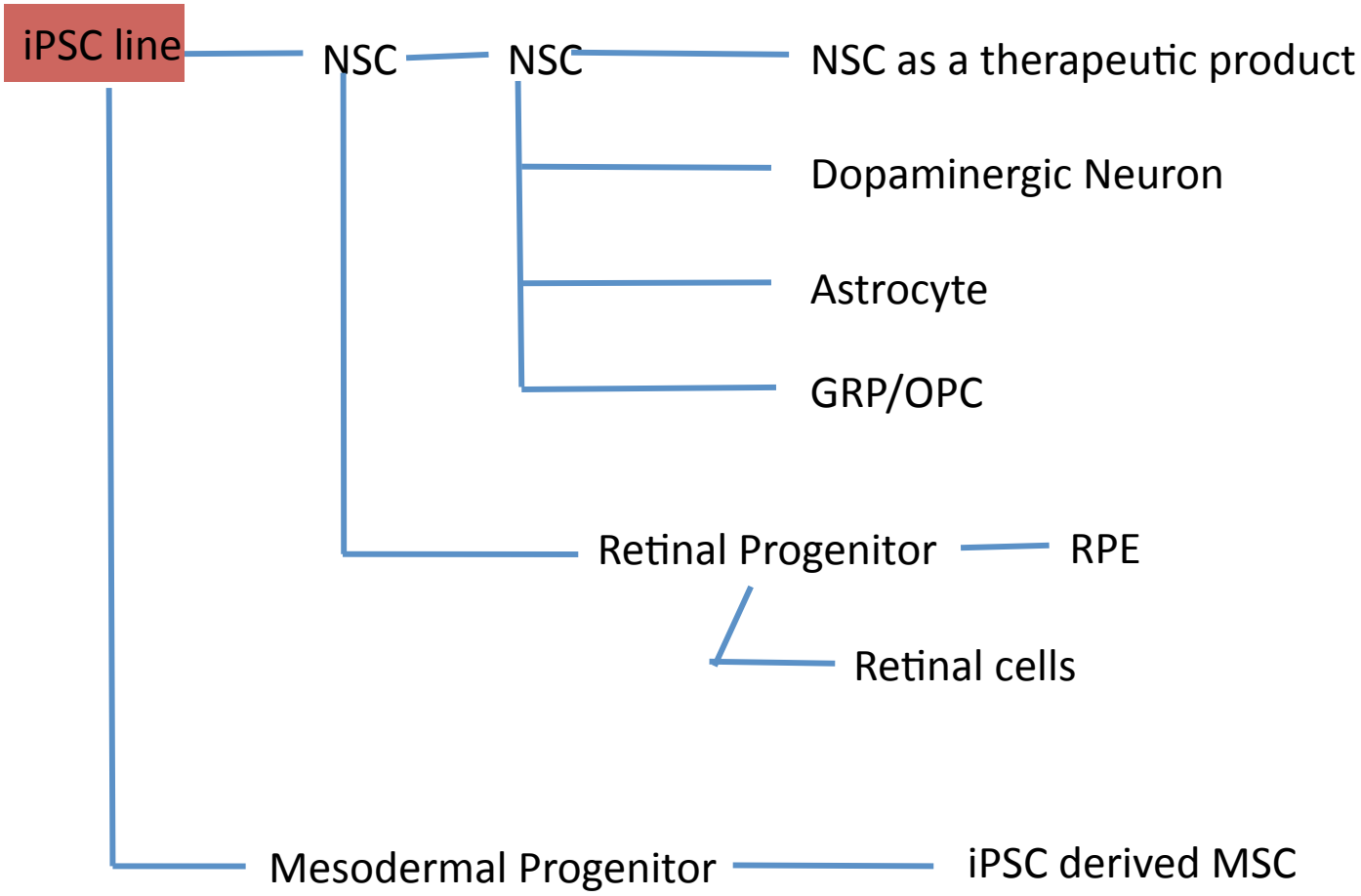
What we are asking is for clarity and proposed comparability criteria

Current Model of therapy using iPSC as an example

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

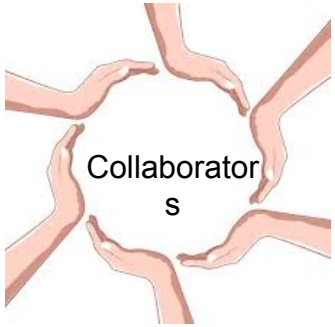
New MCB should meet same specs as the old and the final product should meet the same release criteria

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