USE OF DEVICES AND MANUFACTURING EQUIPMENT IN CELLULAR THERAPY

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Introduction

- Who am I?
  - Serving as chair of ISCT's Devices Working Group.
  - The DWG is thinking about gathering data about devices and equipment in cell therapy—BUT…
  - The DWG has not achieved consensus on how or whether to collect data on presence of devices/equipment in cell therapy production.
  - These remarks should be regarded as personal ones. All errors or misconceptions within them are solely mine.

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What are common Equipment and Devices for cell production?

- Thinking of them by “type” rather than “brand”
  - Collection systems (apheresis, debulking)
  - Separation systems (beads, optical sorting, elutriation)
  - Expansion systems (culture reactors)
  - Co-culture systems
  - Gene transfer systems
  - Washing/concentration systems
  - Storage systems (refrigeration, freezing, thawing)
  - Injection/administration systems (infusion, injection, catheters)
- Need to expand this to a full equipment typology

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What would one try to illuminate by gathering data?

- Which systems are equipment and which are devices?
  - This appears to be dependent on how systems are used in a cell production process flow
  - It may be that a particular system can be device in one production process and equipment in another– if so how does one tell?
- How are investigators using equipment/devices in relation to required reagents? In which systems/production flows do users specify reagents or do equipment manufacturers?

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What does one NOT want to collect data on?

- Not interested in which institution has what equipment or processes
  - All data must be de-identified
- Not interested in “brand” oriented data
  - Not “marketing” or “sales” surveys.
  - Requires some agreed “typology” of equipment to use in identification.
    - i.e. “optical cell sorter” rather than “BD facsAria”
    - This also helps with aggregation

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Prototype Process & Equipment Survey

- Requires:
  - (1) a simple "typology" of process flows (horizontal columns)
  - (2) a "typology" of equipment/device systems to use when filling in the boxes in the columns

"Unprocessed"

Process Type	Type I	Source	Acquire	Formulate	Infuse
How Many Products of this type?					
GMP?	yes				
GTP?					
Other?					

Source	Equipment / Reagents	Acquisition Step	Formulation Step	Infusion Step
allo pbmc	Equipment	apheresis	spinning/washing	systemic infusion
		thawing equipment	refrigerate	
gm-csf (mobilizer)	Reagents			

"Selected"

Process Type	Type II	Source	Acquire	Select	Formulate	Infuse
How Many Products of this type?						
GMP?						
GTP?						
Other?						

Source	Equipment / Reagents	Acquisition Step	Selection	Formulation Step	Infusion Step
auto pbmc	Equipment	apheresis	bead selection hsc	washing	systemic infusion
				cryopreserve	
mobilizers	Reagents		anti cd34 beads	dmso	

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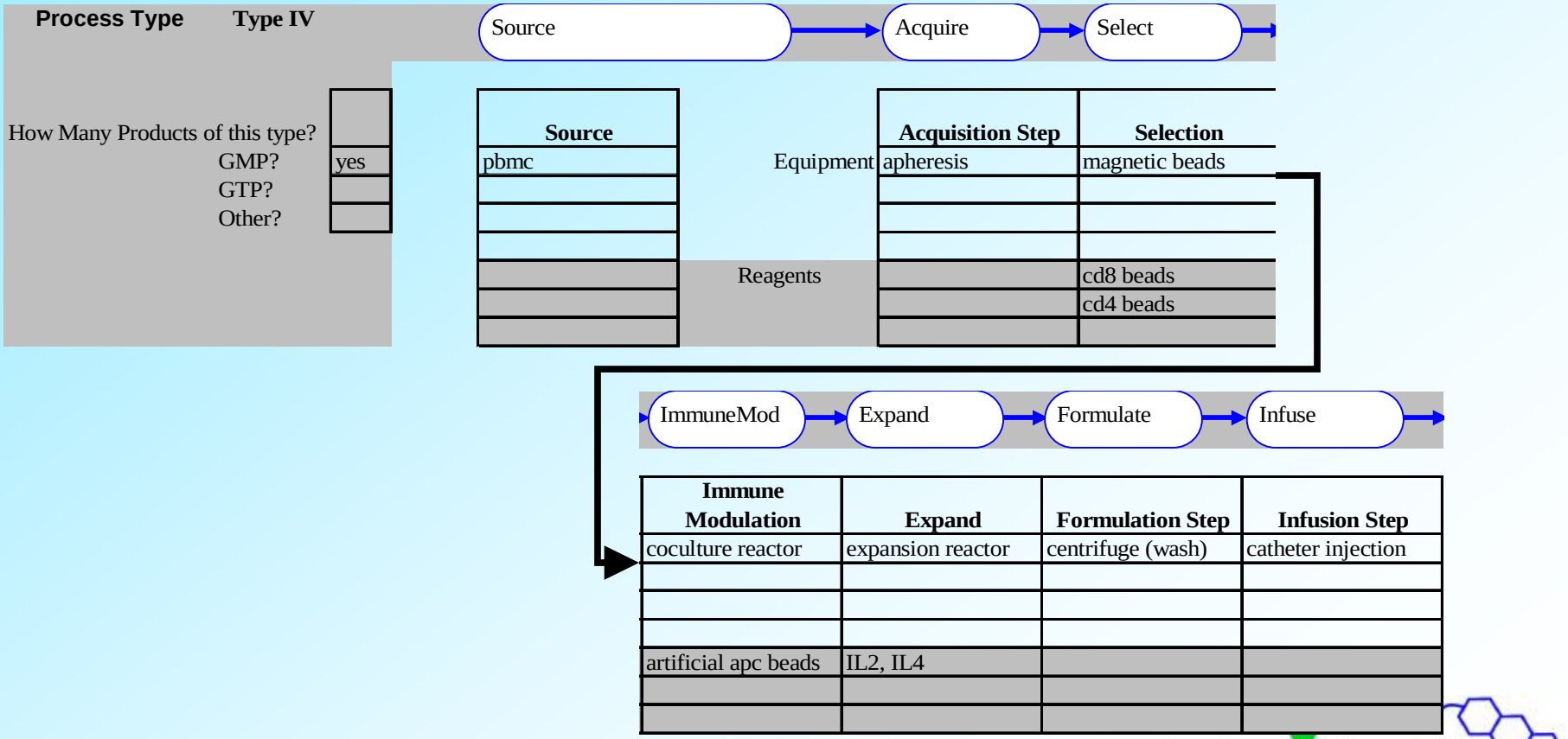
Another process type

“Immune Modulated”



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Five Candidate Process Types

- Unprocessed
- Selected

May be “minimal”

- Selection + Expansion
- Immune Modulation
- Gene Modulation

- Need to investigate if 5 types is sufficient

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Such a system gives a place to connect data types

- We are essentially allowing/asking to connect
- Process design
- Equipment/Device hardware
- Required Reagents (for each process step)

Process Type **Type II**

Source → Acquire → Select → Formulate → Infuse

How Many Products of this type?	
GMP?	
GTP?	
Other?	

Source		Acquisition Step	Selection	Formulation Step	Infusion Step
auto pbmc	Equipment	apheresis	bead selection hsc	washing	systemic infusion
				cryopreserve	
mobilizers	Reagents		anti cd34 beads	dmso	

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Other Questions this kind of data will help with

- Can fit with stakeholder questions
- Allows identification of where equipment is in a process flow.
- Allows some understanding of where requirements on equipment change with which step or which step in the sequence the equipment lives in.
- Allows one to ask is a system equipment or device– and check if that is changing based on how (which step) the equipment is being used
- Allows one to ask how many different reagents are being used with an equipment system
  - Few may suggest reagents are the equipment manufactureres problem
  - Many may suggest they are the users problem

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Process

- To collect this type of data through ISCT we will have to
  - Pilot a survey to confirm or agree on
    - Equipment typology
    - Process typology
  - Operate a general survey of the cell production centers
    - Looks more like qualitative interview than multiple choice e-mail survey– but may be doable as excel sheet with macros.
    - Hoping for reasonably widespread response
  - Analyze
    - Qualitative data (at expected response rates) will get Qualitative analysis
    - Follow-up questions about other issues could be placed in this context, which will certainly make more sense
      - Ä Ex: which equipment come with full validation packages for your use and for which do you have to do protocol specific and non specific validations.

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Problems or Opportunities

- This is actually treading into an area of “standards”
  - If I may comment on the IC industry, which has many complex multi-step production process flows in cleanrooms
  - In that industry there are “standards” for describing and reporting multi-step process flows and the equipment sets that “perform” each unit process step.
    - Complete with standards committees to write those descriptions and the typologies.
- This might be better developed along those lines– in which case the process and equipment standard could be used in reporting all descriptions of cell production processes from the beginning– and we could just look this sort of information up, instead of collecting it.
  - Is there such a reporting standard today?
  - How does the FDA compare one process flow to another?

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Comments and Discussion?

- Follow up comments to me at john-gilbert @ piconomics.com will be collated and re-circulated to the stakeholder attendees.

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