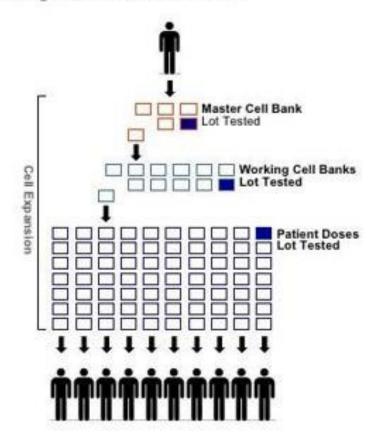
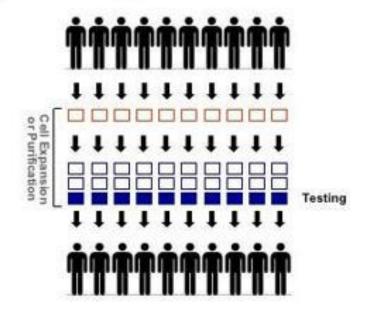


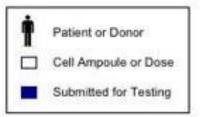
Cell therapy production

Allogeneic / Universal Donor



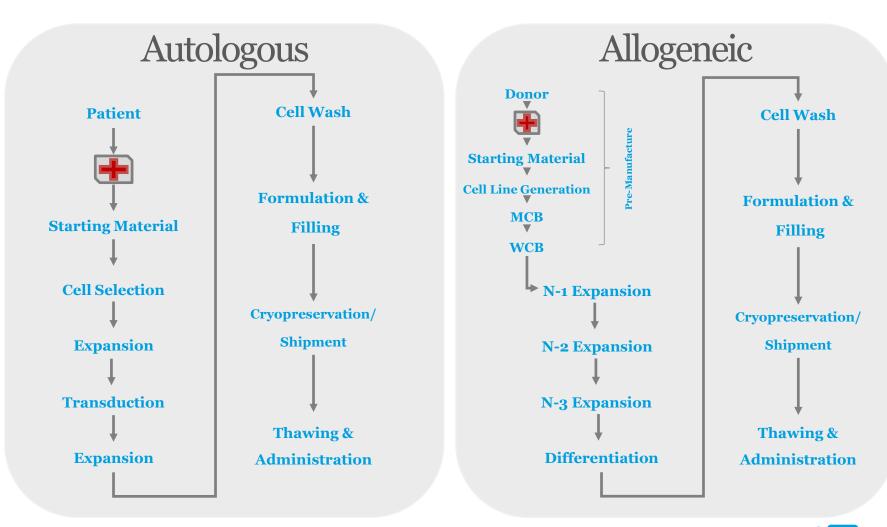
Autologous / Patient Specific





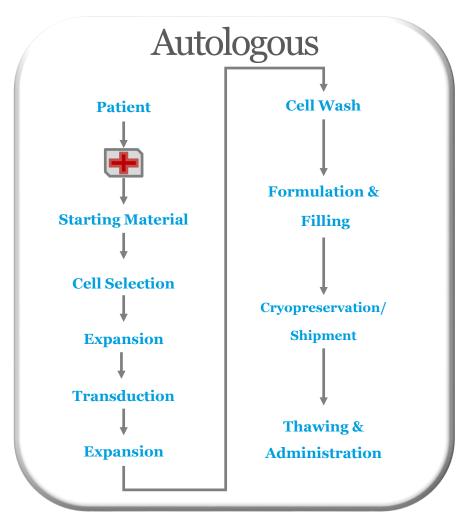


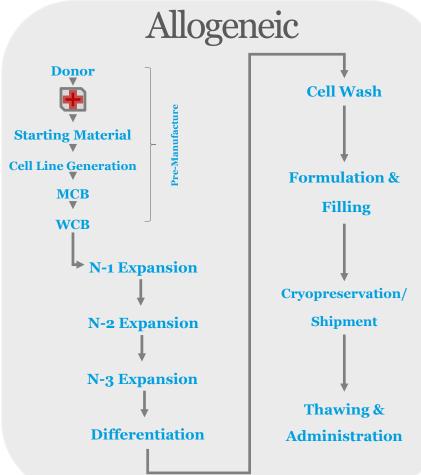
Process stream for cell therapy products





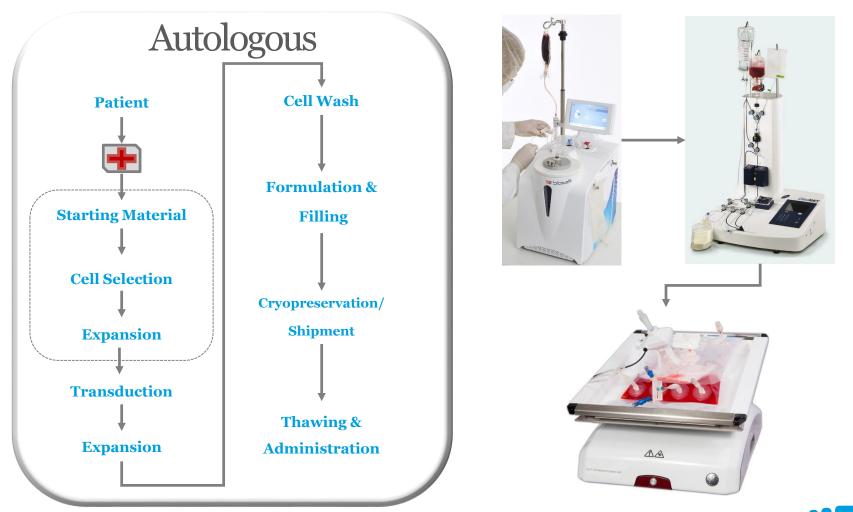
Process stream for cell therapy products



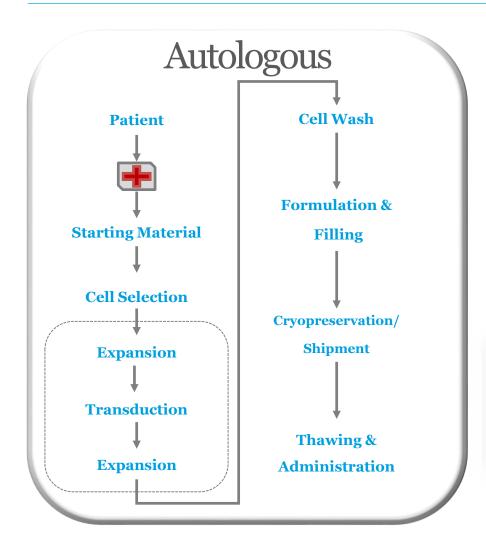




Technology selection: automated processing options



Technology selection: cell expansion performance



Current Scale Requirement <100mL- 1- 2L



Manual Technologies; Multiple Units



Automated Technologies; Single Unit

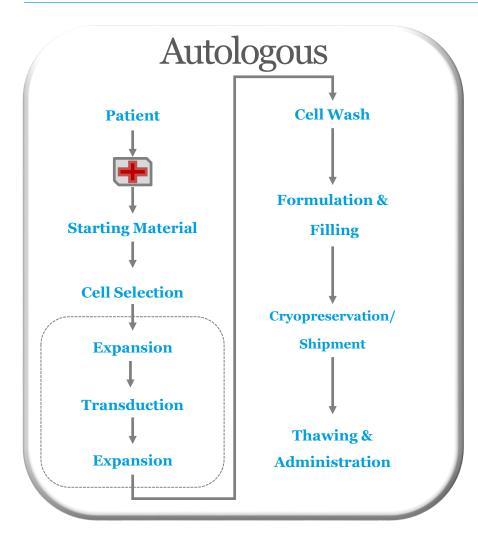




Potential Automated Technologies; Single Unit/Multiple Unit

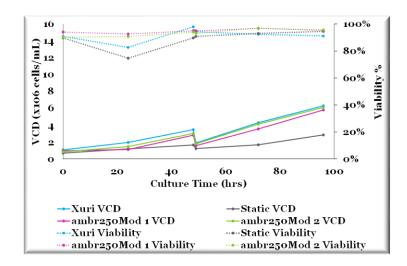


Technology selection: cell expansion performance



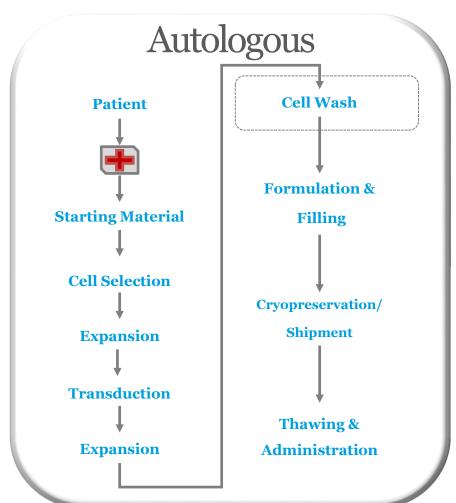
Current Scale Requirement <100mL- 1- 2L







Technology selection: cell wash





Manual Technologies; Multiple Units



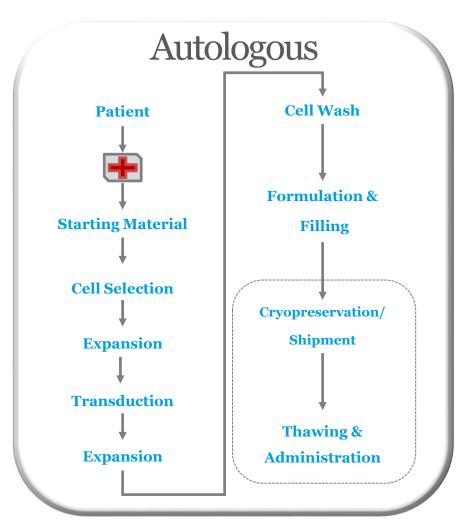
Automated Technologies; Single Unit



Automated Technologies; Single Unit



Technology selection: controlled rate freeze/thaw





Controlled Rate Freezing within GMP Environment



Controlled Product Thaw at Clinical Site



Failure rate reduction: process connections

The product – gene-modified T cell with an open ongoing Phase I trial

The problem – open process, labour intensive, almost 1000 manipulations, 72% needle-based.

The approach – incremental changes over 2 generations to facilitate ongoing clinical trials with ongoing automation and optimisation for 3rd generation product

Results - Reduction in CoGs achieved by increasing throughput (31%), and reducing failure rate (29%), to which automation is the greatest contributor



	Manual Process		First Improvements		Second Improvements	
Manipulation Type						
	Number	%	Number	%	Number	%
Needle	705	72	109	21	69	37
Spikes and other	209	21	20	4	12	6
Tube weld and seal	64	7	399	75	107	57
Total	978		528		188	



Key challenges

Process

Meeting Dose Demand

Technology Development

Process Development & Understanding

Scale up/Scale out

Process Robustness

Manufacturing

Technology Development

Process Translation to GMP

Manufacturing Facility Availability

Training & Staff Availability

Quality

Product Characterisation

Impurity Characterisation

Assay Development

Automation and Data Challenges

Regulatory

Final Product Definition

Risk Analysis

Product Origin

Clinic

Patient Recruitment

Patient Eligibility

Clinical Protocol Complexity

Starting Material Sourcing and Administration

Logistics

Patient Location & Scheduling

Starting Material/Product Shelf Life

Starting Material Shipment and Storage

Product Shipment, Storage and Administration



Key challenges

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Product Shipment, Storage and Administration



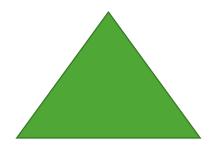


Manufacturing centre

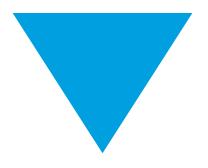




Manufacturing process fitting challenges



Product Quality
Process efficiency
Process robustness
Product safety
Operator safety
Containment



Reduce risk of contamination Risk of cross contamination Reduce operator error Reduce unnecessary movement



Facility layout stages

1. Process Mapping:

• This is a confirmation and "fill the gaps" exercise to ensure a moderate level of process detail at the early stages of facility fitting

2. Equipment List:

 The equipment list is generated based on information provided by the collaborator and checked against the generated process map

3. Process Schedule:

• The selected equipment requirement is mapped and process schedule is created. This is checked against the yearly batch and yield requirement, ensuring that the equipment is sized correctly and the space contains the correct number of equipment units.

4. Scenario Choice:

• At this stage the client can provide some scenario choices based on their current process development data, production and business strategies

5. Facility Layout Options:

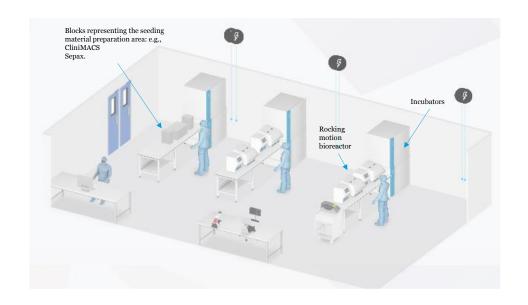
• 3D layouts are generated for each selected scenario based on the information provided. The collaborator can "visit" their module options using a virtual reality headset



Autologous process example

Layout and capacity constraints can significantly impact:

- Product quality
- Yearly production
- Cost of goods
- Processing parallel patient batches in the same cleanroom is typically implemented but companies are working towards this as it will required for cost effective production
- Stress testing and layout modelling provide greater understanding prior to making a commitment to a production output



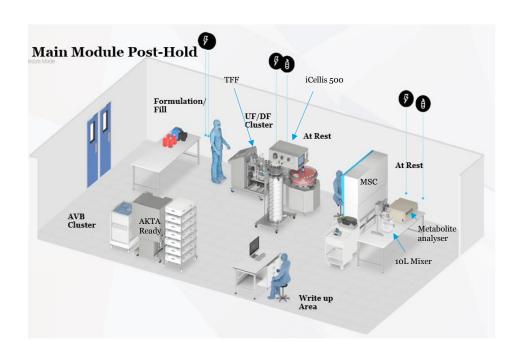


Viral vector process example

Facility layout options and configurations can be explored

Precisely modelled equipment allows to assess:

- Equipment orientation
- Equipment access
- Auxiliary equipment positioning
- Waste and people flow
- Operational space
- Expanding equipment library is available which allows to create and browse available cleanroom accessories





Into the future

- The created layout can be viewed using a virtual reality headset.
- The viewer can "walk" through the module and the facility.
- Assessment of the layout suitability using a first person view.

Future Potential

- Airflow modelling in the room
- Single use connections modelling
- Virtual tours
- Virtual operator training







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