Transfer and optimisation of ATMP manufacturing

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Aim As novel therapies progress through clinical development the manufacturing requirements will inevitably change requiring the optimisation and transfer of Phase I ready processes from smaller facilities, often in academic establishments, to larger facilities with greater capacity e.g.CMO, own facility or serviced production centres such as the CGT manufacturing centre. Robust methodologies, that are operationally efficient, for Technology Transfer (TT) are essential if manufacturing capacity is to keep pace with clinical requirements. The negative impact of a suboptimal TT process can be significant from both a clinical and financial perspective. Using a clinically relevant T cell process we developed a procedure to capture the critical steps to ensure a robust, reproducible process that was operationally efficient and delivered a successful outcome for an active immune oncology clinical trial.

Tech Transfer Master Plan: A high level document which describes the approach and strategy outlining all of the requirements for TT of the manufacturing process and analytical assays in-line with current GMP standards and associated regulations. The document captures responsibilities, communications plan and project timelines.

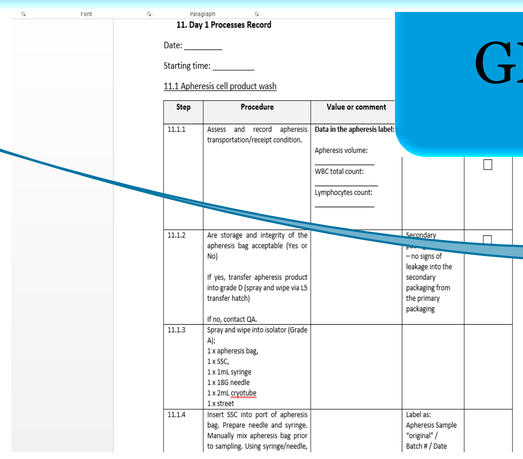
People Forming an effective team with good communication channels is essential. Interactions include:

- Regular (weekly) meetings
- Process and assay observation at Dev. Lab
- Training- Gap analysis & training runs
- Person In Plant- Dev Lab scientist supporting manufacturing team on site.
- Subject matter experts- support engineering run design, validation runs and deviation investigations.

Development Lab

Technical transfer Process

GMP Manufacturing Facility



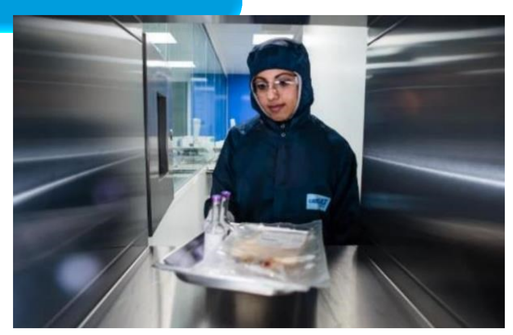
11. Day 1 Processes Record

Date: _____

Starting time: _____

11.1 Apheresis cell product wash

Step	Procedure	Value or comment	
11.1.1	Assess and record apheresis transportation/receipt condition.	Data in the apheresis label: Apheresis volume: _____ WBC total count: _____ Lymphocytes count: _____	☐
11.1.2	Are storage and integrity of the apheresis bag acceptable (Yes or No) If yes, transfer apheresis product into grade D (spray and wipe via LS transfer hatch) If no, contact QA.		Secondary packaging – no signs of leakage into the secondary packaging from the primary packaging	☐
11.1.3	Spray and wipe into isolator (Grade A): 1 x apheresis bag, 1 x SSC, 1 x 1mL syringe 1 x 18G needle 1 x 2mL cryotube 1 x street			
11.1.4	Insert SSC into port of apheresis bag. Prepare needle and syringe. Manually mix apheresis bag prior to sampling. Using syringe/needle,		Label as: Apheresis Sample "original" / Batch # / Date	



Documents Accurate, very detailed documents generated by the Development Laboratory that are version controlled and ensure all of the information transfer is performed successfully. Documents that are required include:

- Equipment specification and SOPs
- Materials- Source, purchasing information, storage, stability and specification with example CoCs or CoAs
- Process- Development reports including design space knowledge, flow diagrams, detailed process description, SOPs, Batch Manufacturing Records (BMRs)
- Analysis (Development tests, In-process and Release)- Development reports, flow diagrams, detailed process description, SOPs, specification, test requests for CROs.
- Process Risk assessment- FMEA style
- Training records for manufacturing team training at Dev Lab including test results to assess qualitative judgements.
- Health and Safety- MSDS; Risk Assessments
- Supply chain requirements for Starting Material, samples, Drug Product including temperature, packaging, monitoring and 3rd party service providers.
- Storage and Stability for Drug Product
- Labelling- Samples and Drug Product.

Technical Transfer Report Generated by the manufacturing facility and summarises the TT batches / assay transfer performance together with any deviations/failures encountered. Acceptance criteria is reviewed against the results and recommendations made.

Conclusion Using risk based methodologies we have successfully 'tech transferred' an immunotherapy manufacturing process from our development laboratories to a CMO for GMP manufacture and clinical supply. By documenting this process into a clear and detailed Standard Operating Procedure we have created a robust and reproducible methodology for the future that mitigates against the risk of increased product variability and failure. This SOP can be applied to any manufacturing process to accelerate clinical development programmes and reduce the significant risk of moving manufacturing facility.

We work with Innovate UK

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