Northern Alliance
Advanced Therapies Treatment Centre

Think Big and Think Early to Prevent Failure at Commercial Scale

This document was produced by Simon Ellison, Simon died in the Spring of 2020 after a short illness. He is much missed within the Northern Alliance. He played a transformational role in adapting and enhancing supply chains for cell and gene therapies, part of his commitment to rapid and effective delivery of these advanced therapies to patients over a number of years. We remember Simon with admiration. In recognition of his contribution we note it here.

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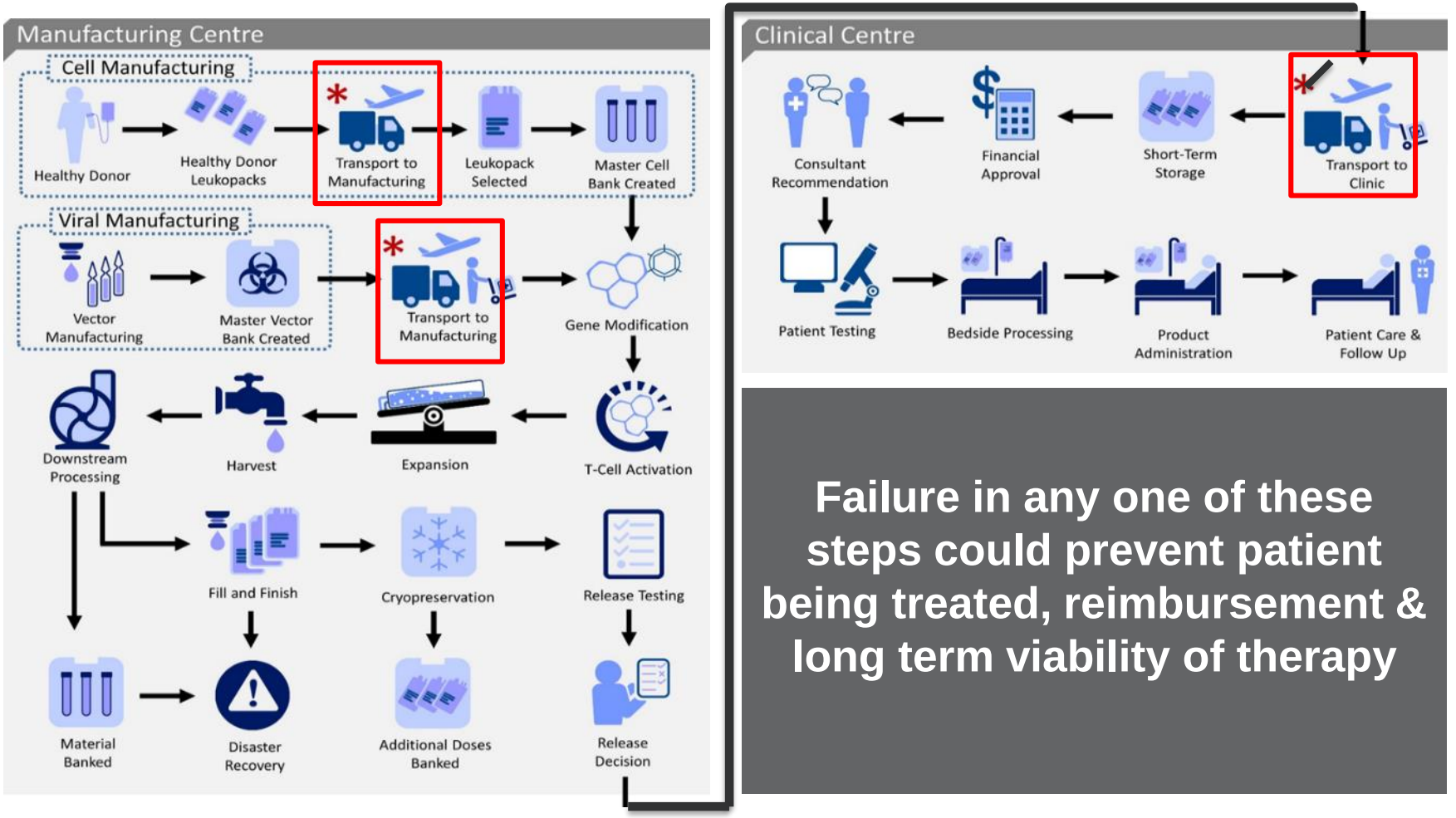
Think Big and Think Early to Prevent Failure at Commercial Scale

Date: May 30th 2019

By: Simon Ellison

AmerisourceBergen

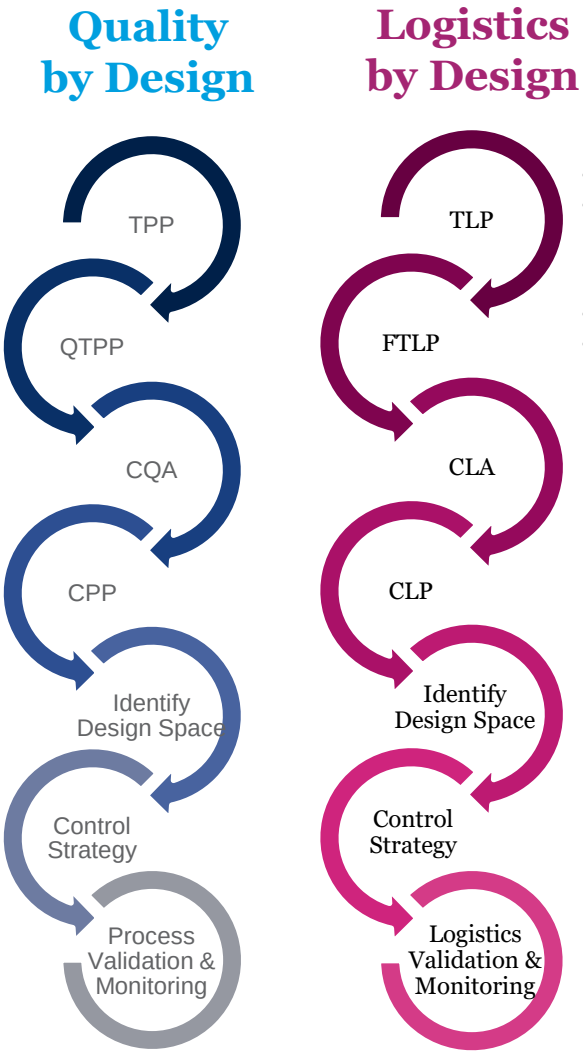
Is Logistics a Critical Manufacturing Step?



Failure in any one of these steps could prevent patient being treated, reimbursement & long term viability of therapy

Chimeric antigen receptor–T cell therapy manufacturing: modelling the effect of offshore production on aggregate cost of goods
Richard P. Harrison, Ezequiel Zylberberg*, Simon Ellison, Bruce L. Levine. Cytotherapy, In Press

QbD Evolving into Logistics by Design



- **Target Logistics Profile**
- Overarching objectives of a commercial logistics strategy with respect to supporting business goals, supplying market needs, maintaining regulatory compliance and facilitating clinical adoption.

- **Focused Target Logistics Profile**
- Prospective summary of the commercial logistics strategy traits that need to be achieved for all components of the value chain, to ensure successful delivery of product to patient whilst maintaining chain of custody and identity

- **Critical Logistics Attribute**
- A physical, temporal, informatic or operational property that needs to be within an appropriate limit, range, distribution or tracked and traced, to ensure the desired logistics strategy is fulfilled.

- **Critical Logistics Parameter**
- A logistics parameter whose variability or failure would impact a critical logistics attribute and therefore should be monitored or controlled to ensure the desired logistics strategy is fulfilled.

- **Identify Design Space**
- The design space or operating ranges for the CLPs are elucidated through practical assessment using supporting tools, such as Design of Experiments (DoE) or through the testing as part of logistics development activities

- **Control Strategy**
- A planned set of controls, derived from current logistics understanding that ensures service performance and quality. Controls may include parameters and attributes related to physical or informatic characteristics and include frequency of monitoring and control.

- **Logistics Validation and Monitoring**
- A MAA/launch ready logistics system functional on a global footprint with regular performance review to support real time data driven decision making to further optimise the logistics undertaking.

Ellison*, McCoy*, Bell, Frend, Ward (*Joint 1st Author), Logistics by Design – A framework for advanced therapy developers to create optimal Logistics Platforms, Cell and Gene Therapy Insights, Dec 2018, 1019 - 1039

Manufacturing Strategy Driven by Shelf Life

Different clinical collection times enable different flights to be utilised

Shipping Window & Risk

Strategic Impact

Fresh

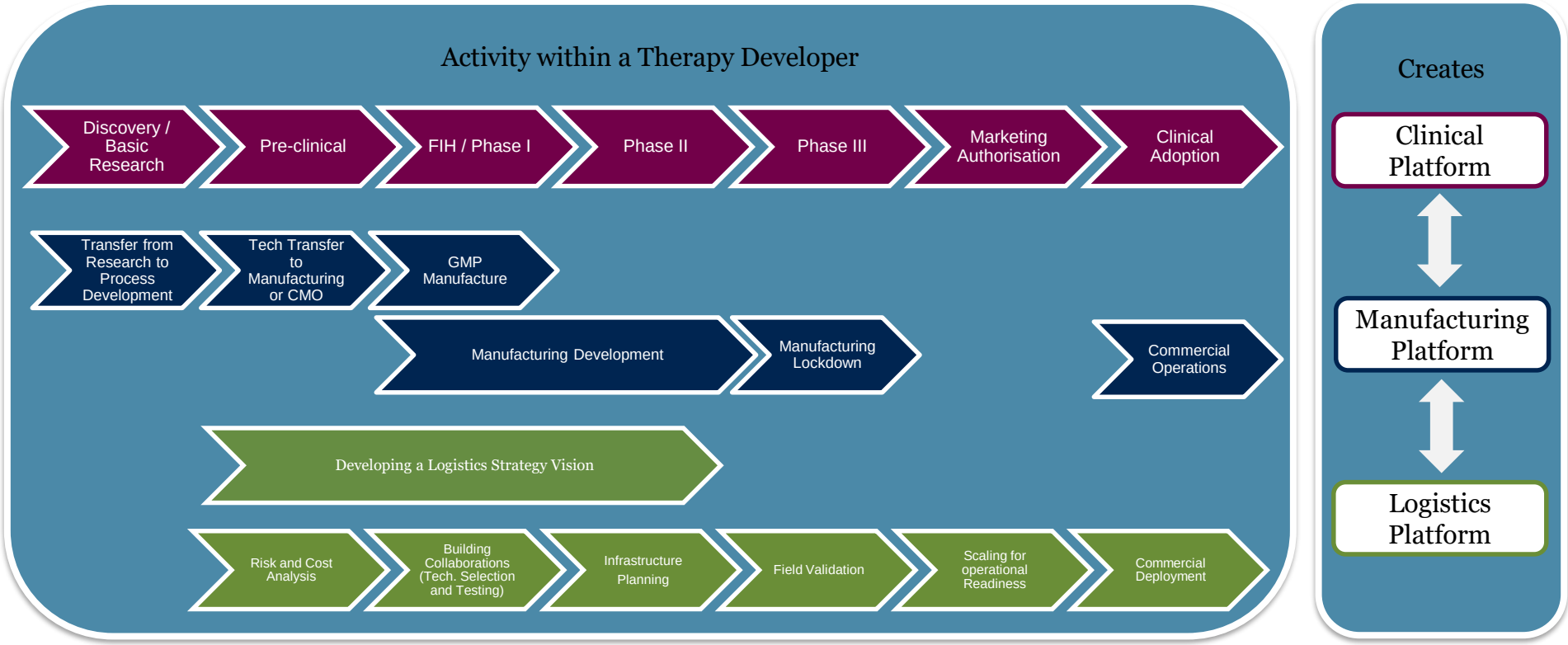
- If donation OR therapy OR monitoring sample has a limited shelf life
- ➢ Multiple manufacturing sites
- ➢ Need to control regulatory, manufacturing equivalence, etc

Cryo

- Has to be possible for ALL shipping
- ➢ Single large scale manufacturing site possible
- ➢ Reduced cell viability
- ➢ How manage/control thaw

Original data from Ellison*, McCoy*, Bell, Frend, Ward (*Joint 1st Author), Logistics by Design – A framework for advanced therapy developers to create optimal Logistics Platforms, Cell and Gene Therapy Insights, Dec 2018

LbD Aligns Development



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LbD Applied

GE Healthcare And World Courier

Collaborate to Drive Commercialization of Cell and Gene Therapies

Partnership

Therapy Developer

GE Healthcare

World Courier
AmerisourceBergen

Creates

- Clinical Platform
- Manufacturing Platform
- Logistics Platform

Where knowledge,
reach and partnership
shape healthcare delivery.