STREAMLINING TECHNOLOGY TRANSFER

Kevin Turney
Director of Process Development
Amgen

ISPE Boston Chapter
June 18th, 2020

Introduction – Kevin Turney

- **Director of Process Development, Amgen**
- Global Network Lead for Technology Transfer, Attribute Sciences, conducting transfers across multiple modalities.
- Responsible for Technology Transfer Team delivering to method transfers across Amgen internal/external network (6 Internal facilities and 15+ external partners).
- Directly supported technology transfers varying from Amgen's first synthetic production facility in Singapore, Manufacturing of the Future (MoF) biological production, and Oncolytic virus production.
- PhD Analytical Chemistry
- Currently in Cambridge, MA

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STREAMLINING TECHNOLOGY TRANSFER

PERSPECTIVES FROM BIOPHARMACEUTICAL COMPANY

Biopharmaceutical Technology Transfer

3.1.2 Technology Transfer

The goal of technology transfer activities is to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product realisation. This knowledge forms the basis for the manufacturing process, *control strategy*, process validation approach and ongoing continual improvement.

Technology transfer projects may take place at various points during the product lifecycle. Successful transfers depend on robust project management processes combined with appropriate product and process understanding. They require partnership, cooperation, and coordination between sending units and receiving units to ensure successful and efficient completion, such that the receiving unit can manufacture, test, and release a safe, efficacious, and quality product comparable to that of the sending unit.

ICH Q10 paragraph 3.1.2

ISPE GOOD PRACTICE GUIDE TECHNOLOGY TRANSFER 3rd EDITION

Technology transfer is the execution (technical and process knowledge) and management of all activities required to successfully reproduce the manufacture of a defined process and/or performance of an analytical method from one facility to another.

Why we conduct Technology Transfers and why are they complex

Business Drivers

Sets Timing and Scope

- **Capacity**
- **Capability**
- **Centralization**
- **Intellectual Property**
- **External Factors (…BREXIT)**

Industry Trending

Increasing difficulty

- **Synthetics and mAb… Varied therapeutic proteins, virus, siRNA, CAR-T, Antibody Drug Conjugates, etc.**
- **Novel modalities increasing in capacity**

Types of Transfers

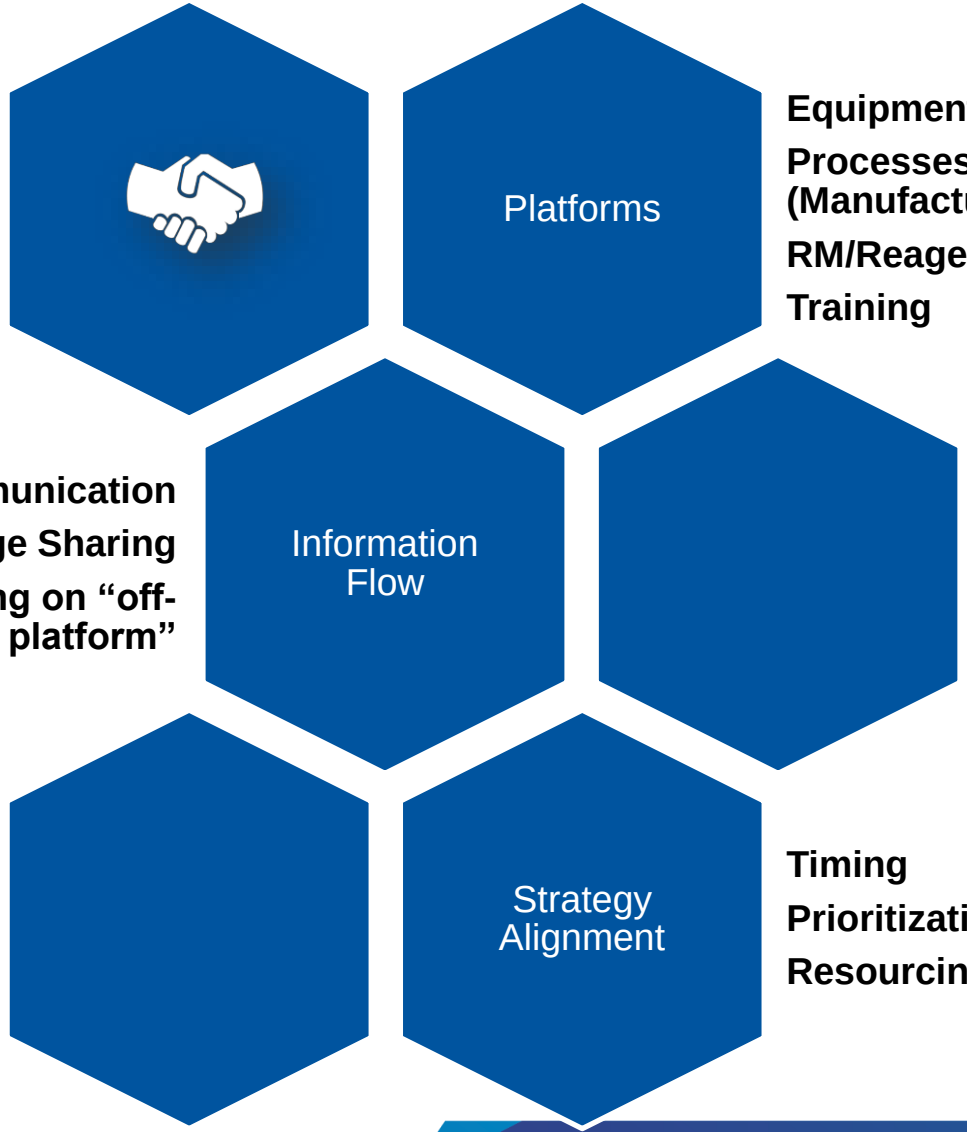
Where.. And Stage

- **Internal only (sending/receiving)**
- **External (receiving)**
- **In-licensing (External sending)**
- **Commercial Programs, late stage, early stage**

Examples

TT of commercial process from Internal Network to Contract Manufacturing Organizations (CMO)
TT (New Product Introduction) of clinical programs from Internal Process Development (PD) to CMO
TT (NPI) of clinical programs from Contract Research Organization (CRO) to CMO

Internal Versus ~~External~~ Technology Transfers



Equipment
Processes (Manufacturing/SOPs)
RM/Reagents/Standards
Training

Communication
Knowledge Sharing
Focusing on "off-platform"

Timing
Prioritization
Resourcing

Technology Transfer Phases and Deliverables

Site Selection → Tech Transfer → Commercial Manufacturing

Team Formation and Planning

- Project Team
- Kick-off meetings
- Gap Assessment
- Project Charter
- Materials Management
- Training Curriculum
- Safety Evaluation

Information Transfer

- Transfer Documenta
- Detail Gap Assessments
- Process Parameters
- BOM
- Raw Material assessment
- Analytical Transfer plan
- Testing strategy

Implementation Transfer Activities

- Machinability runs
- Pilot runs
- Characterization Studies
- Engineering runs
- Analytical Transfer execution
- Media Fill/Filter Validation strategy
- Validation Plan
- Change Control

Process Performance Qualification Execution

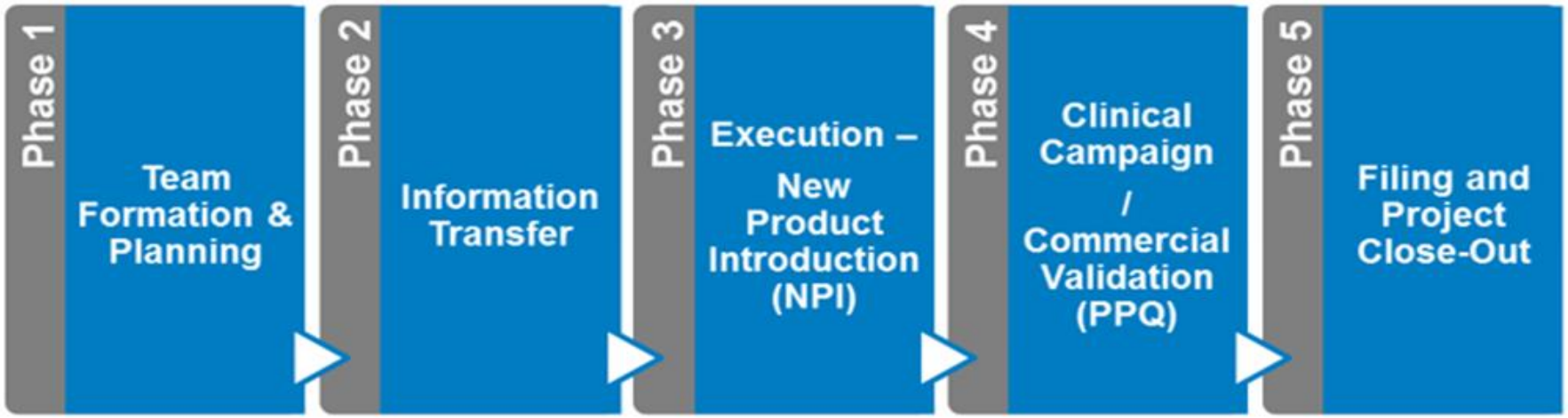
- Validation Master Plan
- Validation Protocols
- Manufacturing execution
- Testing release
- Final reports

Filing/Close out

- Filing preparation
- PAI
- Stability studies
- Lots delivery

Stage Gate Process for Ensuring Successful Technology Transfers

- DEFINED TT PHASES: Technology Transfer can be broken into **defined phases** and each one can require a **Stage Gate review before moving to the next phase**.
- CLEAR DELIVERABLES FOR EACH PHASE: Stage Gate review purpose is to ensure **all critical items from the current phase are completed before moving to the next phase**
- GATED APPROACH WITH APPROVALS: **Stage Gate forms** are related to the program requirements and complexity. Stage gates may be combined or eliminated with justification in the **Tech Transfer Plan**.



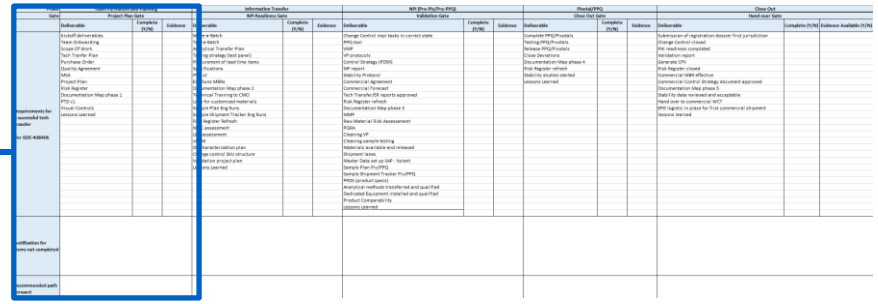
Team Alignment on Deliverables early provides benefits

Phase	Team Formation and Planning		
Gate	Project Plan Gate		
	Deliverable	Complete (Y/N)	Evidence
Requirements for a successful tech transfer	Kickoff deliverables		
	Team Onboarding		
	Scope Of Work		
	Tech Tranfer Plan		
	Purchase Order		
	Quality Agreement		
	MSA		
	Project Plan		
	Risk Register		
	Documentation Map phase 1		
	PTD v1		
	Visual Controls		
	Lessons Learned		
Justification for items not completed			
Recommended path forward			
Lessons Learned	What worked? What did not?	Impact? ideas?	

Specifics are project dependent

Capture lessons learned

EXAMPLE FORMS



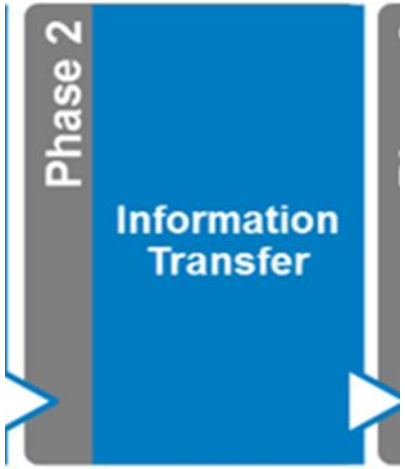
Step 1: finalize list of key deliverables (remove what not applicable)

Step 2: Verify completion of deliverables and provide evidence

Step 3: Justify and assess missed deliverables

Step 4: Provide team recommendation

Use of gap assessments for knowledge transfer and understanding

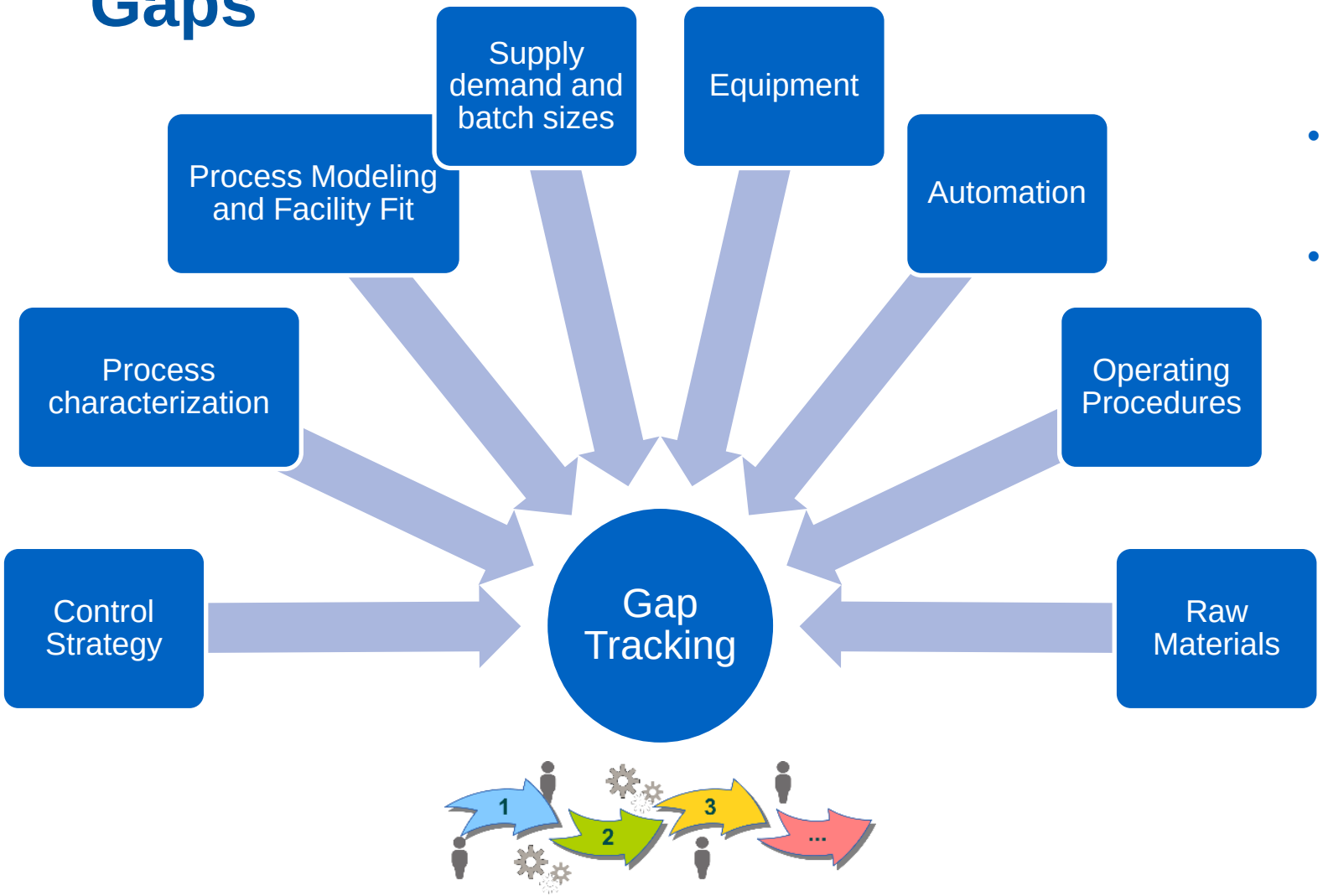


"Make-a-Batch"/"Test-a-Batch" exercises are detailed analysis of process fit into the receiving facility capabilities and operations.

- Assessment is completed by **process/testing experts** providing knowledge while receiving site provides **facility expertise**
- **Alignment between requirements and facility** is done to determine best possible implementation strategy while identifying potential gaps and misalignments

Solid Foundation for Transfer…

Detailed Walk Through of Process to understand Knowledge Gaps

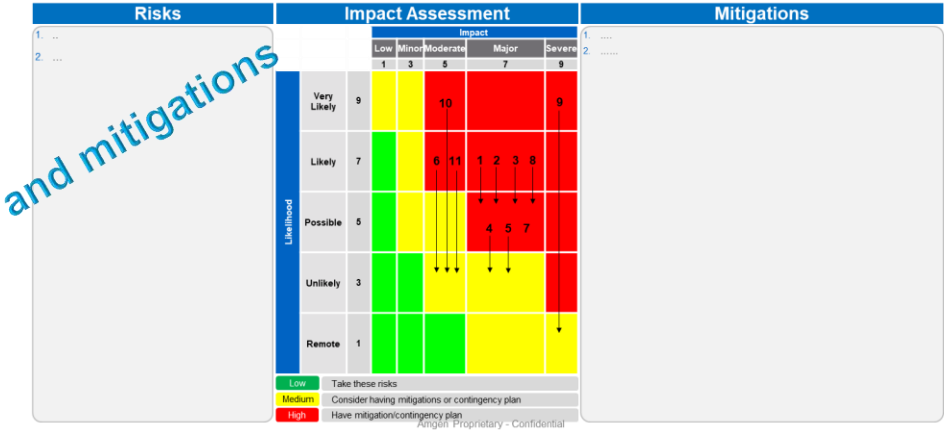


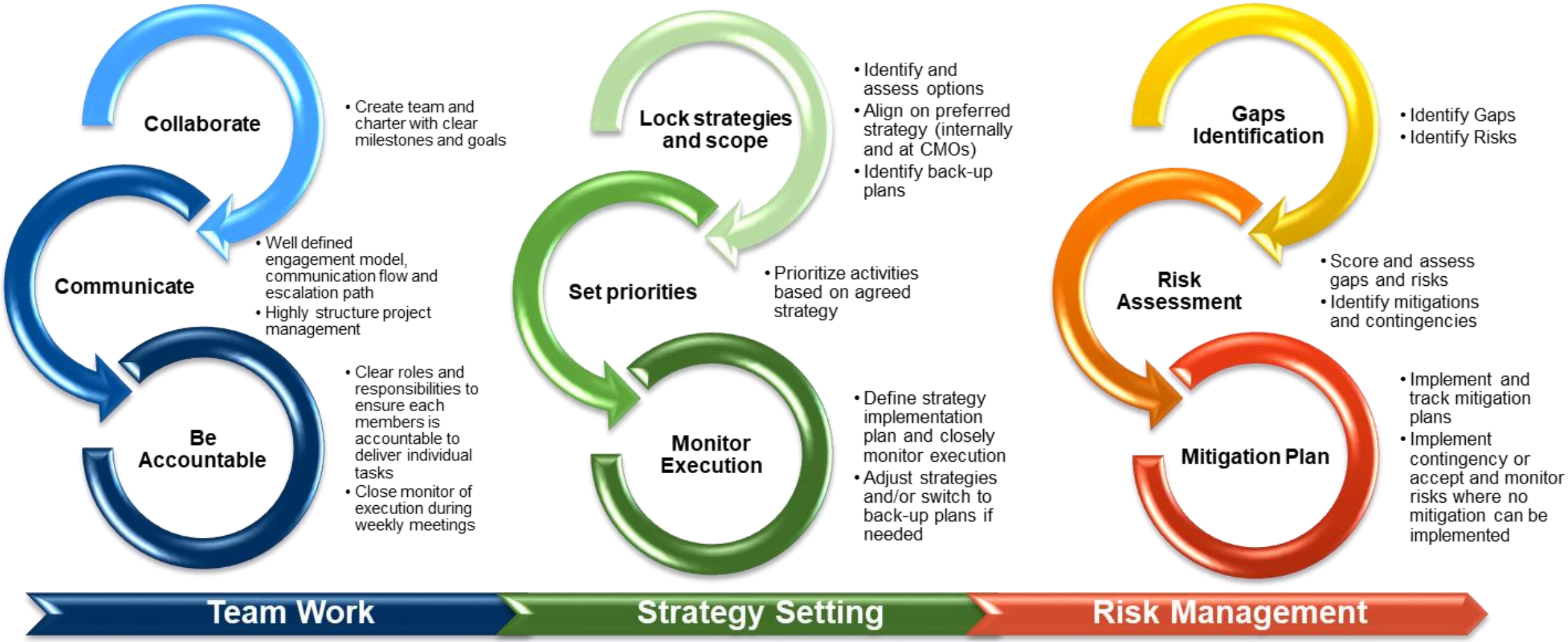
- **Business process used to ensure that all gaps are identified**
- **Knowledge exercise:**
  - **Transfers existing process knowledge**
  - **Identifies receiving site modifications needed to meet process requirements**
  - **Identifies required site studies to support process development**
  - **Defines TT scope of work and project timeline**

Knowledge Transfer Process

Pre Work	MaB/TaB	Follow up
• Primary Documentation • Process Transfer Document • Existing Manufacturing Procedures, Batch Records, SOP's • Facility Fit • Process Model • Commercial Process Description	• 2-3 Day Meeting • 10 -20 people • Detailed review of processes parameters and design • Identifies processes and facility gaps	• Identify all facility fit issues and rationale for making any suggested process changes • Determine potential cause/mechanism of failure and process control detections/preventions • Propose multiple potential mitigations, discuss pros/cons, and develop recommended actions • From options, define a preferred path forward for mitigation – Risk Assessment

identify key risks and mitigations





"IN THE MIDDLE OF DIFFICULTY LIES OPPORTUNITY." – ALBERT EINSTEIN