Production Transfer

How to ensure that the targets will be successfully met

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Eskişehir Turkey, 25th May 2012

a Novartis company

Agenda

- **What is Production Transfer in Pharmaceutical Industry?**
- **What to consider for Production transfer project?**
- **Evaluation: How a funnel process will ensure decision**
- **Business Functions / Roles & Responsibilities**
- **Key for success**
  - Incorporate lean principles into the transfer project & existing transfer protocols
  - Facilitate the flow of scientific knowledge
  - Discuss openly latest during kick-off
  - Risk Management – Some basics
  - Project Risk Matrix
  - Risk Assessment – Follow-up Plan
  - Sustain quality in a more effective and productive manner with lean
- **Take away**
  - Summary for successful Production transfer
  - Workload and amount of transfers
  - Transfer Process Re-designed

What is Production Transfer in Pharmaceutical Industry?

In short, production transfer in pharmaceutical industry is the move of manufacturing activities from one site to another site; this might concern a partial or complete move of manufacturing steps.

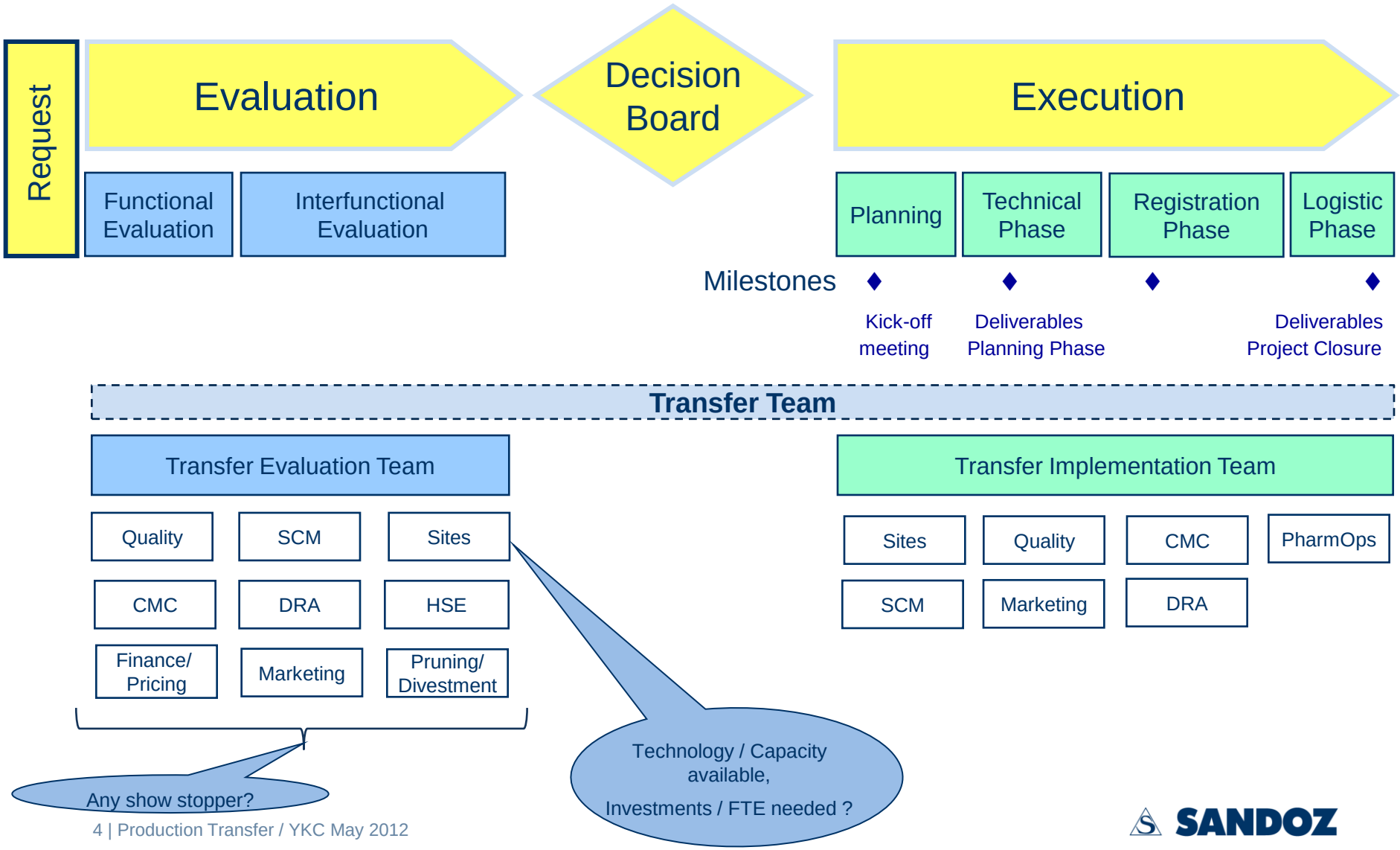
Generally the production transfers occurs at the following points:

After Development: Move from development scale to industrial scale production ⟶ LAUNCH

Not in scope today

Within the life cycle : ⟶ PRODUCTION TRANSFER for which the reasons can be very diverse (e.g. Capacity optimization, flexibility within manufacturing network, cost saving, market access....)

Production Transfer Process



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There are different phases during a transfer

Evaluation and decision phase	Planning/ preparation phase	Execution phase	Assessment / Post transfer phase
▪ Check feasibility (e.g. technical, quality, regulatory, HSE)	▪ Inform involved team members	▪ Perform analytical method transfer AMT	▪ Proof technology acceptance
▪ Elaborate options including business cases for decision committee	▪ Prepare kick-off meeting	▪ Perform manufacturing of feasibility and validation batches	▪ Define follow-up activities and closing criteria
▪ Decide	▪ More detailed assessments	▪ Perform other key technical activities (e.g. Comparative dissolution, Stability....)	▪ Approve reports
▪ Communicate decision, nominate manager , include in databases	▪ Prepare and approve protocols	▪ Perform the registration	▪ Close transfer
	▪ Share technical documentation	▪ Perform the change over plant	
	▪ Prepare readiness of receiving site		

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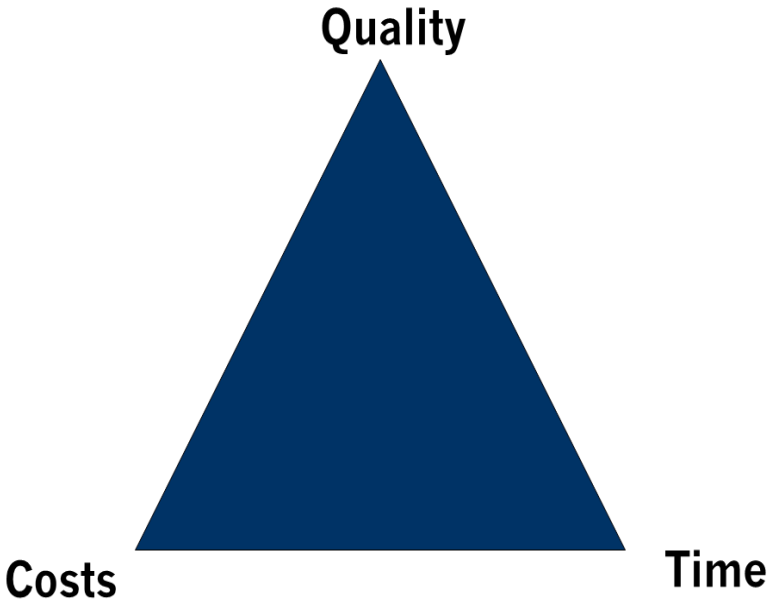
What to consider for Production transfer project?



- Normally there are 3 targets (restrictions).
- It requires experience to balance in the right manner.
- Risk management is an important tool to achieve this

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Project management tools are suitable for Production Transfer

Project

A project is a problem / task scheduled to be solved (Harvard PM)

Production Transfer

A product needs to be transferred from a Transferring site (TS) / Giving site (GS) to a Receiving site (RS) within a defined time

Link

Common principles

- A project / transfer plan will be elaborated and should be monitored until finalization
- During implementation we have to consider guidelines / permits
- Meet Customer expectations (internal / external)

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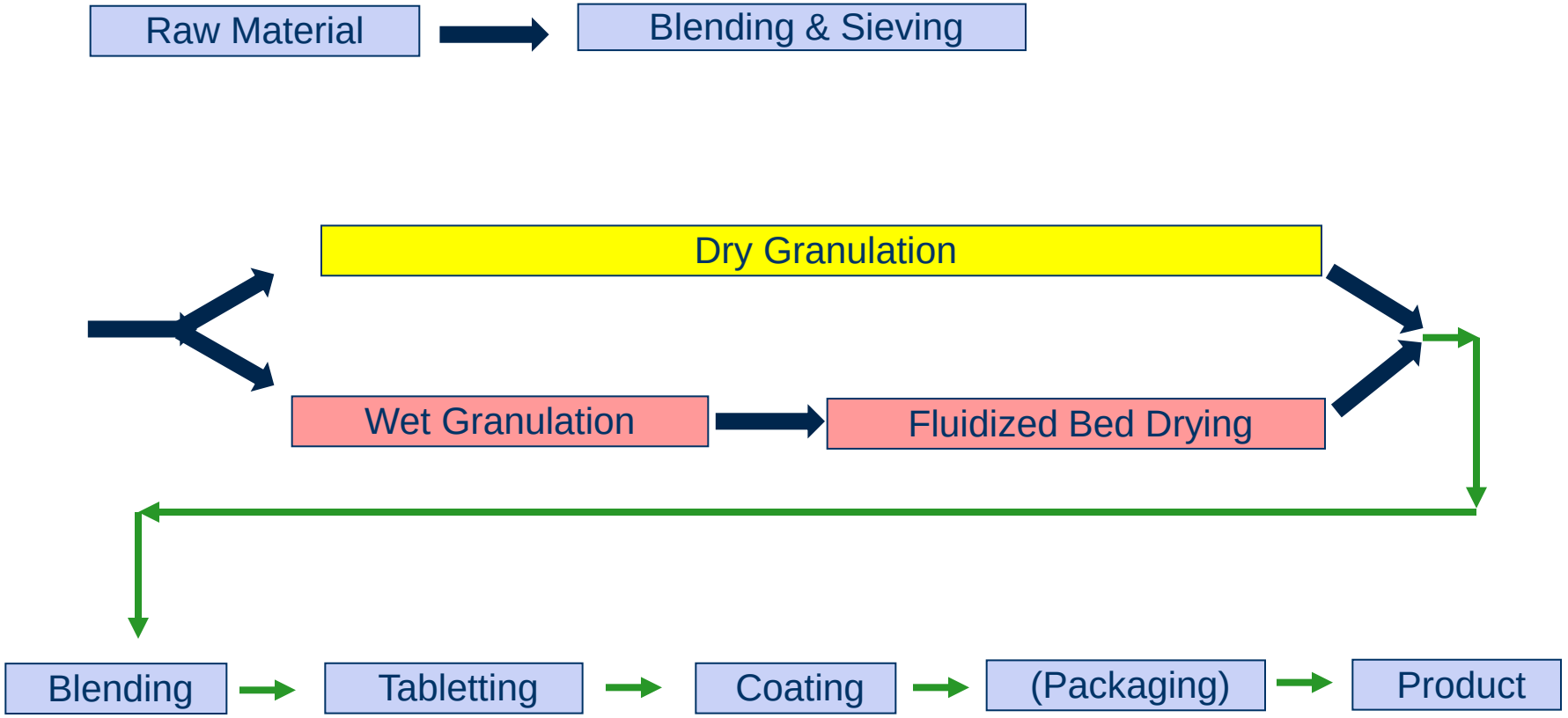
Production Transfer: e.g. Solid Tablet Processing



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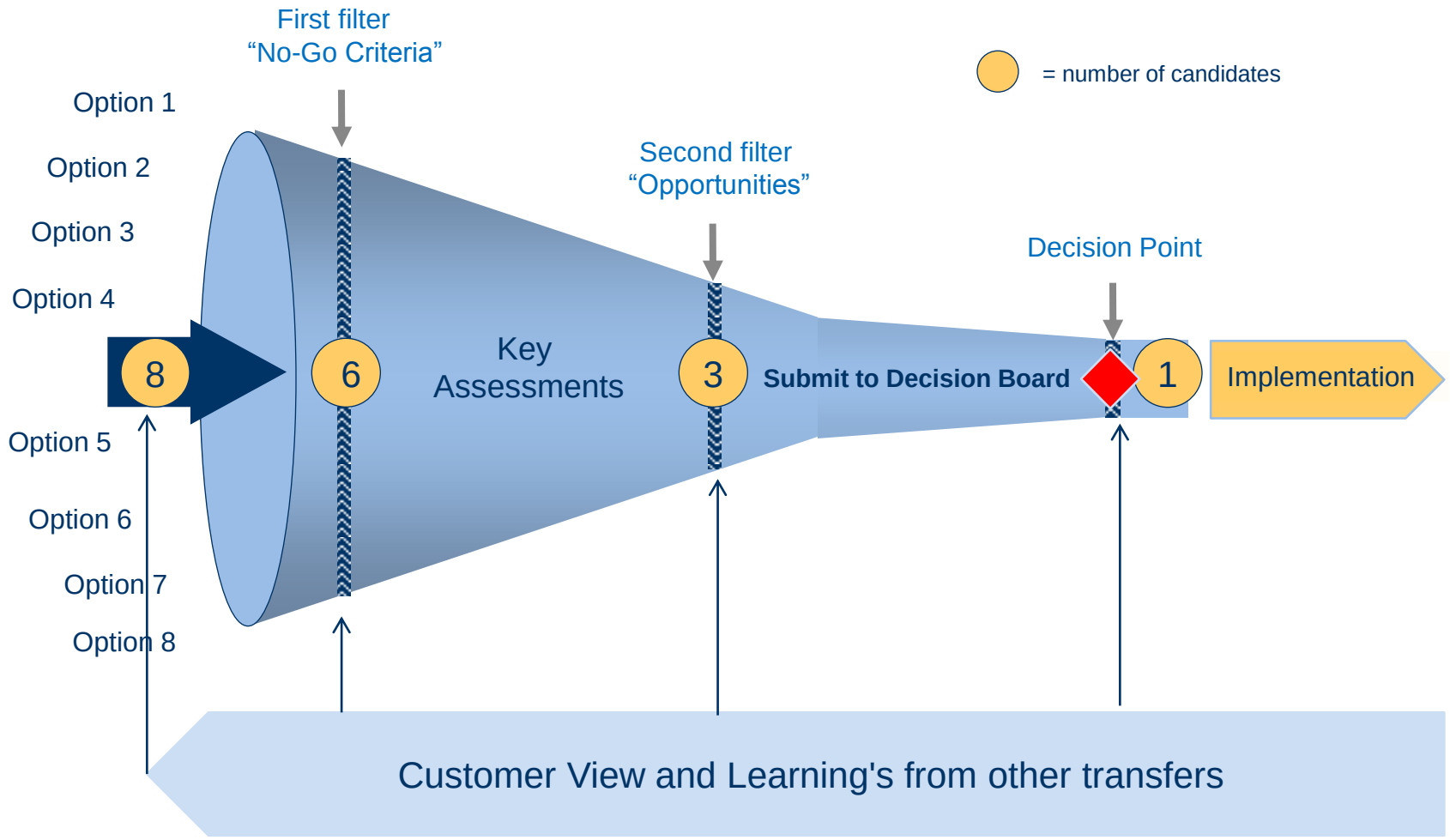
Evaluation: How a funnel process will ensure decision



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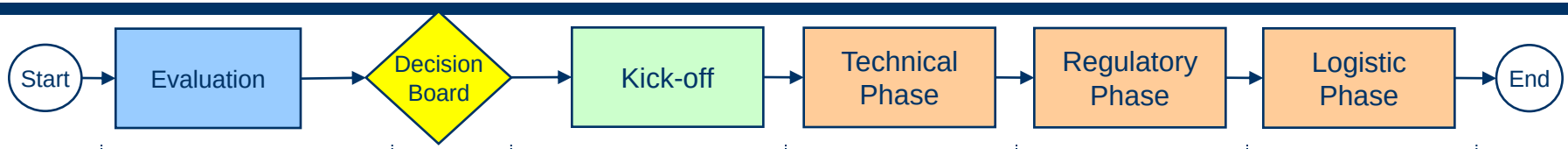
Business Functions / Roles & Responsibilities 1/2



Requester	Initiate requests by filling standard templates for proposals		Remains informed on the project progress			
Transfer manager	• Select the Evaluation Team for detailed evaluation • Summarize and compile comments from evaluation Team • Complete business case / Propose final recommendation to decision board		• Lead the end to end implementation of the project • Assemble the implementation Team, • Assess & communicate the Project scope and kick-off the project	• Lead the end to end implementation of the project • Approve extended project team and project plan (milestones and timelines) • Ensure the Project Management role • Close project / Capture Lessons learnt		
Giving Site	• Provide current manufacturing information on the product		Member	• Support the giving site with expertise.	Ad-hoc Member	• Agree on the ramp-down of supply
Receiving Site	• Provide information on capability and capacity		Member	• Prepare and execute the technical project plan • Update Milestones status (e.g. investment, validation, availability of key doc for CMC...) • Close Phase and Capture Lessons learnt	• Provide CMC with necessary data for registration file preparation	• Ensure the ramp-up of the supply
HSE	• Provide information on HSE concerns		Member	• Ensure the implementation of HSE principle	N/A	• Ensure the implementation of HSE principle with regards to transportation

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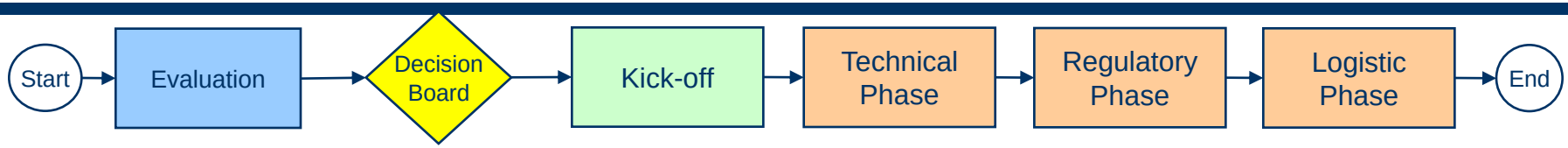
Business Functions / Roles & Responsibilities 2/2



Quality	• Provide information on the product quality status		Member	• Ensure the QA requirement are in place	• Ensure the availability and correctness of all QA document	• Ensure the proper release and compliance
SCM	• Provide information on the future supply set-up		Member	• Prepare future supply set up • Organize all inbound material necessary for Manufacture	Ad-hoc Member	• Execute the change over • Close Phase / Capture Lessons learnt
CMC	• Provide information on the technical regulatory requirement		Member	• Support and advice manufacture on regulatory concern	• Provide Tech Reg. document	Ad-hoc Member
DRA	• Provide information of Regulatory affairs consequences		Member	• Provide Regulatory Strategy & Time line: Type of submission and supporting technical documentation needed • Close Phase and Capture Lessons learn	• Proceed with submission • answer HAs question if any • Inform Team about the approval	Ad-hoc Member
Marketing (Incl. Div. & Pru.)	• Provide project impact on the markets		Ad-hoc Member	Ad-hoc Member	Ad-hoc Member	Ad-hoc Member
Finance / Pricing	• Support on financial items and provide impact on pricing		Ad-hoc Member	Ad-hoc Member	Ad-hoc Member	Ad-hoc Member

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Key for success: Incorporate lean principles into the project

- **Involve Customers** from the evaluation process until implementation
- **Encourage team work**: Empower transfer team leader(s) and members
- **Knowledge-management / Continuous improvement**
  - Involve experts from global functions / other sites
  - Encourage a feedback culture, e.g. speak-up, closing reports
  - Share Specific know-how and check-lists
- **Pull principle:** Receiving site has the lead. Exceptions 3rd party transfers (responsibilities cannot be delegated) and launches
- Use **pilot scale batches** to avoid write-offs/waste whenever possible
- **Mission and task setting during kick-off meeting** when team members and stakeholders will be aligned.
  - Maintain permanent communication within the team (Calls, e-mails...)
  - Capture agreements and share updates with all others by minutes

Key for success: Facilitate the flow of scientific knowledge

- Global Transfer Project Manager (GTPM) and Local Transfer Team Leaders (TTL) evaluate during start-up phase in which areas (e.g. QA/QC, HSE) additional experts from Global or other sites are required.
- Manage trouble shooting by involving experts on short notice
  - Global experts for Galenical manufacturing to ensure:
    - Learning's and expertise for specific topics e.g. tableting, coating
    - Checklists to avoid common obstacles e.g. avoid sticking during tableting
  - Global R&D experts.
    - Share learning's when small scale batches were manufactured or launches performed
    - Identify necessary parameters to be optimized during scale-up . Evaluate robustness?
- QbD (Quality by Design) – Quality risk management e.g. during handover from R&D to TechOps, living document, also applicable for site to site transfers
- Consult database with product specific development documents if available

Key for success: Discuss openly latest during kick-off

1. **Technical assement**
   Process evaluation and risks
2. **Regulatory assessment**
   Including Local / Global aspects
3. **QA / QC Aspects**
   Robustness of methods, GMP
4. **HSE Assessment**
   Product classification
5. **Sourcing**
   Local versus Global, suppliers reliability

Kick-Off meeting

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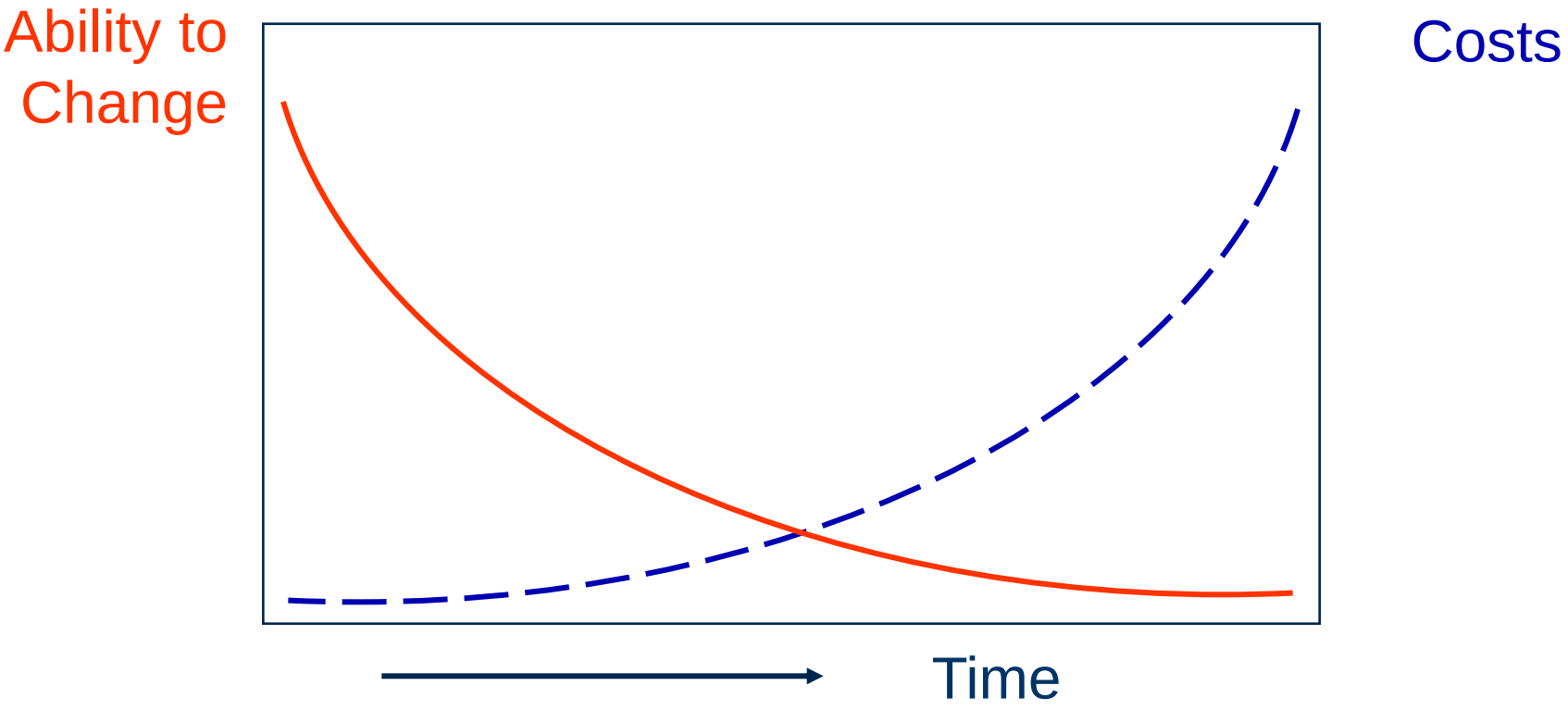
Key for success: The typical project profiles

Why front end loading is so important during evaluation and starting phase



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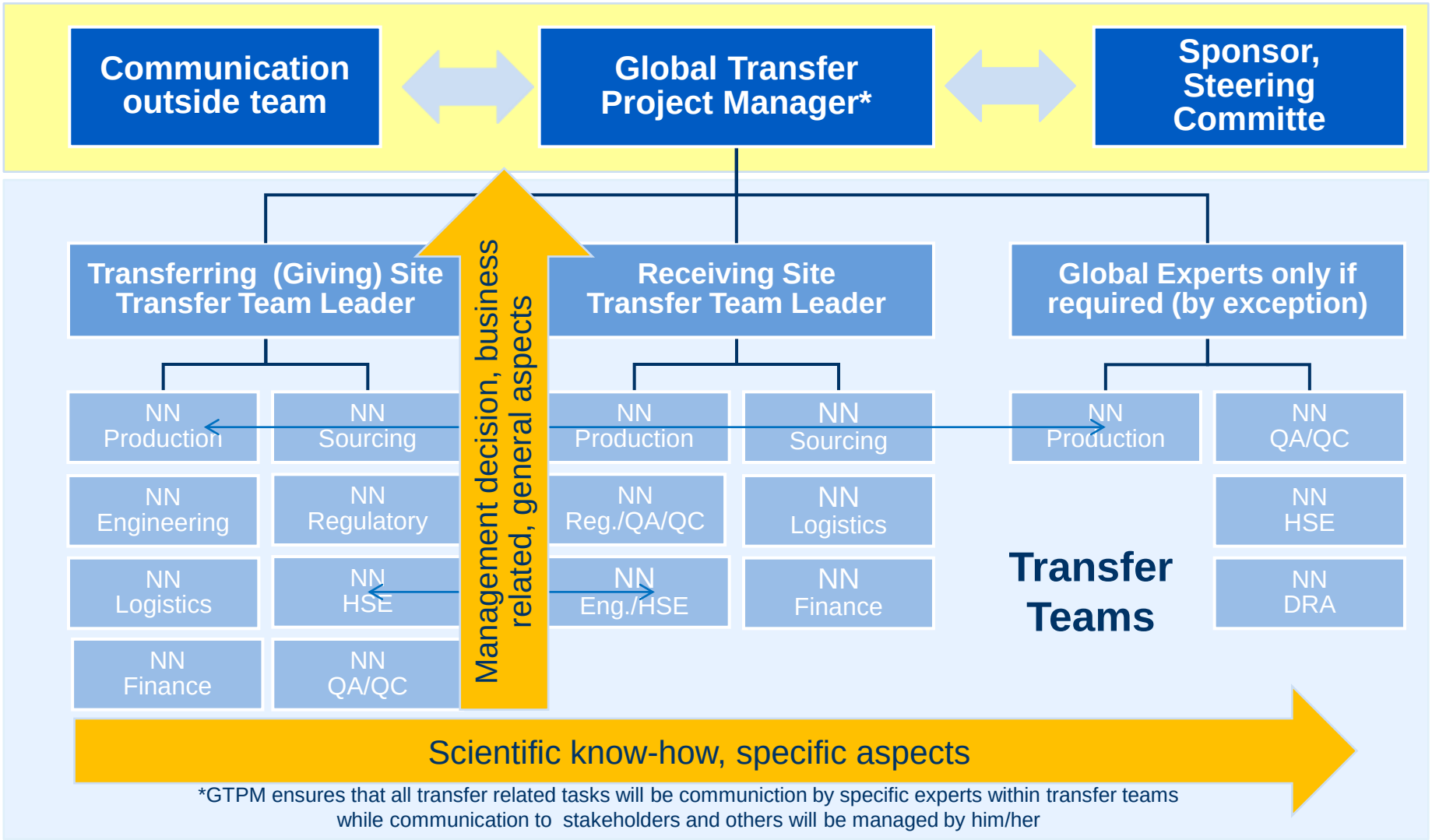
Key for Success: Define clear objectives and communication lines



*GTPM ensures that all transfer related tasks will be communiction by specific experts within transfer teams while communication to stakeholders and others will be managed by him/her

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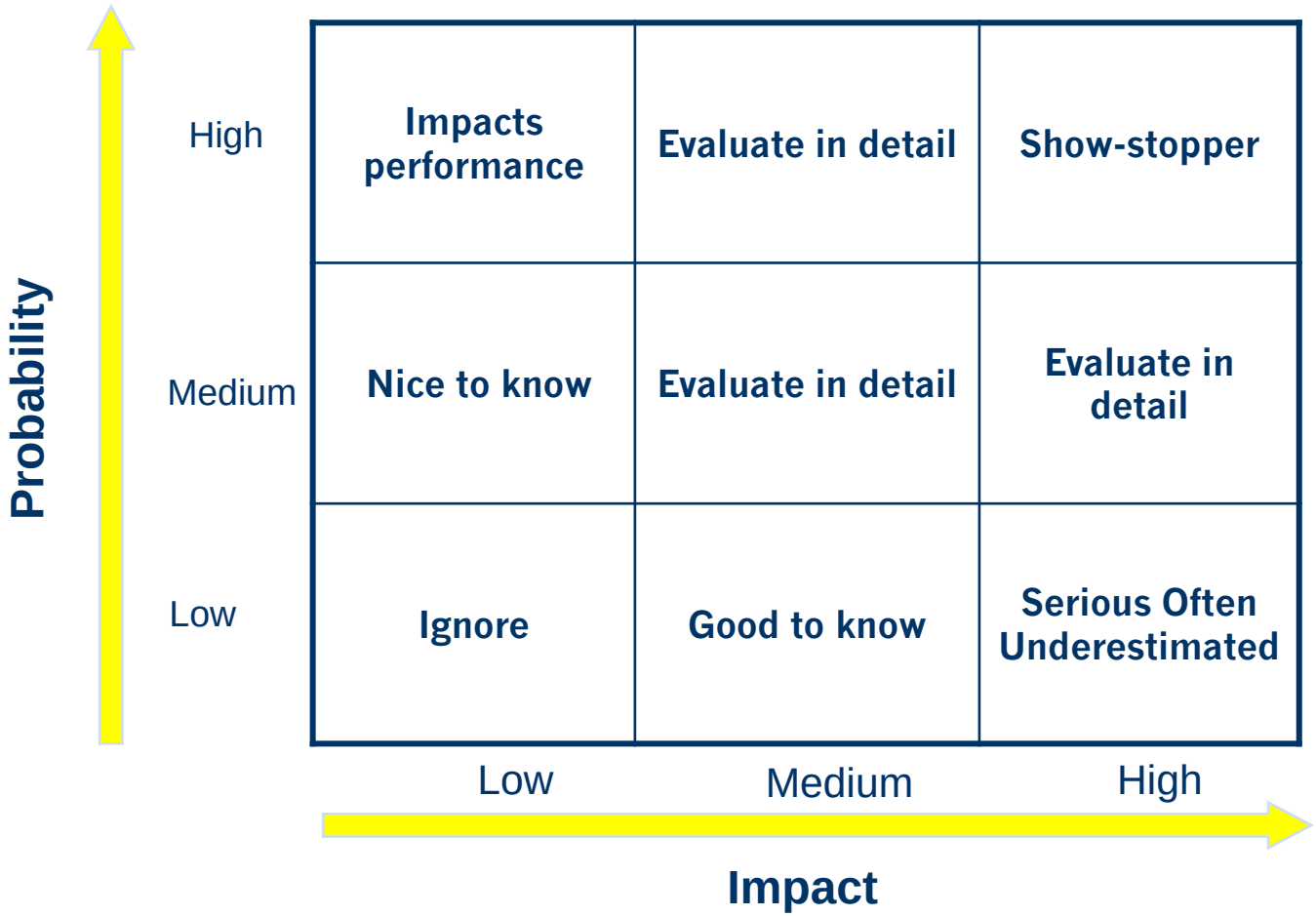
Key for success: Risk Management – Some basics

- Common Tool for HAZOP/HSE studies and investment projects
- How to handle: Talk with the team ..... Don’t hide
- Most decisions are risk dominated because there are often uncertain forecasts or data
- Minimize the risk of unexpected happens. Any manager can manage a project where nothing unexpected happens. Expect the unexpected!!!!
  - Deal with them
    - Avoid them
    - Shrink them
    - Contain them
    - Share them
    - Or pay somebody else to carry them (e.g. outsource, to be excluded)

Key for success: Project Risk Matrix

Elaborate a Project Risk Matrix with team and cluster the cases according to following scenarios



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Key for success: Risk Assessment – Follow-up Plan

Evaluate carefully the potential risks with teams, get their buy-in and ensure the follow-up plan

#	Risk	Impact (L,M,H)	Probability (L,M,H)	How to mitigate?	By Whom	Until When

Key for success:
Sustain quality in a more effective and productive manner

- One Global Operating Procedure GOP with defined Roles and Responsibilities
  - Mandatory for all transfers. Adaptations possible e.g. launches or 3rd party transfers (tasks can be delegated but not responsibility).
  - One decision process managed by the Decision Board. (e.g. @ Sandoz Global Product Allocation is the owner for all transfer related activities and is responsible to align with others).
- Global Quality is responsible for content and maintenance. Use an IT based change control system for change management
- Using a funnel process to come to one joint solution and to avoid doing re-work afterwards.
  - During evaluation phase several options will be assessed. Coming closer to the decision the number of options will be reduced. At same time more details will be evaluated.
  - During decision board meeting, preferred option and a few other will be reviewed.
  - After decision has been taken focus is on fast implementation and not to re-evaluate

Global Transfer Project Managers – Case 1

- They should not see themselves like this

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Global Transfer Project Managers – Case 2

- …. and should not be seen like this….

Take away – Key for successful Production transfer

- **Basic principles**
  - Involve of customers / stakeholders from early beginning (front end loading) to define overall tasks and mission
  - Empower local transfer leaders and teams whenever possible by using defined R&R's
  - Pull principle for implementation (if possible)
- **Facilitate the flow of scientific knowledge**
  - Ensure a knowledge management culture including learning's from what went wrong or could be improved. Do not misuse to celebrate achievements only.
  - Align experts having different expertise during kick-off and implementation
  - Share learning's with development .
  - Involve manufacturing experts (if necessary)
- **Reduce costs, risks and time related to project**
  - Risk management is a useful tool to identify hidden risks and to assess relevance. Based upon elaborate a mitigation plan. It will become part of transfer documentation.
- **Sustain quality in a more effective and productive manner**
  - One Global operating process in accordance with global QA
  - Defined sub-processes with clear guidelines referring to GOP
  - For decision taken choose one process with milestones (funnel process)
  - IT based change management system

Take away: Workload and amount of transfers

The workload and amount of transfers depend on many factors which will impact all together

Both highly experienced and committed teams at both sites
→ empowered teams , less interaction by global transfer project mngr.

Teams have good skills and committed to perform transfer → Only limited, regular updates with transfer teams required

Both teams are committed to follow agreed project plan and have standard level of experience → monitor progress according to plan

One of the site teams will not be committed, conflicts between some members → higher involvement required (mediator, ensure that team will stay focused and other team members not affected)

Unexperienced teams, issues, hostile transfer or general conflicts between teams → high workload for GTPM due to crisis management

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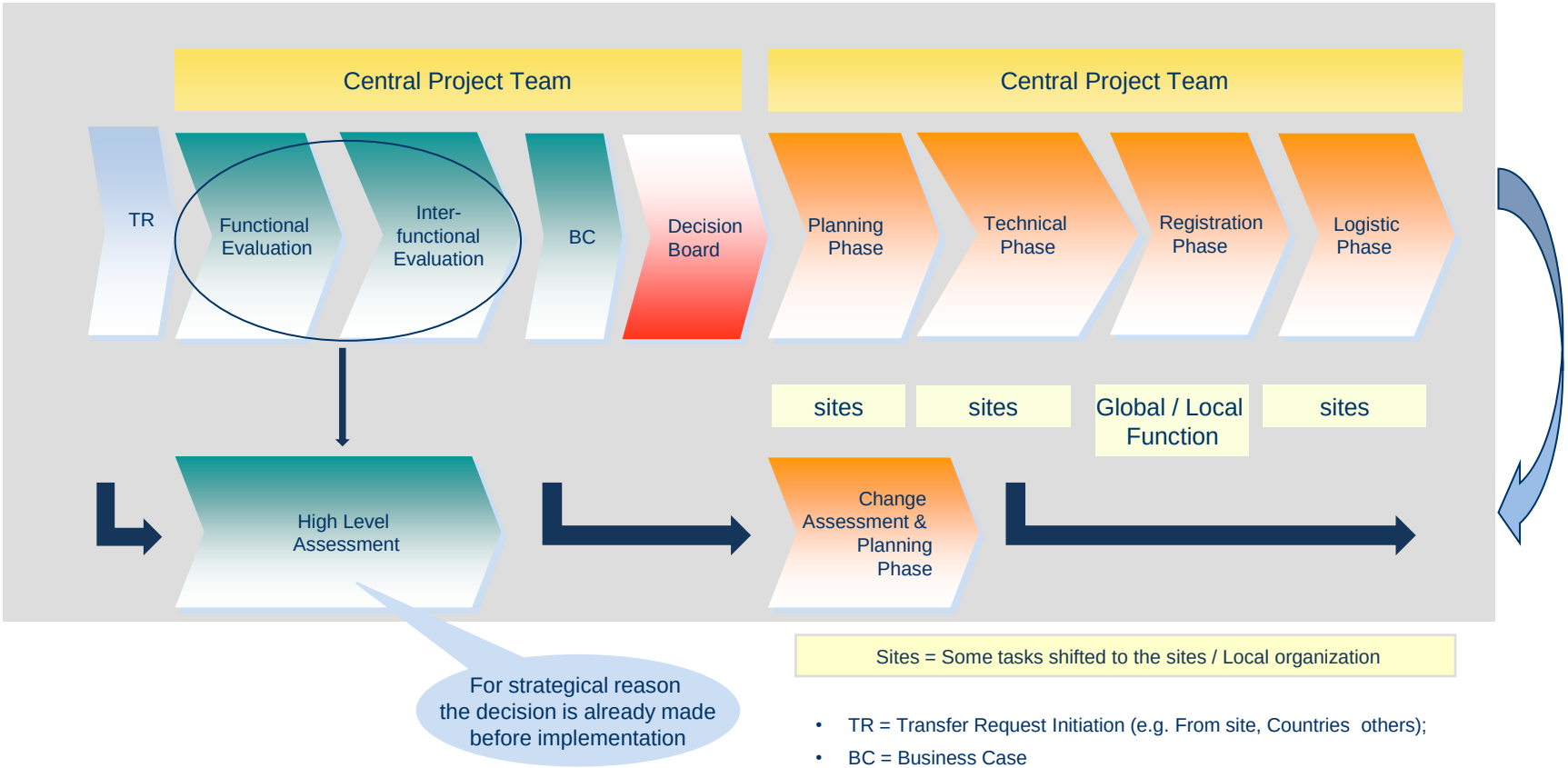
Take away: Transfer Process Re-designed

- Sequential process with partially duplicated activities... to a more streamlined process with more flexibility, parallelized steps and enhanced responsibilities ... and to even shorter timelines for a strategy driven transfer



- TR = Transfer Request Initiation (e.g. From site, Countries others);
- BC = Business Case

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Try to avoid this .... If it happened avoid next time.

Sometimes…..

Thanks for your attention and interest

And an hint to my colleague
Dr. T. Kiesser
who supports me in the preparation