

De-risking for Successful Development

An approach to increase Probability of Success

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Considering High Level of Risk within Development a De-risking Strategy is a « Must Have » to Increase Probability of Success

- Days of easy target and easy development are over:
 - High number of late stage failures (PhII – PhIII)
 - Complex and unknown etiology and MoA requiring clinical learning
 - Complex processes and products requiring tight controls
- Delay in Development projects decreasing their value and attractiveness
- Aggressive and unrealistic timelines leads to numerous assumptions and/or dangerous shortcuts in development and missing information
 - Increasing number of assumptions leads to unexpected and failing results
 - Missing information compromises success and registrability (i.e. RTF)
- High Risk/High Reward development strategies based on unproven assumptions translate in low Probability of Success of product registration

While Risks in Design and Execution of Development Plan are Understood; Risks with External Capabilities May Be Overlooked

- External Capacity /Capabilities usually selected as an attractive option to cover gap early in development:
 - Considered relatively low risk, short term and easy to implement
- However any choice and decision during development will be there for long time and engage you for the future:
 - From early phase to Registration and Supply
- External partner de facto long term partner, will be part of your file
 - Must be covered by an extensive contract
 - Consider external partnership as an extension of your internal capacity/capability and differently from a supplier
 - Need to be managed as internal with responsible, budget and controls
 - If not managed could become higher risk than internal option

De-risking Strategy will Secure Increase Probability of Success

Strategies and best practices for de-risking your Development

Risk with Design:

- Unproven assumptions without justification
- Missing key activities or studies
- Unrealistic timelines

- Identify and challenge assumptions
- Challenge activities and timelines
- Simulate outcome and gaps
- Identify risks and adapt plan with mitigation actions

Failure in Execution

- Unexpected or failing results
- Delay against plan
- Increasing cost / resources needs

- Perform active risk management
- Target increase Probability of Success
- Assess results and impact for next steps
- Organize active learning from failure
- Perform active Root cause analysis

Lack of Capabilities/Capacity:

- Rely solely on External competence
- Non alignment of Quality requirements
- Non Compliant operations for registration and supply
- Lack validation of supply
- Process non transferable/scalable
- Process not reproducible/comparable
- Capacity not sufficient for supply
- Process changed without control

- Contract covering short and long term responsibilities and engagement
- Resolve actively competence and compliance gaps
- Manage through "Man in the plant"
- Perform active risk management
- Review and approve all relevant documentations
- Manage transfer competence

Examples

- Process with specific IP and no contract in place, unique provider, cannot transfer - they manage you
- Facility used in early development non existing anymore or changed or non compliant
- Change ownership of CMO and/or lack of competence
- Compliance issues with CMO may put your company in a very difficult situation to be forced to recall your products
- Multiple requests made for Quality audits not satisfied
- Process changed and not transferred
- Request to invest in order to be compliant, validate process and/or write documentation for submission not in contract. Managing supply of material between different plant internal and external
- How to manage a CMO and technology you do not know or master? Get someone to follow up and manage it as this will be your product and process