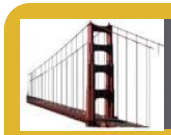

Bay Clinical
R&D Services

Target Product Profiles

An Essential Tool in Development and Strategic Management of New or Modified Drugs/Biologics/Devices

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What is a Target Product Profile?

- A Target Product Profile (TPP) is a summary of the drug development program described in terms of labeling concepts
- It is prepared by the all departments of the company involved in the development of the therapeutic or diagnostic agent
- Its submission to the FDA is voluntary but has specific benefits*
- The TPP is a "living document" evolving and maturing with increasing knowledge and experience

*The FDA has recently withdrawn its draft guidance on TPPs. However, elements of the TPP, basic principles and subcomponents such as the Quality TPP (QTPP) are still included in guidances on Quality by Design (QbD)

TTPs and the Pharmaceutical Industry

- Detailed TPPs have a key role in the pharmaceutical industry in Strategic Program Management (SPM)*
- TPPs explore various labeling scenarios
  - Target, Minimal, Optimal
- TPPs estimate (for each scenario)
  - Probabilities of Success
  - Development Costs
  - Personnel
  - Manufacturing
  - Market Penetration / Competitors

* Strategic Program Management is a series of practices and procedures, which characterize the extent to which an organization creates effective linkages between excellent project management practices and excellent business practices
Heerkens, G. (2007). Introducing the revolutionary strategic project management maturity model (SPM3)- PMI® Global Congress

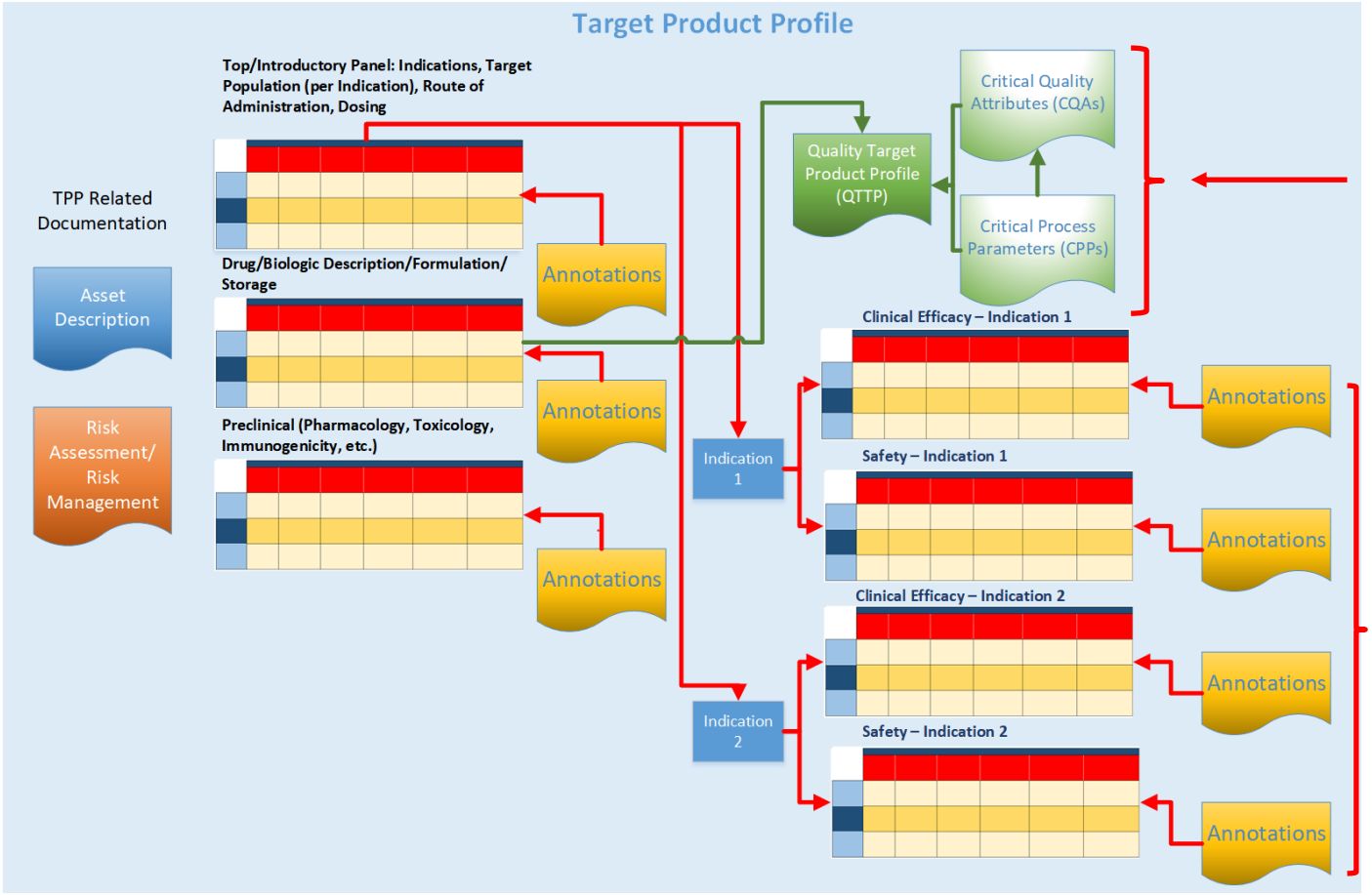
TPP and Quality by Design (QdD)

- Quality by Design (QdB) is a development methodology based on detailed scientific understanding of the test therapeutic agent (its properties and manufacturing process), has predefined objectives and employs effective controls and risk management
- Quality by Design principles are included in the ICH guidances Q8, Q9 and Q10
- These guidances deal mostly with the quality and risk management of the drug/biologic product. As such, there are provisions therein that address the Quality Target Product Profile (QTTP), an essential subcomponent of the TTP
- ICH and FDA are currently extending key elements of QbD to clinical trials.
  - Draft guideline E8(R1): General Considerations for Clinical Trials, May 2019

Assembly of an Industry TPP

- A common template should be used for all products, bringing consistency to the process
- A TPP is assembled for each product entering development and each new indication for an existing drug/biologic
- Input is elicited from various departments. Assembling a TPP is a team effort
- The owner of the TPP is usually the Project Manager who coordinates the activities of specific product development team
- The TPP constitutes an important evaluation tool in "gate reviews", if such reviews are enabled by the organization

Components of a TPP



Elements and utilization of QTTP are covered by the ICH Q8 Guidance

Annotations must be detailed and properly documented to provide a comprehensive explanation for the choices made in the TPP

TPP General Statement

Project Name	(Name)
Project Description	Summary description of the product
Project Category	Is the project is an additional indication for an existing drug or a new project?
Strategic Fit and Value	How well does this drug/biologic fit with the core expertise and capabilities of the company?
Value to Patients	What is the specific value of this drug/biologic to patients? Does it offer therapeutic, safety or ease of use advantages over existing or upcoming drugs/biologics
Company's competitive position	Does the company have a competitive advantage?
Company's IP position	Brief summary of the IP position regarding this drug
Rationale for success	Brief summary as to why the developing team believes that this product would
Factors for success	Brief statement as to the company's core competencies and market conditions that would drive a successful outcome
Key risk factors	Brief statement identifying possible risks
Consequences for not pursuing the project	What would happen if this project is not pursued?
Possible alternatives to this project	Are there any alternatives to this project?

TPP Description of Therapeutic Agent

	Description of Therapeutic Agent				
	Active Ingredient	Purity	Form	Formulation	Stability/Storage
Optimistic	=Target	Purity better than that of competing drugs	Form that improves treatment compliance	Formulation that increases stability without any safety concerns	Increased stability at room temperature
Target	Description of the Active Ingredient (AI)	Purity at the same range as competing drugs	Same as that of competing drugs	Same as that of competing drugs	Stability and storage same as that of competing drugs
Minimal	= Target	Purity lower than that of competing drugs, but without any effect on efficacy or safety	=Target	=Target	=Target

This particular TPP module can be substituted by the QTTP, if desired.
The QTTP will provide more information on certain parameters of the new drug (see slide 11)

- The above panel presupposes that the new agent belongs to the same compound class as preexisting or competing treatments
- If not, or if it is a drug in an indication previously served by biologics (or vice versa), then it needs to be redesigned accordingly
- Additional properties, such as the identity and concentration of contaminants or the utilization of any particular delivery devices, may be added to this description

TPP Summary of Efficacy

	Primary Indication				
	Primary Clinical Endpoint (s)		Target Patient Population	Route of Administration	Treatment Regimen
	Clinical Outcome 1	Clinical Outcome 2			
Optimistic	Meets the primary and a number of secondary endpoints that may result in claims	>Target Or =Target	>Target Or =Target	>Target (if more than the target routes are tested) Or =Target	> Lower doses and/or less frequent administration may provide advantages
Target	Meets the primary endpoint(s) of the pivotal study (or studies)	Provide entries if more than one primary endpoint	Target (Describe target population)	Target (Describe target route(s) of administration)	Target (Describe target regimen)
Minimal	= Target	= Target (if essential for regulatory success)	=Target Or <Target If successful in a more limited population	= Target Or < Target If the least desirable tested route is successful	> Higher dosing and more frequent administration than target that may still be acceptable

TPP Summary of Safety

	Primary Indication				
	Safety		Drug Interactions	Precautions	Contra-indications
	Clinical	Non-Clinical			
Optimistic	>Target if fewer and less severe AE profile Or =Target		>Target if fewer and less severe interactions Or =Target	>Target if no or fewer precautions Or =Target	>Target if no or fewer contraindications Or =Target
Target	Target safety is usually equivalent to the known safety of the same class or similar classes of compounds that have been approved	Laboratory or other findings similar to those observed for the same class or similar classes of compounds that have been approved	Interactions similar to those observed for the same class or similar classes of compounds that have been approved	Precautions similar to those observed for the same class or similar classes of compounds that have been approved	Contraindications similar to those observed for the same class or similar classes of compounds that have been approved
Minimal	= Target (<Target would be acceptable if risk/benefit ratio is favorable)	= Target (<Target would be acceptable if risk/benefit ratio is favorable)	=Target (<Target acceptability criteria should be explained)	= Target (<Target acceptability criteria should be explained)	= Target (<Target acceptability criteria should be explained)

Additional Elements of TPP

- The TPP may contain additional elements regarding:
  - Product design and formulation
    - Contaminants
    - Any delivery system associated with the drug
  - Projected dates of submissions, regulatory approval and launch
  - Cost of goods, pricing, market size
  - Target, optimistic and minimal conditions may be set for these elements

How to Assemble a TPP

- Utilize the following:
  - Define properties of the drug in preclinical development
    - Pharmacokinetics
    - Toxicology
    - Efficacy in animal models
  - Select target indication(s)
    - Structure a TPP for each indication that may require additional development
  - Examine approved claims of competitors (efficacy and safety)
  - Examine the competitive environment for compounds currently in development and likely to be approved in the near future
  - Elaborate on minimal and optimal profiles

TPP as a Strategic Planning Tool

- Clinical Development
  - TPP scenarios can be used for:
    - Design of clinical studies
    - Design of detailed timelines
    - Evaluation of risks and creation of mitigation plans
    - Estimation of the possibility of success
    - Estimate budgets/personnel
- Regulatory /Clinical
  - Estimation of likely approval dates in various geographies
- Manufacturing
  - Evaluation of manufacturing options/expenditure
- Marketing
  - Estimation of costs of goods
  - Estimation of pricing
  - Estimation of marketing campaign costs
  - Estimation market penetration (focus groups)

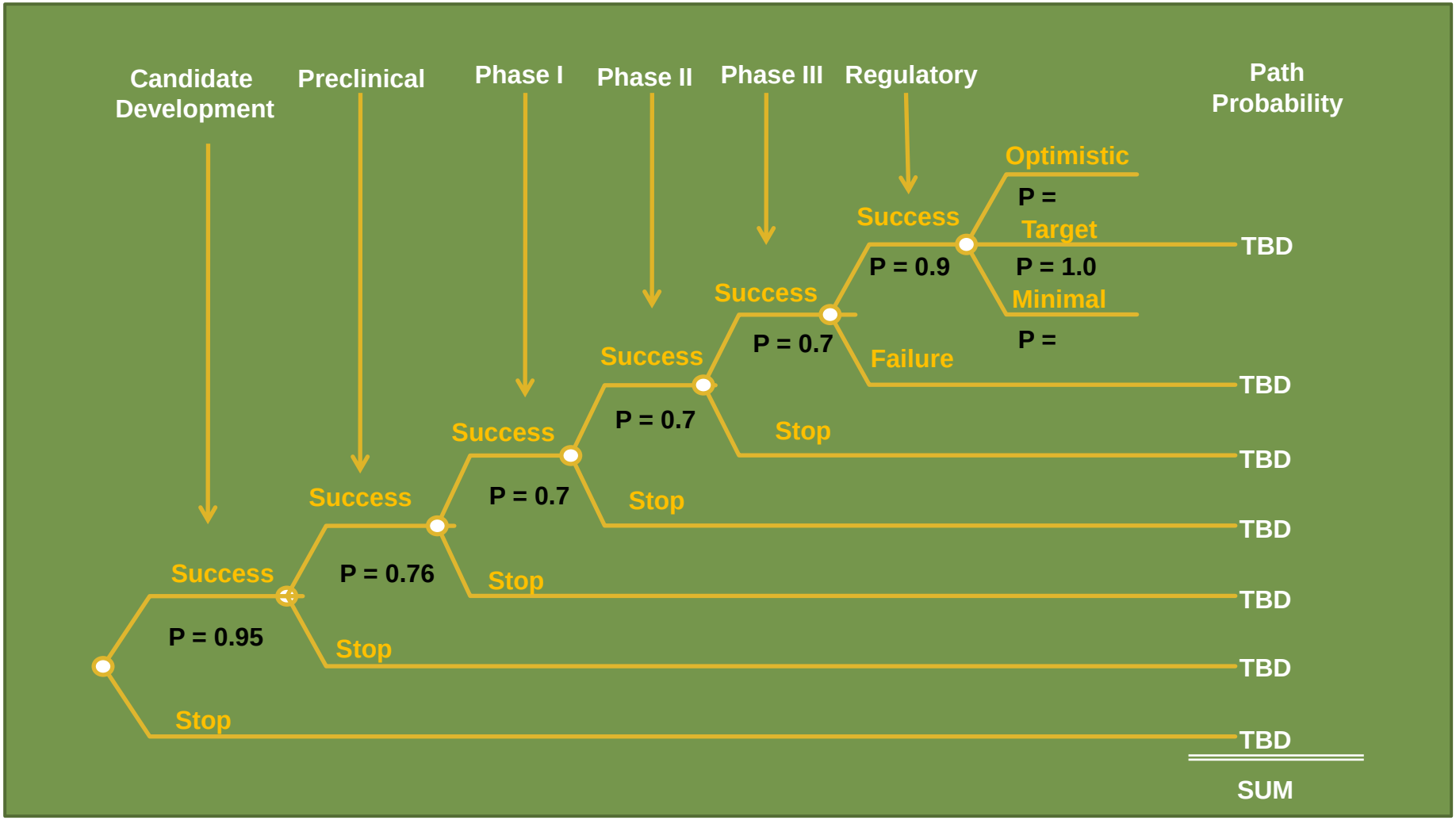
Utilizing TPPs in Development

- TPPs utilized correctly can:
  - Assess risks and create risk mitigation plans for all stages of clinical development
  - Assign a probability of success at each phase of clinical development and each indication targeted
    - Assumptions of probability of success at any stage of development should be explained and contrasted to industry norms
  - Promote a team-based approach
    - Compiling TPPs is a team-based activity that enhances collaboration among project team members and increases awareness of the project's critical issues throughout the organization

Risk Identification and Mitigation Plan (Clinical Development)

Risk #	Risk	Impact (1 to 5)	Risk of Occurrence (1-5)	Mitigation Action Plan	Ownership (Enter Appropriate Department)	Date for Action
1	Phase 1 study (Describe Risk)	1= minimal impact 5 = maximal impact	1= unlikely 2= possible 3= probable 4= likely 5= very likely	Enter mitigation plan (Note if the occurrence of the outlined risk leads to program discontinuation)		
2	Phase 2 study: (Describe Risk)	1= minimal impact 5 = maximal impact	1= unlikely 2= possible 3= probable 4= likely 5= very likely	Enter mitigation plan (Note if the occurrence of the outlined risk leads to program discontinuation)		
3	Phase 3a study (Describe Risk)	1= minimal impact 5 = maximal impact	1= unlikely 2= possible 3= probable 4= likely 5= very likely	Enter mitigation plan (Note if the occurrence of the outlined risk leads to program discontinuation)		
4	Phase 3b study (Describe Risk)	1= minimal impact 5 = maximal impact	1= unlikely 2= possible 3= probable 4= likely 5= very likely	Enter mitigation plan (Note if the occurrence of the outlined risk leads to program discontinuation)		
5	Regulatory	1= minimal impact 5 = maximal impact	1= unlikely 2= possible 3= probable 4= likely 5= very likely	Enter mitigation plan (Note if the occurrence of the outlined risk leads to program discontinuation)		

Example of Development Plan Risk Tree Analysis based on TPP



Summary

- TPPs are excellent tools for:
  - Planning the development of a novel agent
  - Obtaining accurate and helpful feedback from regulatory agencies
  - Estimating the project risks
  - Evaluating the possibility of success
    - Comparing possibilities of success of other product configurations and indications
  - Evaluating the total costs of development
  - Estimating the market opportunity
  - Retaining focus throughout the development process