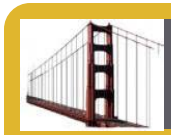

Bay Clinical
R&D Services

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 and TPPs

- The FDA strongly advocates the use of a TPP although it does not mandate it
- The FDA has prepared a Template included in a recent draft guidance [http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm080593.pdf]
- For each element of the label, the template proposes
  - **Target:** Language in the Package Insert that the sponsor hopes to achieve
  - **Annotations**:Summary information regarding completed or planned studies
  - **Comments:** To provide clarity
- The TPP template links each labeling concept to a specific study or other source of data

Selected FDA Responses to TPP Submissions

- Study Endpoint Reviewer
  - TPP used during endpoint review of a special protocol assessment
    - "The target label language in the TPP helped me evaluate and give the sponsor detailed-feedback on what else would be needed to support the desired labeling statements."
- Medical Reviewer
  - TPP submitted as component of Briefing Document for EOP2 meeting
    - "The Indications and Usage part of the TPP was helpful for us to provide additional advice on the necessary information to collect in Phase 3 to meet the companies proposals (if possible)."

Selected FDA Responses to TPP Submissions

- Division Director
  - TPP submitted Phase 1-3
    - “Success in drug development is, in some measure, like success in a sport. Take ice hockey as an example. A winning team knows not only where the puck is, but also anticipates where the puck is going to be. A sponsor develops a TPP to clarify where, ideally, the product is going to be.”

TTPs and the Pharmaceutical Industry

- Detailed TPPs have an increasing 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

Assembly of an Industry TPP

- A common template is used for all products
- A TPP is assembled for each product entering development and each new indication for an existing drug/biologic
- Input is elicited from various departments
- The owner 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

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 Summary of Efficacy

	Primary Indication				
	Primary Clinical Endpoint (s)		Target Patient Population	Route of Administration	Treatment Regimen
	Clinical Outcome 1	Clinical Outcome 2			
Optimistic	It is possible that secondary endpoints may result in additional claims	>Target Or =Target	>Target Or =Target	>Target Or =Target (if more than one route is tested)	> Lower doses and/or less frequent administration may provide advantages
Target	The primary endpoint of the pivotal study or studies	Provide entries if more than one primary endpoint	Target (Describe target population)	Target (Describe target route 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 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
    - Purity
    - Contaminants
    - Storage Conditions
    - Shelf Life
    - 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)

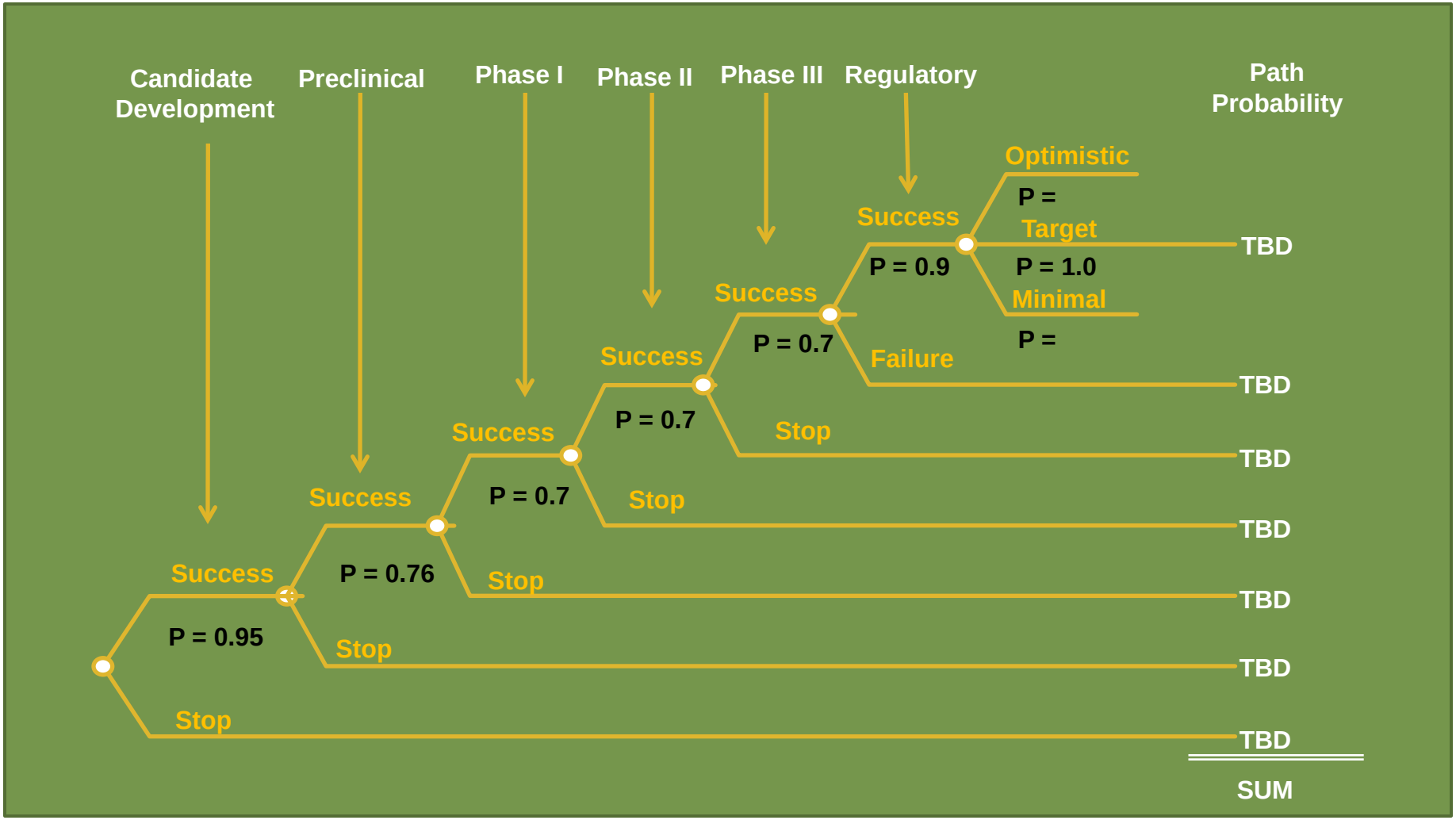
Utilizing TPPs in Development

- 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

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