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Research Article

TARGET PRODUCT PROFILE: AN ESSENTIAL TOOL IN DRUG DEVELOPMENT

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Abstract:

A Target Product Profile (TPP) is a strategic development tool which summarizes a drug product's development goals, ideally as expressed in terms of its labelling and promotional concepts. It is prepared by the all departments of the company involved in the development of the therapeutic or diagnostic agent. A systematically developed TPP can ensure alignment of objectives across company departments, accelerate development timelines, minimize development risks, and eventually lead to an optimal product. The Strategic Evaluation Framework augments the TPP with the additional information necessary for the assessment of a product's commercial potential. The Strategic Evaluation Framework constitutes the yardstick to track the developing product's actual clinical profile versus that necessary for commercial success and there by serves as the guide for strategic clinical development decision making.

Keywords: Pharmaceutical development; Strategic Evaluation Framework, Target Product Profile

1. TPP (Target Product Profile)(1)

A Target Product Profile (TPP) is a strategic development tool which summarizes a drug product's development goals, ideally as expressed in terms of its labelling and promotional concepts. The TPP document format correlates each development goal to planned or completed clinical testing and/or development activities. The TPP process early and consistently in product development discussion with the FDA maximizes the

efficiency and clarity of key development decisions ("Beginning with the end in mind"). TPP is a product of joint, pan-industry/FDA collaboration.

Background

In 1997, a Clinical Development Working Group composed of representatives from the FDA and pharmaceutical sponsors began discussions on ways to improve sponsor and FDA interactions in the drug development process.

The working group recommended use of a template that provides a summary of drug labeling concepts to focus discussions and aid in the considerate between sponsors and the FDA.

Experience with TPP-focused meetings with sponsors at the FDA has indicated that such documents can be useful .An efficient dialogue between a sponsor and the FDA during the drug development process can minimize the risk of late-stage drug development failures, increase the possibility that optimal safety and efficacy data are available in a timely manner, improve labeling content, and possibly decrease the total time involved with drug development.

1.1 Objective:[2]

- Modify TPP into a strategic development process.
- Clarify the pathway to introduce key development concepts (Biomarkers, PRO's, new disease states, product-differentiating attributes, etc).
- TPP's Value Proposition: "Do the planned or completed clinical activities support the labelling or promotional concept indicated?"

1.2 Purpose of a TPP:[1,2]

TPP is to give a format for discussions between a sponsor and the FDA that can be used throughout the drug development process, from pre-investigational new drug application (pre-IND) or investigational new drug application (IND) phases of drug development through post marketing programs to follow new indications or other considerable changes in labelling.

The TPP embodies the notion of beginning with the goal in mind. That is, the sponsor specifies the labelling concepts that are the goals of the drug step up program, documents the specific studies intended to support the labelling concepts, and then uses the TPP to assist in a productive dialogue with the FDA.

The ideal version of what the sponsor would like to claim in labelling guides the design, conduct, and study of clinical trials to maximize the effectiveness of the development program. Ideally, the final version of the TPP will be similar to the annotated draft labelling submitted with a new drug application (NDA) or biologics license application (BLA).

1.3 Attributes of a TPP[1,2]

The TPP provides a report of the overall intent of the drug development program, and gives information about the drug at a particular time in development.

TPP has planned according to the key sections in the drug labelling and associates drug development activities to specific concepts intended for inclusion in the drug labelling.

The sponsor can draft and update relevant sections of the template that are intended to support the specific statements in labelling. The sponsor can also use these updated versions of the TPP in preparation for discussions with FDA review staff to identify the most important development goals for the drug.

The TPP has a dynamic summary that changes as knowledge of the drug increases. For best possible use, we recommend that the TPP be updated regularly to reflect new information about the drug and changes in the clinical development program.

1.4 Advantages of a TPP [1,2]

A well-organized TPP can save meeting time for conversation of issues by eliminating the need for a sponsor's introduction to the history of the drug development program. Sponsors can also use a TPP to update their interactions with FDA review staff by individual TPP entries and sections that have been previously discussed from entries that are the current or future focus of a discussion.

This process can reduce the need to return the established entries, unless the development goals change or new scientific issues emerge.

The use of a TPP has especially important at pre-new drug application (pre-NDA) and pre-biologics license application (pre BLA) meetings, when it be able to help the review staff focus on a sponsor's goals and make sure previously discussed items have not changed when the sponsor submits an NDA. In a Briefing Document, a sponsor can use a TPP to quickly update new FDA or sponsor personnel who join the program.

A TPP enables a sponsor to pursue the desired outcome (i.e., approval and optimal labeling of a safe and effective drug) in the most efficient manner with respect to FDA interaction because all such interaction is focused on the explicitly stated goals of the development program.

2. TPP as a Strategic Planning Tool [3,4]

Clinical Development

TPP scenarios can be used for: Plan of clinical studies

Design of complete timelines

Costing of risks and creation of mitigation plans

Review of the possibility of success

Estimate budgets/personnel

Regulatory /Clinical Estimation of likely approval dates in various geographies

Manufacturing review of manufacturing options/expenditure

Marketing

Estimation of costs of goods

Review of pricing

Review of marketing campaign costs

Review of market penetration (focus groups)

3. Utilizing TPPs in Development [3,4]

TPPs utilized correctly can:

- measure risks and create risk improvement plans for all stages of clinical development
- Assign a possibility of success at each phase of clinical development and each indication targeted assumption 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

4. Benefits of the TPP Process [5]

- Patients, Healthcare Providers, FDA and Industry Can Benefit from TPP: TPP Leverages "beginning with the end in mind."
- Identifies and clarifies supportive clinical plans and/or development activities prior to executing pivotal trials ("Avoid surprises").
- Pathway of early, clearer dialogue and oversight for key development concepts (e.g. Biomarkers, PRO's, new disease states, product-differentiating attributes, etc).
- Coordinates FDA reviews over more than one office (e.g. combinational products).
- Creates an external process around which sponsors and the agency may optimize their internal procedures to create greater efficiency and contribute to lowering product development costs.

5. The Strategic Evaluation [6]

The primary goal for the Strategic Evaluation Framework is to ensure that pharmaceutical product development is driven by a marketplace need to facilitate strategic product go / no-go decision making and to enhance development programs so that they better integrate marketplace value drivers.

Moreover, the Strategic Evaluation Framework provides a clear format for intra-company project team progress discussions as well as serves to better communicate a product's value to investors, portfolio executive and senior administration. Building the framework around the FDA's TPP definition removes the need for multiple versions of a TPP for different purposes.

Thus, the framework incorporates the FDA's definition of the TPP, but adds to it to capture other essential parameters that place the patients, doctors and payers top-of-mind. No single part of the framework should be utilized in isolation, as it is the collective body of information that supports the decision-making function.

The Strategic Evaluation Framework functions through enforcing a constant benchmarking of the evolving product in development relative to the original characteristics of a therapy that would be both differentiated and solve some as yet unmet market need. The components of the Strategic Evaluation consist

1. **The Target Market Profile**

(TMP) is the foundation for the structure. Without accepting the market, any product profile will only be an unsupported guess at the capacity of the product to be successful. While the details may be enhanced as more is learned about he market, the key facts contained in the TMP should change only when there is a major market shift.

2. **The Strategic Target Profile**

(STP) is the vision for the product and is created based upon the unmet needs of the market as defined in the TMP. While staying within the realistic bounds of the company's core capability, it is the profile of the desired product to be built. Since it is important to maintain a consistent strategy, it should change only when an update to the TMP makes it completely necessary.

3. **The TPP is the profile**

At first, this profile will be the same as that in the STP. However, per the FDA's guidance, it will be updated as clinical data comes in to reflect the latest characteristics of the drug you want the regulatory authorities to grant.

To use the Strategic Evaluation Framework to guide the strategic clinical development decisions that set the foundation for commercial success, companies must estimate how the most likely drug candidate (the latest version of the TPP) fits against the original vision for the product (the STP).

In this comparison, it will quickly emerge how far the clinical trial results deviate from the original vision for the product (the STP), and therefore how well or how poorly the resulting drug will serve the market's unmet needs.

Flow chart of strategic assessment mention below.

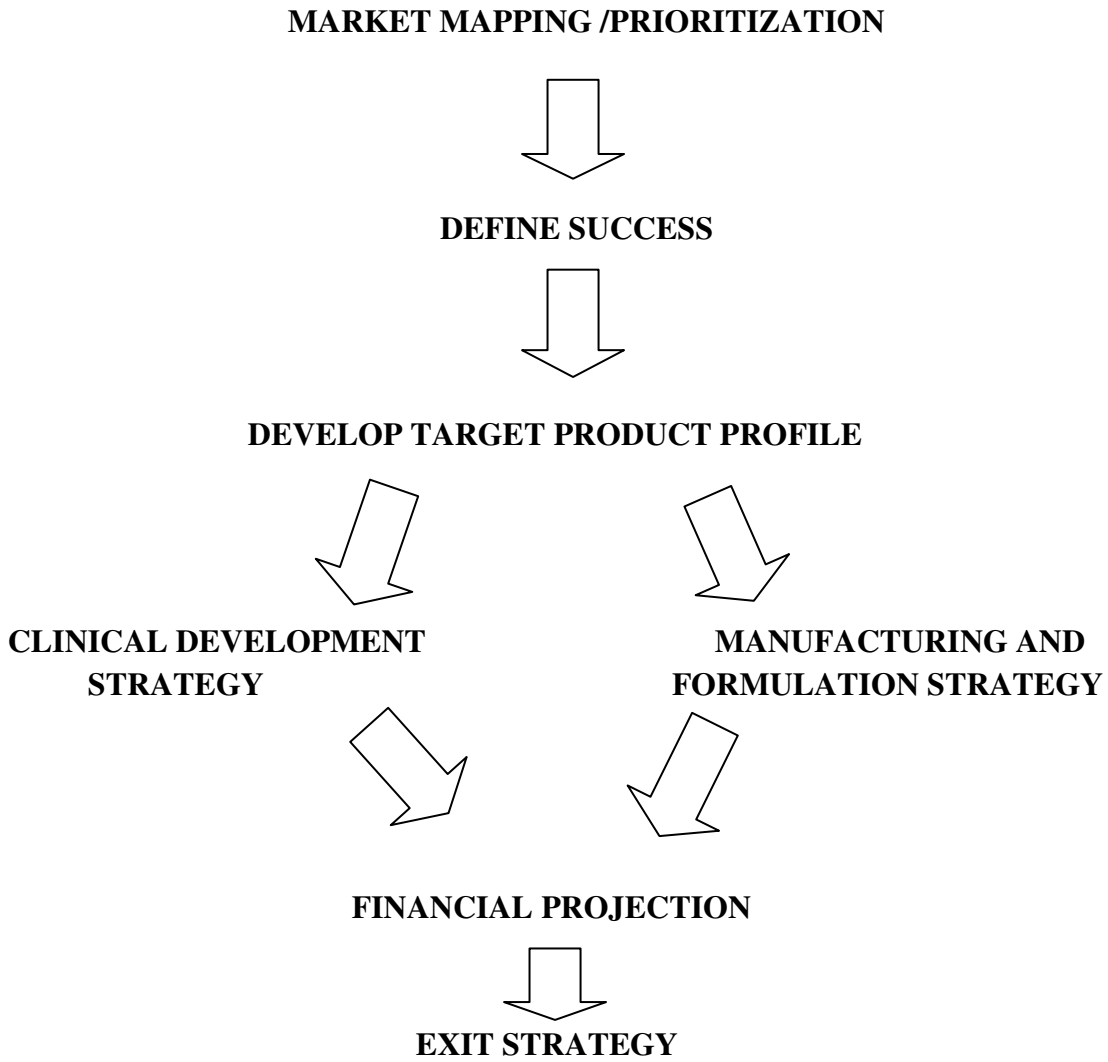

Figure 1: flow chart of strategic assessment.

Table-1: Key information contained within the strategic evaluation framework.

	Target Market Profile (TMP)	**Strategic Target Profile (STP)**	**Target Product Profile (TPP)**
Purpose	Captures all of the key information about the market	A vision for a product that will meet the needs of the market	A record of the drug that is most likely to launch
Content	Therapeutic area / disease Unmet needs Patient populations Drivers of use Competitive assessment Economic cost of disease	Target attributes (desired label) Value drivers Pricing Patient share Revenue – Profitability Pharmacoeconomics Investments (R & D, COGS,SGA) Cost of goods Licenses, Royalties	Indications and usage Dosing and administration Contraindications Warnings and precautions Adverse reactions Description Clinical pharmacology Clinical studies Storage and handling
Rigidity	Created before the STP or TPP. Details are updated as findings emerge, but core facts change only in response to major market events	Set at the beginning of clinical development and updated only when necessitated by changes in the TMP	Updated as clinical and pharmacologic findings emerge and in response to guidance from regulatory authorities

5. TPPs -Current Practice [6,7]

The FDA positioned its draft guidance on the TPP as facilitating better communication between the sponsor and the regulatory body because it summarizes the drug development program in terms of intended labeling content and claims. But while the structure of the FDA guidance facilitates efficient discussion with regulatory bodies, the product's profile usually does not embody the market insights necessary to determine the commercial viability of developmental programs.

For example, achieving a statistical primary endpoint in pivotal clinical trials may well be sufficient for regulatory authorization, but may not give a compelling addition to the therapeutic armamentarium: the result might yield a marketed product that does not deliver a good return on investment for the company.

The end of Roche's HIV program is a good example of choice making regarding the developing characteristics of actual products inrelation to the marketplace needs and anticipated return.

The FDA-defined TPP contains only limited anticipation of market needs in the form of promotional claims and is devoid of pricing assumption and other important information that is necessary to properly evaluate a drug' s value in the portfolio.

Returning to the Exubera example, had Pfizer accurately understand the marketplace wants for insulin products, hundreds of millions of dollars in improvement and marketing costs could have been re-allocated to other projects.

The authors do not suggest that Pfizer (or the other companies pursuing inhaled insulin) made an easily avoidable mistake – market needs have to be anticipated many years in advance.

However, this example is provided to demonstrate the consequences of misreading the market needs, and hence the importance of gauging them as accurately and early as is possible.

6. Drug Development process: TPP [7,8]

One of the most important considerations during the early stages of the development of a new medicine is to develop a Target Product Profile (TPP). This TPP can be based upon the headings of a Summary of Product description and give the company's ideal characteristics for the product, e.g. target indication, pharmaceutical form, route of administration, shelf life and storage characteristics.

This document is important because it can be re-visited throughout development to consider whether the company still has a product which will be suitable from a authoritarian, industrial and patient point of view.

For example, a company is developing a new migraine treatment which patients will be expected to take home and self administer as needed, it is likely that the TPP will reveal the ideal that the product should be a tablet or capsule to be taken orally and stored at room temperature. Whenever development it becomes apparent that the product can only be formulated as a liquid which must be administered by injection and stored at -80°C, then

clearly the company may decide that they do not have a commercially viable product and development may be terminated.

In order to assist companies developing new medicines, many guidelines are accessible by the regulatory establishment in Europe and the US, and globally approved guidelines are also available developed and published under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

These guidelines cover many scientific and regulatory aspects of the manufacture and non-clinical and clinical testing of medicinal products. They are often precise to particular therapeutic indications, for example diabetes, HIV infection or osteoarthritis, or type of product - biotechnology products or new chemical entities (NCE).

This focus of the guidelines on therapeutic indications and type of product is main because it means that early in development judgements can be made as regards which guidelines are applicable to a specific development programme.

It be essential to understand this because whilst regulatory guidelines are not officially binding, they do represent the agencies' current thinking on particular topics and any deviation from the guidelines must be justified.

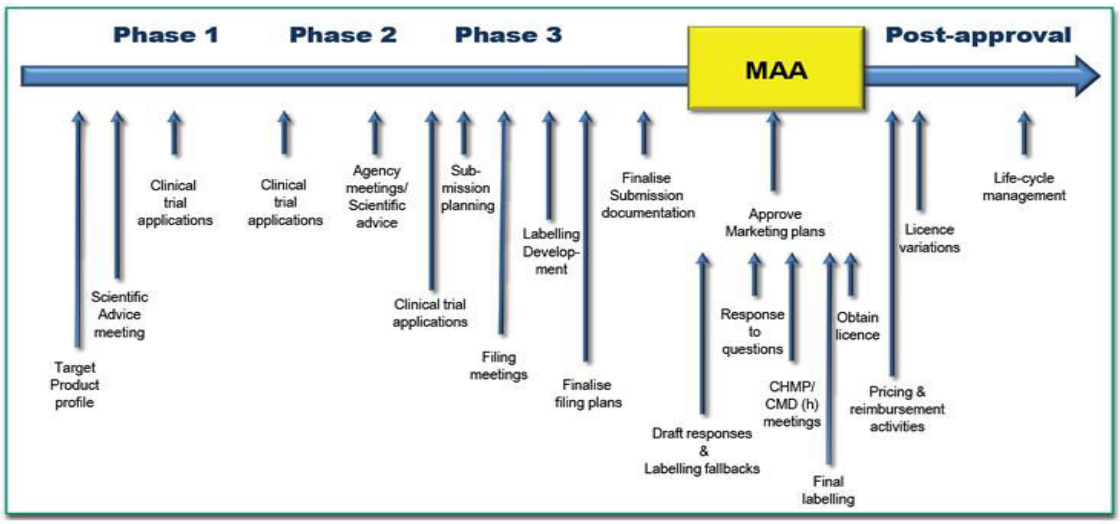

Figure 2: Regulatory interactions throughout the development process.

Example of TPP

A hypothetical antifungal agent about to enter Phase 1 studies was used. Existence an early stage compound, the final dose is still to be determined. For the development scientist, this leads to indecision as to what the eventual formulation concentration will be and possibly whether the compound is adequately soluble.

Table-2: Commercial TPP for a Hypothetical Antifungal Agent About to Enter Phase 1 Studies.

Product Attribute	Wants	Musts
Drug-related		
Indication	Treatment and prophylaxis of systemic candidiasis	Treatment of systemic candidiasis
Route of administration	IV	IV
Dose range	50–100 mg	<300 mg daily
Product-related		
pH	pH 5–8	Greater than pH 3.5 and less than pH 9.5
Packaging type(s)	Glass bottle and plastic bag with ability to be hung	Glass bottle or plastic bag with ability to be hung
Storage conditions	Room temperature	Room temperature (long term and in-use)

The example contains a number of instances where the desired product attribute differs from the true requirement. For example, it can be popular for advertising to launch in both a plastic bag and a bottle. Still, the TPP captures the true necessity, which in this case is just one package type.

Litheness has also been built in to the TPP. For example, at this stage in improvement, it cannot be clear if a solubilizing agent such as a cyclodextrin is required. Because the use of a cyclodextrin can need a technology license, the potential impact of the license on cost of goods sold (COGS) is noted under "Freedom to Operate."

Conclusion:

Drug and other Health Care Discovery/Developments involve complex processes requiring integration from beginning to FDA Approval. Target Product Profile is an integrator and communication tool. The earlier the Target Product Profile is used, the greater the possibility for successful development. The Strategic Evaluation Structure as per a scaffold that addresses explicitly the many functions and uses for product profiles, and the need to focus on the marketplace and individual customer value rather than on product attributes alone. Collectively, the components of the Strategic Evaluation Framework help guide the strategic clinical development decisions that set the foundation for commercial success.

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