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Target Product Profiles in Drug Research and Development – What are they and what are the benefits

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INTRODUCTION

TPPs are descriptions of key features needed in a new treatment for a disease and are used to guide and drive drug research and development. They can save time and aid communication with regulatory agencies, they can provide direction for drug development programmes, they can help to stop inappropriate drug development and save resources, they can point the way to the critical experiments, and they can summarize drug profiles to varying stakeholders. As we shall see, TPPs have different meaning and structure dependent on usage. Here we intend to explore and clarify.

TPPs can be broadly divided into 3 related forms

- Aspirational. A fixed description of the essential attributes of a treatment for a disease, derived from a wide ranging understanding of the disease in question, the medical and commercial opportunity, the regulatory hurdles, any real or potential competitors, the access and re-imbursement environment, and the goals of the developing organization

- Emerging. As the drug undergoes trials its properties are revealed. This will describe the likely attributes in terms of indication, patient population, efficacy, safety, adverse events, dosage and administration as data becomes available through experimentation and trials and the performance of the treatment becomes clearer. This will inevitably have a shorter term focus, and will change as the drug moves through development

- Regulatory. The desired labelling concept and goals for the treatment in development, targeted during the development and regulatory process for the drug. This facilitates regulatory interactions during the drug development process by outlining the desired labelling and driving the discussion on the trials and data needed to support those claims

Each of these are useful to different groups of stakeholders, they can be used as an internal document to define and guide drug development within commercial organizations, they can serve to advertise the necessary profile for a treatment for a disease that a public funding group is seeking, they can be used to define data needs and hence clinical trial design for regulatory groups, or they can be used to showcase the performance of a drug in order to attract development funding from commercial backers

It is not essential that any of the TPPs described are developed for a new drug, but they serve to streamline the development process, clarify communication and make best use of resources. Also TPPs do not deny a science led development strategy, rather they are there to provide a broad working construct with essential key attributes. As such they should be not seen as a process barrier – rather they should support serendipity, optionality and adaptation. Indeed, with an unexpected discovery in an existing project, ATPPs can be developed which reflect the new disease area or patient population which could be treated

In the next section to this discussion, we intend to explore each of these TPPs in turn. We will take a detailed look at their purpose and goals, and examine what information and guidance should be included for each, and at each stage of development. There is no fixed template for TPPs, but we will provide some examples as to what has worked well for each of the categories outlined above.

Aspirational TPPs (ATPPs)

ATPPs provide the context for and set targets along a range of key criteria that are required to be met for a new treatment. They are constructed with the needs of patients, physicians, payers and the developing organization in mind and thus require an in-depth understanding of those needs. They are intended to be fixed, and will not change as the properties of any new treatment become known. In this way they set out the aims of a drug development programme and act as a guide to focus efforts and set targets.

The key requirements for the treatment may not be expressed through efficacy and safety alone. For example, the treatment may be needed to reduce the number of days of hospitalized per year, it could provide a more stable formulation that permits flexible transport and storage, it could lead to less frequent dosing which provides improved compliance, or it may deliver a reduced potential for abuse. These key criteria will be built through a detailed understanding of patient, payer, physician and market needs and could include:

- Product vision
    - Therapeutic area
    - Indication
    - Unmet need
    - Key benefits that the treatment will provide
    - Patient population
    - Patient pathway
- Positioning
- Competition
- Efficacy profile
- Safety and tolerability profile
- Dosage, duration and regimen
- Formulation
- Target price and prescriber

Ideally ATTPs need to be fixed and stable over a number of years as they serve as a long term guide for research and business development groups. Thus the time horizon of an ATPP is typically 5 to 10 years, but in practice they should be reviewed and updated at regular intervals to reflect changes in the commercial and medical environment. If there are critical time factors (ie a competitor nearing launch) then this time line would be detailed and provide a basis for decision making given the progress of the competitor. They can also signal trends in disease areas and where new treatments may be needed in the future.

ATPPs lay out the critical elements that need to be demonstrated. It is also good practice to describe the minimally acceptable level of the key criteria that must be reached, and if any of those criteria are critical, non-negotiable or not subject to trade-off with other criteria. This guide can help set the hurdles during development and speed decision making when results of studies are known.

ATTPs can also serve to build company strategy in terms of which disease areas they wish to focus on now and in the future. They can highlight any gaps in the current portfolio and guide not only internal research organisations but align business development search and evaluation activities.

Emerging TPPs (ETPP)

As a drug moves through development its properties, activity and effect on disease are revealed. ETPPs are used to summarize these aspects for the drug given the current understanding of the drug's performance and how they align with the critical elements of the Aspirational TPPs.

ETPPs typically describe the value critical aspects of the drug from the developer's perspective - which may be the potential usage and uptake in patients for a commercial drug developer, or how the drug can enable access to hard to reach neglected diseases from a not-for-profit drug developer, or even how the approach may drive the science in a new area and foster innovation from a more academically focussed developer. ETPPs should cross reference the critical requirements of the ATPPs, unless the drug in question is in a new and unexpected area where no ATPP exists. Some examples of the elements of ETPPs are:

- Efficacy and toleration profile
- Number of hospital days saved
- Stability data for the formulation which will enable access to difficult to reach geographies
- Performance in a specific patient population
- Dose reduction due to use in combination therapy
- Regimen and dosage advantages
- Manufacturing advantages
- Bacterial resistance versus other antibiotics

Some of these elements might be known – for example the results of a phase one trial may reveal the safety in healthy volunteers. But other elements may be yet to be established – for example efficacy in a general patient population may need to be determined in a phase 3 trial

ETTPs can quickly describe a drug in development and its intended profile. Hence they are a way of advertising the product and its "unique selling points" to a potential partner when it comes to funding the next stage of development.

For a commercial drug developer ETPPs can also drive a valuation. Eg by showing how the new drug will be used and uptake in a particular patient population this can lead to a forecast of patient numbers and ultimately to a valuation taking into account market share, access, pricing, and cost of sales. Depending on the stage of development of the drug some attributes may not be fully established fully as described above. But by considering what is known (ie through early clinical data) and by taking into account a range of possible outcomes of these unestablished attributes a range of value can also be developed. As the drug progresses and more is known, this value also becomes clearer and less uncertain. The very best ETTPs will lay out the acceptable trade-offs between the critical criteria, and those criteria where no trade-off is possible

Comparing ETPPs to ATPPs can lead to a discussion concerning the probability of the meeting the critical criteria of the ATPPs, and hence a plan of how to resolve those questions by doing the right experiments, and efficient use of resources in the phases of drug development

Regulatory TPPs (RTPP)

RTPPs describe the aims of a drug development programme in terms of labelling concepts. They can be used by regulatory agencies to quickly see the claims the developer is aiming for with a new drug and therefore the data, experimentation and clinical trials needed to support these claims from the regulatory perspective.

An RTPP is a valuable reference document that helps the drug developer and regulatory agency understand the entire drug development process, from pre-investigational new drug application (pre-IND) through post-approval programs to pursue new labeling claims or indications. An RTPP is not a necessarily a fixed description of the aims of drug development, but may change as more becomes known about the nature of the drug under development.

Possible sections of an RTPP could include:

- Therapeutic area
- Indications and usage
- Patient population
- Dosage, dosage form and administration
- Claims and labelling
- Clinical pharmacology
- Proposed clinical programme and data to be provided
- Toxicology programme and data to be provided
- Contraindications and drug interactions
- Adverse reactions
- Warnings and precautions
- Potential for abuse
- References

A well-organized RTPP enables the drug developer to make best use of resources through focused interactions with regulatory agencies. It can also help to:

- Ensure the alignment of data collection and trial end points with regulatory requirements
- enable the timely collection of safety data
- improve labelling content
- potentially reduce the time to patient

However, care must be taken with RTPPs. They can certainly enable the regulatory process, but may not lead to successful drugs from the developer's perspective. Careful referencing of the ATPP should be made to ensure that the developer's critical objectives for the drug are being met, or experiments are being designed and data collected to test whether the drug can meet these objectives.

Here we have described TPPs in terms of 3 different forms to aid understanding of their different uses and forms and who they be most useful for. It is possible to use only one TPP to cover most of the aspects of the 3, but this can lead to confusion, delay and inefficient use of resources. In the next section we discuss ownership, governance and key messages.

OWNERSHIP, GOVERNANCE AND KEY MESSAGES

Clear ownership of TPPs is essential to high functioning drug development organizations. Within profit seeking drug development groups Aspirational TPPs are usually owned by the commercial divisions and can be competitively sensitive documents. With not for profit groups and drug development sponsors ownership is generally in the medical domain and are often outward facing to attract development partners. Emerging TPPs are best owned by a commercial/development partnership in a commercial organisation, or a medical/development partnership is a not for profit group. Regulatory TPPs are best owned by the Clinical and Regulatory functions.

ATPPs and ETPPs can be described as a communication and discussion mechanism between commercial or medical groups outlining disease treatment gaps or other opportunities in the marketplace and research groups describing what a new discovery could mean in terms of its potential to address disease

In high performing organisations the development of ATPPs will be a cross functional effort across research, clinical, pharmaceutical sciences and commercial organisations. They can form a context for the discussion on the merits of new drugs and treatments as they are developed, or reviewed from external sources.

ATPPs fit into company strategy as they lay out what kind of treatments the organisation looks to develop in which disease areas. There is therefore a link to the current portfolio where gaps are highlighted and any shortcomings of drugs in development are made clear. ATPPs can align the business development organisations in their search and evaluation efforts to source external treatments. ATPPS require regular review and updates as market conditions change, regulatory requirements shift, or competitors appear.

For drugs in development ETPPs need to be cross referenced to ATPPS by governance at least annually, and at major milestones eg clinical study read-out. This also insures that the development project continues to align with company strategy.

Key Messages:

- Recognizing the different types of TPPs and how they are used reduces the potential for mis-alignment of objectives within organisations
- High quality, widely understood, and regularly updated TPPs enable clear decision making in the drug development process and can lay out research and business development strategy
- TPPs enable valuation and prioritisation of not only drugs and treatments in development, but also the highlight disease areas most in need of treatments
- They can drive discussion for the optimum development path and hurdles
- TPPs enable effective collaboration across functions

In summary, it is useful to think of TPPs in terms of the three different types mentioned here and an understanding of them may go some way to clear up potential confusion. Good TPPs support communication, can guide the research and business development efforts of drug developers, and are one step to high performing pharmaceutical organisations.

ABOUT THE AUTHORS

Graham Finch BSc BEng MSc

Graham leads the VPA POEM (opportunity evaluation) practice and is providing strategic and analytical guidance to Research and Development and Business Development investment decisions. He has a background in asset and portfolio strategy, commercial analysis and valuation, business development search, evaluation, due diligence and deal terms for licensing and acquisition, market and customer analysis, investment and risk analysis.

Nick Brindley MSc

Nick has a wide experience in a variety of roles from manufacturing and QC to European marketing as well as in commercial development. He has worked at all stages of product development, from working with Research scientists on pre-development compounds and programmes through phase 2 and 3 progression to pre- launch, and across most therapy areas. He was commercial site head on two R&D sites of a global pharma company and has also been responsible for Licensing & Development projects across a number of therapy areas in his various roles. Nick brings a wealth of commercial experience and expertise in the assessment of potential product value and designing development programmes to help achieve that value from both labelling and P&R consideration.

Mike Florence PhD MBA

Mike Florence is part of the VPA Executive Associate Group and heads the VPA OpEx practice. He has many years' experience in Pharmaceutical and Chemical industries delivering step change improvements and projects across manufacturing, supply chain, Research and Development and marketing companies. Mike is a winner of the European strategic risk award for building risk and lean into portfolio management and a sustainable business cycle. Previous roles include Global Project Manager accountable for leading cross functional teams to deliver large and complex portfolio of projects to decision points on time and budget.

Pauline Stewart-Long BSc PhD

Pauline has many years' experience in the pharmaceutical industry with roles in clinical research, project management and portfolio management. This includes managing drug development projects in several therapeutic areas and all phases of development as well as being a portfolio director responsible for a portfolio at a major pharmaceutical company. As VP of Global Project Management she had a significant line management role as well as leading a major change initiative to define the practices and processes associated with the implementation of an enterprise project management system across R&D and is now sharing her insight with a variety of companies.

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