Target Product Profiles

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What You Will Learn

- The Target Product Profile (TPP) and its importance for clarifying objectives in the drug product development pipeline
- Practical strategies for developing and maintaining an effective TPP throughout different development stages
- How to leverage the TPP to speed decision-making and bring the drug product to market

The Target Product Profile

The TPP is the summary from an information gathering process started at the beginning of the project by the drug development team to **guide product development** towards desired characteristics

- Captures the key attributes of the product
- Identifies gaps in current knowledge
- Provides a clear roadmap to reach project goals

The TPP is a **living document** that changes throughout the course of the drug development process

The Drug Development Team

Discovery

Clinical/ Medical

Marketing

Regulatory

CMC (Chemistry, Manufacturing and Controls)

The TPP Format

Attribute	Must/Minimum	Want/Desired
Patient Population	Human adult patients	Human adult patients
Maximum dosage form size	Size 00 capsule	Size 1 capsule or smaller

Building A Preliminary TPP

General categories to consider:

- Indications and usage
- Dosage and administration
- Pharmacokinetics
- Final product considerations

- What disease/condition is targeted?
- Who are the target patients?
- Where is the target market?

Requirements for the TPP are specific to the development phase

Building A Preliminary TPP

General categories to consider:

- Indications and usage
- Dosage and administration
- Pharmacokinetics
- Final product considerations

- How is the dosage form administered?
- What is the dosage strength?
- What is the duration of treatment?
- What should dosage form look like?

Requirements for the TPP are specific to the development phase

Building A Preliminary TPP

General categories to consider:

- Indications and usage
- Dosage and administration
- Pharmacokinetics
- Final product considerations

- What is the mechanism of action?
- What are the pharmacokinetic requirements?
- How and where is the drug absorbed?

Requirements for the TPP are specific to the development phase

Building A Preliminary TPP

General categories to consider:

- Indications and usage
- Dosage and administration
- Pharmacokinetics
- Final product considerations

- What are the stability requirements?
- What are the packaging requirement?
- What are the manufacturing requirements?

Requirements for the TPP are specific to the development phase

Building A Preliminary TPP

Determine phase of drug product development

- Develop a New Chemical Entity (NCE)
- Match an existing product (generic product)
- Improve an existing product

Define the primary project objective

- Determine what is marketable/approvable
- Demonstrate bioequivalence
- Determine what needs to be improved and how to improve

Building a TPP for an NCE

Primary Goal: *Determine what is marketable/approvable*

- What is the patient population?
- What is the target market?
- What is the treatment duration?
- Where is the administration location?

TPP to Develop an NCE

Attribute	Must/Minimum	Want/Desired
Patient population	Human adult patients	Human adult and pediatric patients
Target market	US, EU, Japan	US, EU, Japan
Route of administration	Oral	Oral
Administration location	Home	Home
Number of formulations	2	4
Dosing frequency	Twice daily (bid)	Once daily (qd)
Treatment duration	Chronic	Chronic
Release rate	Immediate Release	Immediate Release
Type of formulation	Solid (tablet or capsule)	Solid (tablet or capsule) for adult, Liquid (solution or suspension) for pediatric
Formulation strengths	15 mg and 30 mg	15 mg and 30 mg for adult 1 – 5 mg for pediatric
Number of formulations per dose	≤ 2 tablets/ capsules	≤ 2 tablets/capsules for adult ≤ 3 mL for pediatric
Maximum dosage form size	Size 00 capsule	Size 00 capsule for adult 3 mL volume for pediatric
Stability/storage of formulation	36 months at 25®C/60% RH	36 months at 25®C/60% RH
Formulation packaging	Blisters	Blisters for adult Reusable bottle with dosing spoon for pediatric

Gaps Identified

- Liquid formulation feasibility
- Drug solubility
- Solid formulation feasibility
- Feasibility of high dose

Building a TPP to Match an Existing Product

Primary Goal: *Demonstrate bioequivalence*

In the generic development phase, many of the key questions normally asked during development of an NCE TPP will have more defined answers.

Therefore, attributes in this phase need to be defined in relation to the similarity of generic product to the reference product

- How similar does the product need to be to the existing product?

TPP to Match Existing Product

Attribute	Must/Minimum	Want/Desired
Patient population	Human adult patients	Human adult patients
Target market	Brazil	Brazil
Route of administration	Oral	Oral
Administration location	Home	Home
Number of formulations	1	2
Dosing frequency	Every 12 hours	Twice daily (bid)
Treatment duration	Acute, 14 days	Acute, 14 days
Release rate	Extended release	Extended release
Dosage form release profile	Similar to reference product in vitro dissolution testing results (Need to establish dissolution method and criteria)	Equivalent to approved reference product in vitro dissolution testing results (Need to establish dissolution method and criteria)
Type of formulation	Uncoated tablet	Film coated tablet
Formulation strengths	100 mg	100 mg and 200 mg
Number of formulations per dose	≤ 4 tablets	≤ 2 tablets
Maximum dosage form size	≤ 1g	Similar size to reference product
Manufacturing Process	Commercially available and precedented in Pharma	Use equipment at manufacturing facility, direct compression preferred
Stability/storage of formulation	2 year shelf life at Room Temperature (15 - 30°C)	3 year shelf life at 30°C/75% RH (same as reference)
Formulation packaging	Blister	Transparent blister

Gaps Identified

- Formulation Components
- Formulation Composition
- Film coating
- Use of direct compression
- Feasibility of high dose
- Stability

Building a TPP for an Improvement Upon an Existing Product

Primary Goal: *Determine what needs to be improved and how to improve*

- What needs to be improved?
- What are the motivations for improvement?
- What are the known limitations?
  - Is therapeutic window known?
  - C_{max} specifications?
  - C_{min} specifications?

TPP to Improve Existing Products

Attribute	Must/Minimum	Want/Desired
Patient population	Human adult patients	Human adult patients
Target market	Global	Global
Route of administration	Subcutaneous	Subcutaneous and intramuscular
Administration location	Hospital	Hospital
Number of formulations	1 fixed dose combination	2 fixed dose combinations
Dosing frequency	Single dose	Single dose
Release rate	Immediate release	Immediate release
Type of formulation	Injectable liquid	Injectable liquid
Formulation concentrations	1 mg Drug A and 1 mg Drug B in 1 mL	1 mg Drug A and 1 mg Drug B in 1 mL 5 mg Drug A and 5 mg Drug B in 1 mL
Injection volume	300 µL	300 µL
Type of formulation	Solution, sterile	Solution, sterile
Preservative	Acceptable levels of standard, precedented preservative(s)	Preservative-free
Stability/storage of formulation	Stable for 2 years under refrigeration (2-5°C) stable for 1 month at room temperature	Stable for 10 years at room temperature
Formulation packaging	Liquid in glass vial, use syringe to dose	Liquid filled syringe with exact dose volume

Gaps Identified

- Stability of Drug A with Drug B
- Feasibility of high dose
- Feasibility of preservative free formulation
- Injectability
- Product stability and packaging

Next Steps

Use the TPP as a roadmap to fill gaps in current knowledge

Design experiments geared towards:

- Addressing project challenges
- Meeting critical product attributes

Remember the TPP is a **living document** and should be revisited and revised as new information is received

Revising the TPP: An OzmoCAP® Case Study

- Compound X already an immediate release (IR) oral dosage form for twice-daily (bid) dosing in human adult patients

- **Goal**: Develop a once-daily (qd) extended release (ER) oral product
  - Reduce dosing frequency for patient compliance
  - Blunt C_{max} to decrease side effects

Compound X Preliminary TPP

Attribute	Must/Minimum	Want/Desired
Patient population	Human adult patients	Human adult patients
Target market	Global	Global
Route of administration	Oral	Oral
Dosing frequency	Twice daily (bid)	Once daily (qd)
Release rate	Extended release	Extended release
Dosage form release profile	**???**	**???**
PK parameters	Cmax ≤ Cmax of IR tablet	Cmax < Cmax of IR tablet

Revising the TPP: An OzmoCAP® Case Study

TPP identified need to understand if Compound X had absorption in the gastro-intestinal (GI) tract

- Developed oral extended release (ER) osmotic capsule, OzmoCAP® dosage form
- Dosed into dogs to evaluate ER absorption *in vivo*

OzmoCAP®

- Oral extended release (ER) osmotic capsule
  - Release drug over an extended period – not enteric (delayed) release
  - Range of drug release durations controlled by capsule
    - Release independent of drug properties
    - Release independent of pH
    - Release independent of position in GI tract
  - Fast development times for feasibility studies in animals
  - PK sampling combined with imaging to directly correlate drug absorption with position in the GI tract
  - Excellent *in vitro-in vivo correlation* (IVIVC)

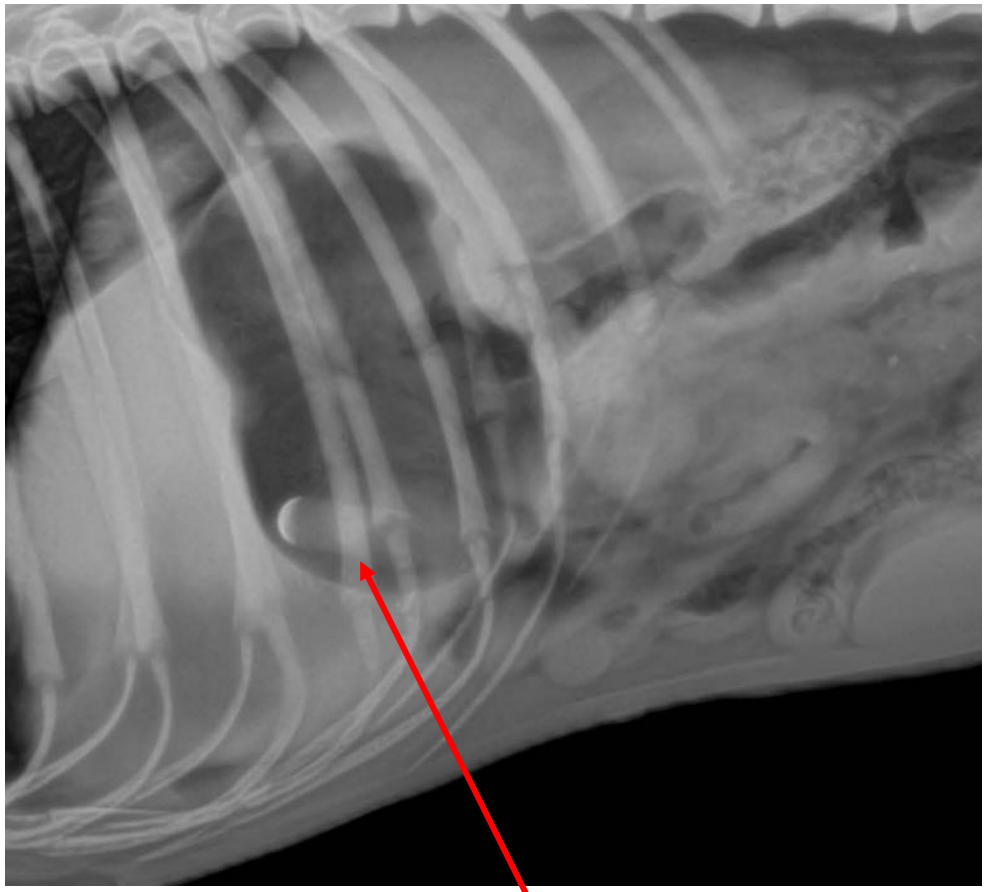
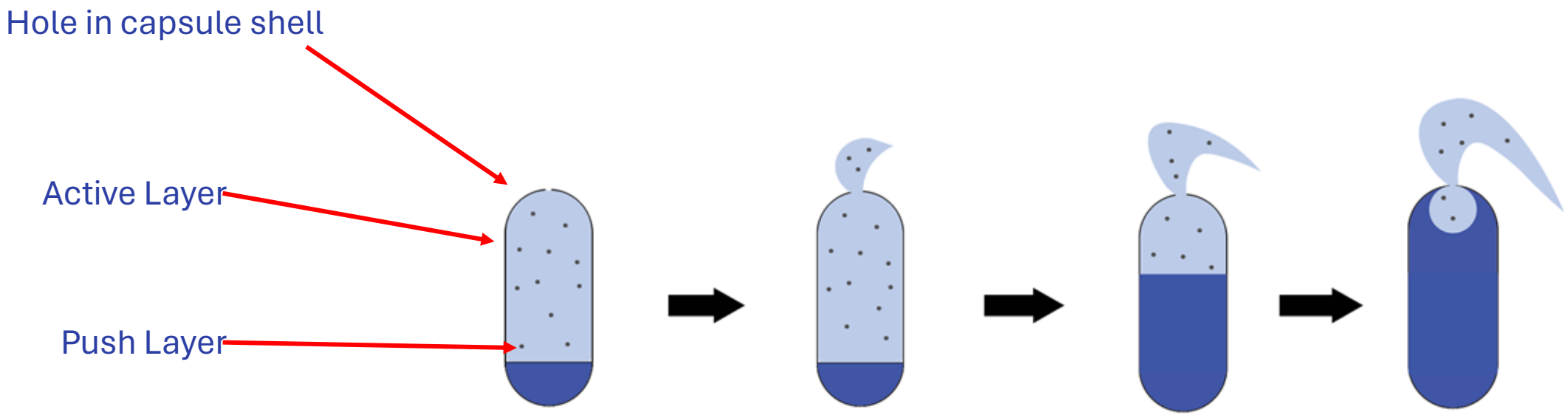


Image of OzmoCAP® in GI of dog

OzmoCAP® Release Mechanism

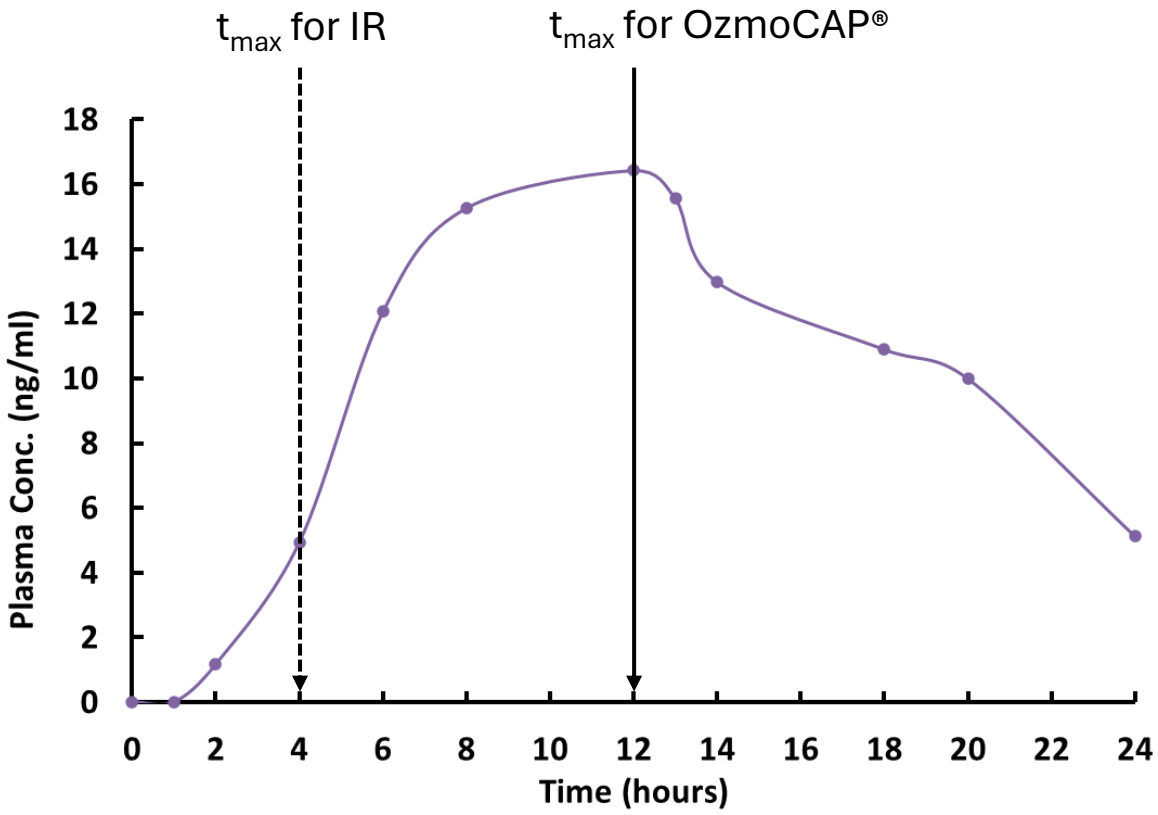


OzmoCAP® Formulating for Extended Release

- Solid API or DP intermediate (e.g. amorphous dispersion) is processed with excipients and compressed into an active layer
  - Dose range is 1-150 mg
- Active and push layers filled into capsule shells
- Capsule shell sealed and ready to dose
- Capsule shells are prepared using a proprietary process
  - Size 00
  - Release profile options:
    - Formulation A: 80% API released in 6 hours
    - Formulation B: 80% API released in 14 hours
  - Each profile is a separate capsule shell formulation

Compound X OzmoCAP® Dog Data

- IR dosage form has 4-hour t_{max}
- Formulation A OzmoCAP® extended absorption and shifted t_{max} to 10-12 hours
- Sufficient absorption in upper GI for ER
- Development of ER dosage form should progress with release durations based on *upper* GI absorption



Compound X Revised TPP

Attribute	Must/Minimum	Want/Desired
Patient population	Human adult patients	Human adult patients
Target market	Global	Global
Route of administration	Oral	Oral
Dosing frequency	Once daily (qd)	Once daily (qd)
Release rate	Extended release	Extended release
Dosage form release profile	**Time (h) / %Release** 0 / 0 **6 / 80** **16 / 100**	**Time (h) / %Release** 0 / 0 **6 / 80** **16 / 100**
PK parameters	Cmax ≤ Cmax of IR tablet	Cmax < Cmax of IR tablet

Summary

- Developing a TPP:
  - Defines critical project goals and product attributes
  - Identifies clear objectives to address information gaps and drive research towards project goals

- Updating the TPP is important to increase development effectiveness and efficiency to speed product to market

Questions?