Disclosures

Shareholder:

- GlaxoSmithKline
- Spero Therapeutics

Consultant:

- Prokaryotics

The opinions expressed in this presentation are my own and are not necessarily shared by my industry colleagues

Target Product Profile
Why Do We Need It?

John F. Tomayko, MD
jftomayko@gmail.com

CARB-X Antibiotic Development Bootcamp
ASM/ESCMID Conference on Drug Development to Meet the Challenge of Antimicrobial Resistance
September 5, 2017
Boston Park Plaza

ARE WE THERE YET?

What is a Target Product Profile (TPP)?

- Is it a map **(Where?)**
- ..instruction set **(How?)**
- …template **(What?)**
- ….commercial document **(Why?)**

“Fail to prepare, prepare to fail”

The True Purpose of a TPP*

(Summary from Tebbey & Rink)

- Provide an ineradicable point of reference for the development of a value-added contribution to the therapeutic treatment paradigm
  - A reflection of the market needs
  - A benchmark
- Achieving regulatory approval alone may yield a marketed product that does not deliver a good ROI for the company
- Attempting to mold the TPP to the unfolding properties of the compound must be resisted as it can lead to errant investment into a molecule that will not provide a solution to the needs of the market
  - The TPP should only be updated when the market conditions change

***Tebbey, Paul & Rink, Charles. (2009). Target Product Profile: A Renaissance for its Definition and Use. Journal of Medical Marketing. 9. 301-307. 10.1057/jmm.2009.34.**

Some Folks Don't Like TPPs

Reason 1

- They stifle discovery; discovery relies on a prepared mind and serendipity not a TPP

Reason 2

- They're useless because they always change

Reason 3

- There is no way that I can deliver that…

Reason 4

- **I just don't like any of that stuff, …and I don't like Mondays**

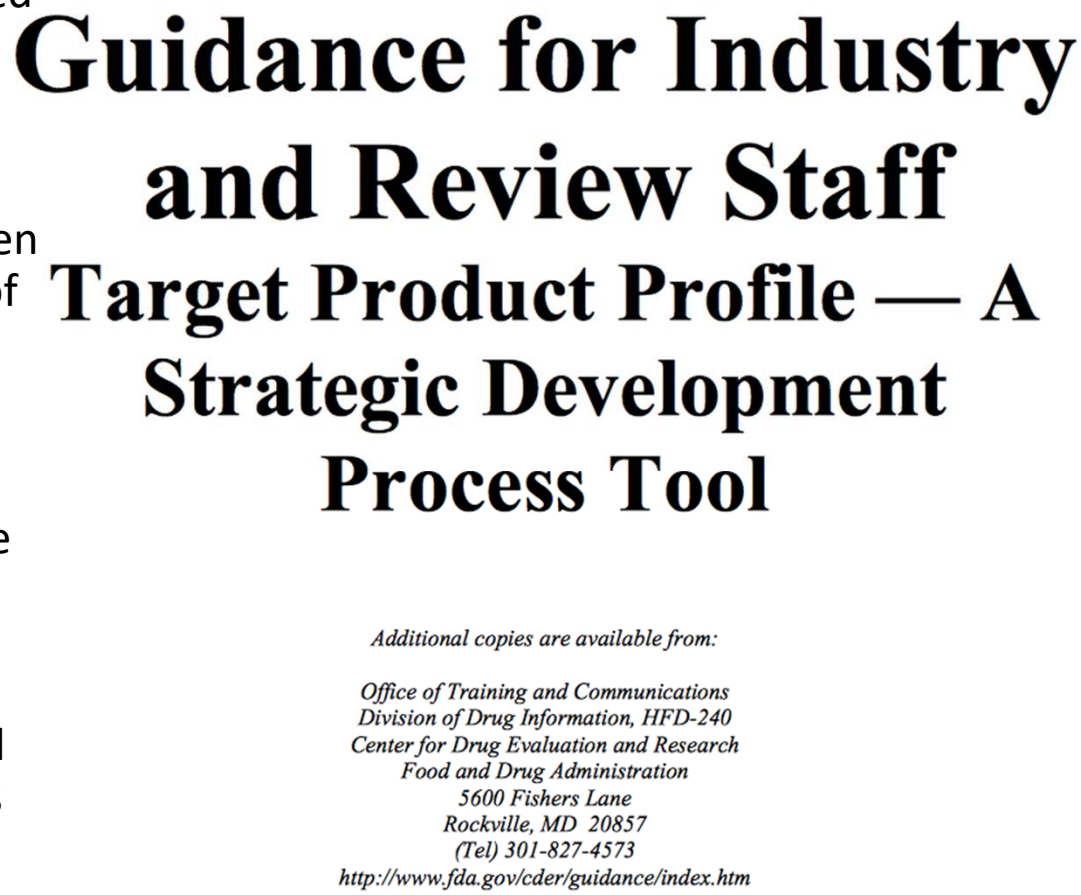
Some Say…

- …the TPP is written by the company developing the treatment, and if it is begun early it can help keep their development work properly focused on the end goal

Some Say…

- ✓ …the TPP is written **by the company developing the treatment**, and if it is begun early it can help keep their development work properly focused on the end goal
- A TPP can be used as a basis for discussions between the company and those regulatory authorities that will assess the product for release to market. A TPP is a document used by pharmaceutical companies that focuses on a desired product label
- Though a TPP initially represents the optimal product, **it is a dynamic document which can be updated as the drug development program progresses and knowledge of the drug increases**

- In 2007 a Clinical Working Group composed of FDA and pharmaceutical sponsors was formed to improve sponsor and FDA interactions regarding the drug development process
- Clearly, an efficient dialogue between the sponsor and FDA, with a goals of the development program in mind, can minimize the risk of late-stage drug development failures
- The TPP provides a statement of the *overall intent* of the drug development program, and gives information about the drug *at a particular time* in development, and is a ***dynamic*** summary that changes as knowledge of the drug increases
- The ideal version of what the sponsor would like to *claim in labeling* guides the design of the TPP



Guidance for Industry and Review Staff

Target Product Profile — A Strategic Development Process Tool

Additional copies are available from:

Office of Training and Communications
Division of Drug Information, HFD-240
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
(Tel) 301-827-4573
http://www.fda.gov/cder/guidance/index.htm

Submission of a TPP is voluntary and is not required for granting an end-of-phase 2 (EOP2) or other meeting with sponsors

Some Say…

- ✓ …the TPP is written **by the company developing the treatment**, and if it is begun early it can help keep their development work properly focused on the end goal
- ✓ A TPP can be used as a basis for discussions between the company and those regulatory authorities that will assess the product for release to market. A TPP is a document used by pharmaceutical companies that focuses on a desired product label
- ~~Though a TPP initially represents the optimal product, it **is a dynamic document which can be updated as the drug development program progresses and knowledge of the drug increases**~~
- ✓ A TPP is a format for a summary of a drug development program that is described in terms of drug labeling concepts and goals, and should be developed with the commercial goals of the product in the forefront

TPPs can be “Valued”

- One should understand the 'added value' of an innovation, ie, meaningful patient benefits compared to current SOC therapies to justify value driven reimbursement
  - How will the new therapy improve patient outcomes compared to the SOC?
  - Are there specific deficiencies with the current SOC that could be addressed– such as an improvement on the AE profile, difficulty with tolerance, non-ideal dosage form or regimen, etc.?
  - What scientific differentiators would need to be evident if the innovation is to be reimbursed and seen as a clinical alternative to standard treatments?
- Market Research can be undertaken to place a value on a TPP
  - Trade off analyses can be made to see what is driving the value
  - Value can be expressed as **base profile**(achieving the target attributes), **upside profile** (achieving some stretch targets/attributes), and **downside profile** (failing to achieve some attributes)

How do you Write a TPP?

TPPs Should be Developed by a Cross Functional Team

- **Discovery and Development**
  - Both early discovery and clinical development teams need something to aim towards;
- **Regulatory**
- **Global Commercial Strategy**
  - Commercial team members familiar with global needs and reimbursement policies are essential
- **Manufacturing (CMC)**
  - Often requires lead time to deliver clinical material
  - TPP can help these separate functions to manage their resources and plan for scale up
- **Portfolio Management**
  - The net present value of a TPP can be determined
  - These can guide investment decisions
  - Frame discussions
- ***Buy in comes from participation in the process***

TPP Name	Desired Profile	Minimum Acceptable Profile	Current Gold Standard Profile	Source
Indication				
Target Label				
Clinical Efficacy (incl. HE endpoints)				
Safety and Tolerability				
Contraindications/ Warnings				
Precautions/ Drug and Food Interactions				
Formulation and Dosing Regimen				
Dose				
Current/ Future Gold Standard				
Current Value Proposition				
Competitive environment at launch				
PoS				

TPP or Asset Product Profile

Description	• A novel (covalent reversible) non-β-lactam serine β-lactamase inhibitor (BLI) that can be used in combination with appropriate β-lactam antibiotics for proven or suspected β-lactamase mediated resistance
Indication	• **Drug-Bl1** is a β-lactamase inhibitor indicated in adults as part of combination therapy with the following β-lactam antibiotics for the treatment of the corresponding β-lactamase producing pathogens: – **Ceftazidime or cefepime**: For Class A ESBLs including CTX-M-14 and CTX-M-15; Class A Carbapenemases including KPC-2 and KPC-3; Class C AmpC cephalosporinases; and Class D beta-lactamases including OXA-48 – **Meropenem**: For Class A Carbapenemases including KPC-2 and KPC-3; and Class D carbapenemases including OXA-48
Efficacy	• Clinical cure rates in combination with appropriate β-lactam antibiotics non-inferior to best available therapy
Microbiology	• **Drug-Bl1** is a potent broad spectrum serine BLI with activity against: – Class A ESBLs including TEM, SHV and CTX-M – Class A carbapenemases including KPC-2/-3 – Class C AmpC cephalosporinases – Class D OXA carbapenemases or cephalosporinases including OXA-48 • Activity and/or potency profile of the β-lactam partner can be further augmented by CB-618 – **Ceftazidime, cefepime**: enhanced potency vs. serine β-lactamase producing (ESBL, KPC, AmpC, OXA-48) but NOT metallo-β-lactamase producing (NDM-1) Enterobacteriaceae – **Meropenem**: significantly enhanced potency vs. serine carbapenemase producing (KPC, OXA-48) but NOT metallo-β-lactamase producing (NDM-1) Enterobacteriaceae; good anaerobe, *Pseudomonas* and Gram-positive activity – [Based on *in vitro* data] **Aztreonam**: enhanced potency vs. β-lactamase producing Enterobacteriaceae, including strains producing metallo-β-lactamases • Activity profile against *Acinetobacter* spp. or Gram-positives unchanged by the addition of CB-618
Safety / Tolerability	• **Drug-Bl1 s**afety and tolerability profile comparable to partner alone
Dosing	• IV infusion, three times a day (TID) in patients with normal renal function, similar to most β-lactam partners; dose adjustments in renally impaired patients
Pharmacokinetics	• Linear PK; rapid tissue distribution; no accumulation; renal excretion; low protein binding; no potential for major drug-drug interactions and no negative drug-drug interaction with partner
How Supplied	• Single vial, separate from β-lactam partner

TPPs Aren't Always Written by the Developer

- UNICEF
  - UNICEF creates Target Product Profiles (TPPs) to communicate requirements for products which are currently not available on the market but which fulfil a priority need to be used in the unique context in which UNICEF and it's partners operate
    - Rapid diagnostics for E.coli, Zika, emergency structures, tents, etc.
    - https://www.unicef.org/supply/index_91816.html
- WHO for TB diagnostics
    - http://www.who.int/tb/publications/tpp_report/en/
- The British Air Ministry listed specifications for aircraft
    - https://en.wikipedia.org/wiki/List_of_Air_Ministry_specifications

- Pull incentives (under consideration)
  - Governments may issue TPPs that define attributes or eligibility requirements for attainment of a market entry awards

Conclusions

- The **TPP is a strategic document** that describes the desired attributes of a product
- Yes, TPPs are a commercial tool
  - It takes a lot of money to discover a good antibiotic, it takes even more to develop it!
  - **Regulatory approval is not the only mark of success**
- Achieving the **TPP is necessary for commercial success** and thereby serves as the guide for determining **asset** value and capital spending
- It is **not a dynamic document** and should not change
  - An Asset Product Profile (APP) should be the dynamic, changing document that reflects your progress towards achieving the TPP
- In the future, **TPPs could be issued by governments**
  - Listing the attributes necessary to achieve a market entry award