# The Target Product Profile

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Nov 5, 2015

# Topics to be Covered

- Overview of TPPs
  - What are they?
  - What is the purpose and benefit of using a TPP?
  - What is usually in a TPP?
- What are the unique issues for a TPP for HIV vaccines?
  - Comparisons with other vaccines
- How can a TPP best be used to support HIV vaccine development?

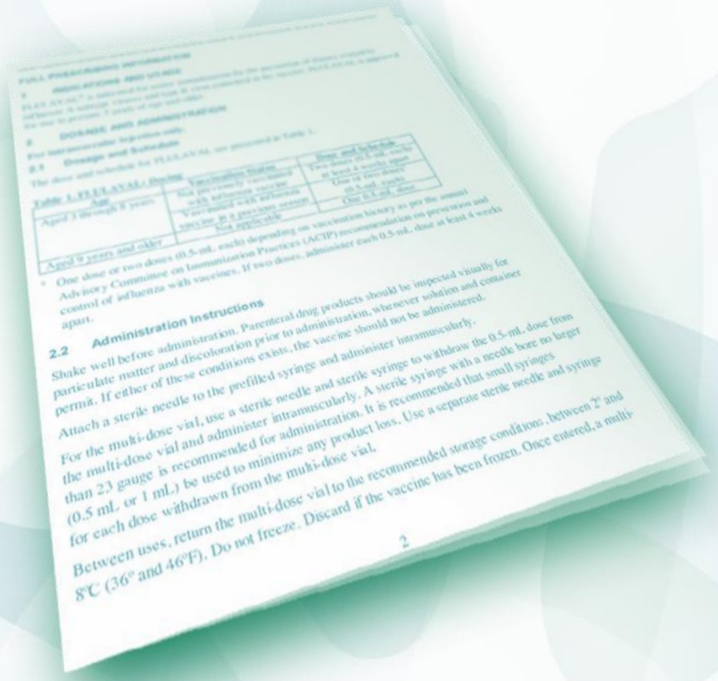
# TPP Background and History

- In 1997, a working group with FDA and industry members recommended developing a template to use during drug development.
  - summarize drug labeling concepts and desired claims
  - focus drug development activities and process
  - facilitate discussions between FDA and product developers
- This led to the development of the **Target Product Profile**

# WHY?

From a regulatory perspective, the product labeling (package insert/product claims) **must** be supported by appropriate studies and data.

In the past, companies might request approval for indications or products that had not been included in the development plan.



Clinical data in men 18-30 years old may permit approval only for men 18-30 years old – not helpful if indication is primarily in men >50

Clinical studies that used a frozen formulation may not support approval of an alternate formulation (liquid, lyophilized)

**FDA Guidance for Industry** "Target Product Profile – A Strategic Development Process Tool" (2007)

| Attribute | Desired Target | Minimally Acceptable Product | Studies that support the target |
|---|---|---|---|
| | | | |

# TPP emphasizes the concept of **beginning with the goal in mind**

The TPP lays out the desired labeling claims/attributes

– indication, target population, product characteristics

The TPP identifies and lists the studies that will be needed to support these claims

# Benefits of a TPP

| Without a TPP – claims are broad and non-specific | With a TPP – claims are well-defined and quantifiable | |
|---|---|---|
| **Label Claims / Attributes** | | |
| "Vaccine against chickenpox" | 80% efficacy in healthy adults after 3 doses | ➔ Defines requirements for efficacy study |
| Storage conditions? | Stable at 2-8°C for 2 years | ➔ Defines formulation and stability requirements |
| **Marketing Concepts** | | |
| Cost? | <$2.00/dose | ➔ Defines requirements for manufacturing and packaging |
| **Public Perception** | | |
| "Everyone will want this vaccine" | Requires 80% uptake for commercial success<br>Requires recommendation by vaccine advisory groups | ➔ Defines needed market research studies |

**Note: The TPP defines the studies that are needed to achieve the desired product**

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# The TPP Today

**The TPP has evolved into a strategic document that is widely used by product developers and has expanded to incorporate additional product attributes not covered by the labeling**

- Marketing attributes
  - Competitive advantage relative to competitor products, cost to produce versus anticipated sale price
- Corporate attributes
  - Portfolio management, ROI
- Governmental/medical affairs
  - Recommendation for use by government/advisory group
  - Potential for reimbursements
  - Assessment of product uptake by medical providers and public

Delineates information needed for product success

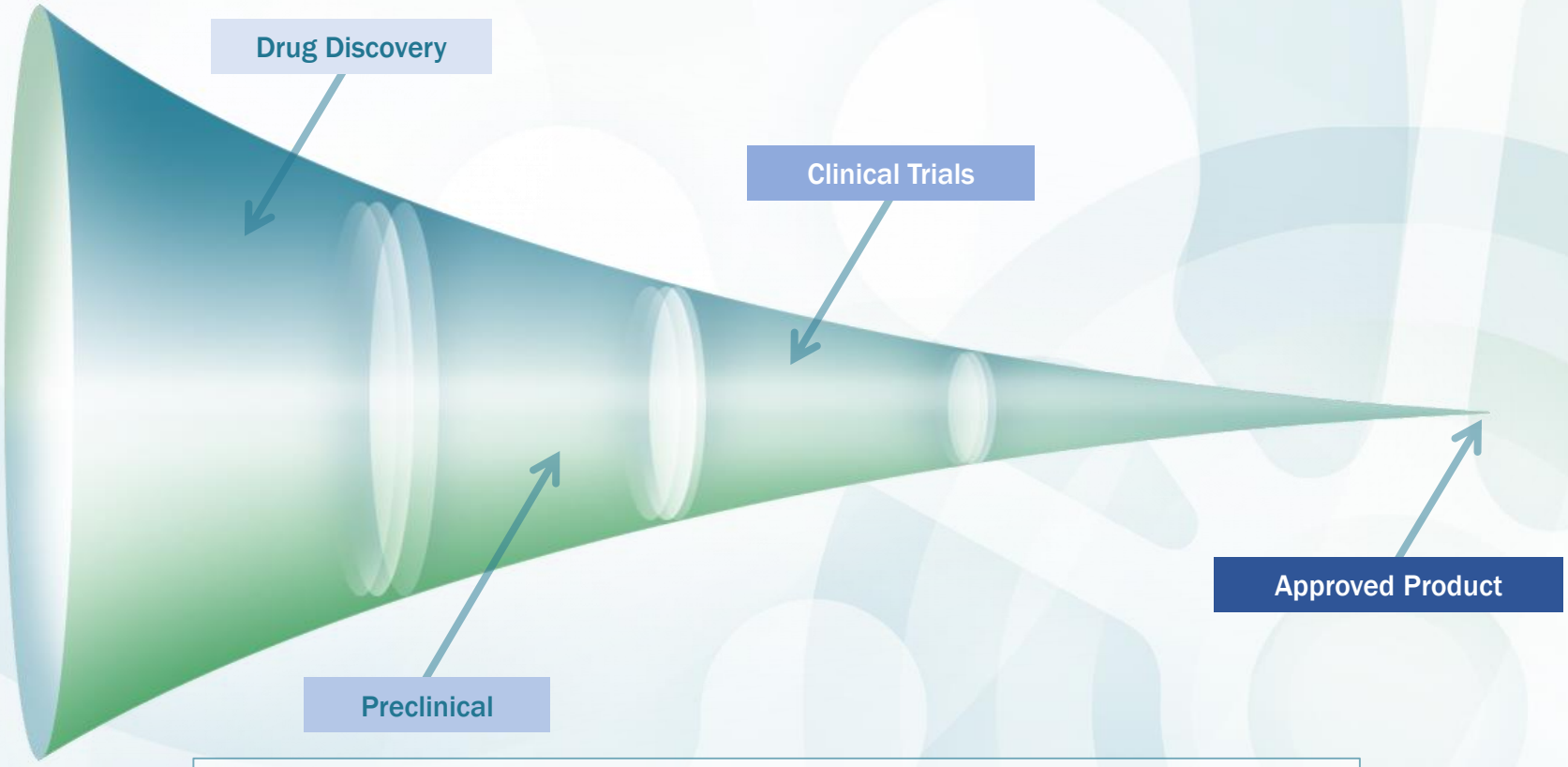
Aids the product development team to ensure that studies address the intended goal

# Attributes of a Vaccine TPP

| Labelling Concepts | |
|---|---|
| Indications | Efficacy (Clinical studies) |
| Target population | Dosage and schedule |
| Components (description) | Duration of protection |
| Product presentation | Safety and Tolerability |
| Route and method of administration | Co-administration |
| Shelf-life and storage | Clinical pharmacology |
| **Additional Attributes** | |
| WHO prequalification | |
| Registration pathway | |
| Target price | |

Specific attributes to include in a TPP are product and project specific – a strategic decision by the project team

# When Should a TPP Be Developed?




- No specific time that a TPP is required
- Earlier TPP helps minimize the risk of irrelevant activities and increase the likelihood that meaningful preclinical and clinical studies are conducted

# Developing a TPP for an HIV vaccine

- Complex development problem
  - Candidate vaccines have been in clinical trials since the 1980s
    - Many studies completed and ongoing
  - Vaccine candidates based on multiple platforms have been and are being tested
    - DNA plasmids, viral vectors, proteins, heterologous regimens
- Relative to many other vaccines
  - An HIV vaccine will probably be complex and multi-component
  - The immunization regimen will involve multiple doses over a long time interval

Where do you start?

# Developing a TPP for an HIV vaccine

- Multiple TPPs for multiple products
- Many HIV vaccine candidates are at an early phase of development - TPP attributes should be designed to answer phase appropriate questions
    - Safety of novel platforms
    - Feasibility of complex regimens, compatibility of multiple components
- No clear consensus on the necessary immune response(s), and what vaccine is needed to stimulate this response
    - What criteria should be used for go/no-go decisions?
        - Immune response equal to, better than, or worse than earlier generation product?
        - What specific immune response is primary?

# Developing a TPP for an HIV vaccine

- Some candidate vaccines are being developed to characterize immune responses in humans

  "Clinical research reagents"

  - TPP attributes were initially developed for a product intended for licensure and may not be relevant for a clinical research reagent
    - Dosage and schedule
    - Stability, product presentation

  **How much optimization is needed?**

Define the goals of your program, select and develop attributes accordingly

# TPP Attributes

## Examples of Licensed Vaccines – Questions for HIV candidates

# Dose and Schedule

| Target |
| --- |
| • Route of administration, dose schedule, adjustments for different populations |
| **Annotations** |
| • This section describes the studies that support the proposed dose and schedule<br>• During clinical development<br>  • The optimal dose and schedule should be established during Phase 2 studies<br>  • The optimal dose and schedule may be selected based on immunological endpoints that are believe to be predictive of product efficacy |

- What studies will be done to evaluate dose regimens?
- What immunologic endpoints will be used to select dose and schedule?

# Dose and Schedule

| Vaccine | Target |
|---|---|
| **HPV** (typical) | Gardasil is administered intramuscularly as a 0.5mL dose at 0, 2, and 6 months |
| **HIV** (example investigational regimens) | • ALVAC at 0, 1, 3, and 6 months → AIDSVAX B/E at 3 and 6 months<br>• DNA at 0, 4 and 12 weeks → MVA at 6 months after the last DNA injection, and a second MVA at 80 weeks after enrollment.as injections |

# Description (components)

| Target |
| --- |
| • Qualitative and quantitative description of the ingredients |
| **Annotations** |
| • This section describes the studies that support the proposed product composition.<br>• For early clinical development<br>  • The product may still be evolving and different formulations and doses under investigation<br>  • The investigational product may be presented in a format that is not commercially viable  approved indication is a goal and the design of a pivotal efficacy study will be only high level<br>  • The initial studies will have safety and immunogenicity targets to allow designing later studies<br>• For many vaccines pre-specified immune responses are often used to "bridge" efficacy results from the pivotal efficacy study to secondary target populations. |

# Description (components)

| Vaccine | Target |
|---|---|
| **HIV** | Env protein - what variant?<br>Adenovirus - strain, insert gene(s)?<br>DNA - backbone, insert antigen(s)?<br>Pox - strain, antigen?<br>Adjuvant<br>• An effective vaccine is likely to require multiple components & and a heterologous prime-boost approach<br>• This type of product is much more difficult to implement relative to most vaccines |
| **HPV** | • Virus-like particles (VLPs) of the major capsid (L1) protein of multiple HPV types.<br>• <100 µg protein/HPV type<br>• Adjuvant to be included |

- What is the scientific justification for the regimen to be studied?
- What studies will be done to support inclusion of a specific adjuvant ?

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# Indication

| Attribute | Target & Consideration | Annotation |
|---|---|---|
| **Indication** | • Identify the specific disease(s) or conditions that the vaccine is intended to prevent or treat<br>• An HIV vaccine may have multiple indications (preventive and therapeutics)<br>  • Prevention of infection with HIV in individuals that are fully vaccinated<br>  • Prevention of transmission of HIV from a fully vaccinated infected person<br>  • Reduction in viral load<br>  • Reduction in active disease in infected individuals | • Studies are required to address each of the desired indications<br>• A minimal target might address one indication, and the desired target might address multiple indications |

# Indication

| Vaccine | Target |
|---|---|
| **HIV** | Prevention of infection/disease in individuals >6 mos. of age |
| **ZOSTAVAX®** | Live attenuated virus vaccine indicated for prevention of herpes zoster (shingles) in individuals 50 years of age and older |

# Clinical pharmacology

| Target |
| --- |
| • Mechanism of action |
| **Annotations** |
| • This section describes the studies that identify potential or confirmed mechanism of action of the vaccine<br>• During clinical development<br>  • The optimal dose and schedule should be established during Phase 2 studies<br>  • The optimal dose and schedule may be selected based on immunological endpoints that are believe to be predictive of product efficacy |

# Clinical pharmacology

| Vaccine | Target |
|---|---|
| **HPV** | • HPV only infects human beings. Animal studies with analogous animal papillomaviruses suggest that the efficacy of L1 VLP vaccines suggest that the efficacy of L1 VLP vaccines may involve the development of humoral immune response.<br>• Humans develop a humoral immune response to the vaccine, although the exact mechanism of protection is unknown |
| **HIV** | • An effective HIV vaccine will likely need to stimulate multiple immune responses. |

# Recommendations and thoughts on using a TPP for an HIV vaccine

- Include the TPP concept in your development program
  - Frequently lacking
- Prioritize attributes
  - If analyzing an immune response is the major objective, decisions on other attributes may be delayed until later in development
- Design your program to address desired TPP attributes
  - Modifications to the program are inevitable. By starting with the goal in mind, delays can be minimized.