Development of a Target Product Profile (TTP)
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Course Number PB-VI01P: Development of a Vaccine During a Pandemic
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Conflicts of Interest: None
Target Product Profiles (TPPs)

“The TPP is essentially an organized “wish-list” of characteristics, features, and attributes that one would like to see in a newly developed medical product once it reaches the market.”

Lee BY and Burke DS. Constructing target product profiles (TPPs) to help vaccines overcome post-approval obstacles. Vaccine. 2010 Apr 1; 28(16): 2806–2809.
Preferred Product Characteristics (PPCs) and Target Product Profiles (TPPs)

• WHO’s Initiative for Vaccine Research (IVR) develops PPCs and TTPs to guide vaccine developers.

• PPCs provide strategic guidance as to WHO’s preferences for new vaccines in priority disease areas and are typically developed prior to phase III clinical trial planning.

• High priority vaccines include: Dengue, HPV, Malaria, Measles-Rubella, Pneumococcal conjugate, Polio (inactivated), Rabies, Rotavirus, Typhoid, Yellow fever.

Preferred Product Characteristics (PPCs) and Target Product Profiles (TPPs)

- TPPs provide technical guidance as to WHO’s criteria in response to emergency or epidemic scenarios.

- Developed to facilitate accelerated vaccine development.

- WHO TPPs are usually formulated early in product development, prior to phase I clinical testing.

- Both PPCs and TPPs articulate vaccine preferences from an LMIC perspective.

https://www.who.int/immunization/research/ppc-tpp/en/
WHO PPCs and TPPs

• Developed with key stakeholders and end-users.
• Primary audience is any entity engaged in global vaccine product development.
• Compliance can facilitate WHO policy recommendation and prequalification.
• Can reduce the time between vaccine licensure and introduction into countries.

https://www.who.int/immunization/research/ppc-tpp/en/
A Target Product Profiles

• Has the ultimate goal in mind.

• Identifies “optimal target” and a “minimal target.”

• Early TPPs may propose estimated targets that can be refined based on manufacturing, non-clinical & clinical results.

• Typically, targets do not change unless the intended use of the product or standard of care changes, or in response to regulatory guidance.

• The final version of the TPP often serves as the precursor to the annotated product label.

https://www.who.int/immunization/research/ppc-tpp/en/
TPP Elements

1. Indication for use
2. Target population
3. Contraindication
4. Safety/Reactogenicity
5. Efficacy
6. Dose regimen
7. Durability of protection
8. Route of administration
9. Coverage
10. Product stability and storage
11. Co-administration with other vaccines
12. Presentation
13. Production
14. Registration and Prequalification
15. Post-marketing surveillance
TPP - Element 1

Indication for use

What do you want the vaccine to do ideally? What would be the minimum benefit that would be acceptable?

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunization protects against COVID-19 infection.</td>
<td>Immunization reduces the severity of COVID-19 disease.</td>
</tr>
</tbody>
</table>

Develop and defend three distinct minimal indications.
TPP - Element 2

Target population

Age, gender, health profile, e.g. pregnant, lactating women

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages and medical profiles.</td>
<td>Adults including the elderly.</td>
</tr>
</tbody>
</table>

Develop and defend two distinct minimal indications.
What populations do you think the vaccine must protect?
TPP - Element 3

Contraindications

What populations should be excluded for safety reasons, children, pregnant women, people w/ allergic conditions?

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>None.</td>
<td>Immune compromised patients.</td>
</tr>
</tbody>
</table>

Develop and defend three contraindications that you think might pose safety concerns as regards your vaccine.
TPP - Element 4

Safety/Reactogenicity

Adverse events (AEs)

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild, transient AEs</td>
<td>Safety and reactogenicity profile whereby vaccine benefits outweigh safety risks.</td>
</tr>
<tr>
<td>No serious AEs.</td>
<td></td>
</tr>
</tbody>
</table>

Describe two or more safety risks that could result from a COVID-19 vaccine that you think would seriously limit the vaccine’s use by the general public.
TPP - Element 5

Efficacy

To what extent does your vaccine work across different outcomes, e.g., preventing death, reducing hospital stay, reducing viral shedding?

<table>
<thead>
<tr>
<th>Preferred</th>
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<tbody>
<tr>
<td>&gt; 70% efficacy (on population basis, including the elderly).</td>
<td>&gt; 70% efficacy (population basis) and &gt;50% efficacy in the elderly.</td>
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</tbody>
</table>

Develop your primary outcome measure and four secondary outcome measures. Propose two pre-determined subgroup analyses.
Dose regimen

Single/multiple dose, time between doses, booster requirements

<table>
<thead>
<tr>
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<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-dose regimen.</td>
<td>No more than two dose regimen one month apart.</td>
</tr>
</tbody>
</table>

Based upon experience with your vaccine platform, propose your preferred and minimal dosing regimen.
TPP - Element 7

Durability of protection

Lifetime immunity, time-limited immunity, need for regular boosters

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime.</td>
<td>Confers protection for at least 6 months.</td>
</tr>
</tbody>
</table>

Based upon experience with your vaccine platform, propose and defend your preferred and minimal estimates of the durability of protection for your vaccine.
TPP - Element 8

Route of administration
injectable, nasal spray, oral delivery

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral.</td>
<td>Injectable.</td>
</tr>
</tbody>
</table>

Based upon your vaccine platform, describe the pros and cons of your route of administration as regards convenience, cost and possible effects on vaccine induced immune responses.
TPP - Element 9

Coverage
Monovalent, multivalent

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivalent.</td>
<td>Monovalent.</td>
</tr>
</tbody>
</table>

Will your vaccine be based on a single SARS-CoV-2 clade or multiple different clades? Indicate the clade(s) that will be the basis of your vaccine and why this (these) clades were selected.
**TPP – Element 10**

**Product stability and storage**
Shelf life, temperature requirements, preservatives

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Critical or Minimal</th>
</tr>
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<tbody>
<tr>
<td>Shelf life &gt; 24 months at -20 °C. Stability &gt; 6 months at 2-8°C.</td>
<td>Shelf life &gt; 12 months at -20 °C. Stability &gt;8 hours at 2-8°C.</td>
</tr>
</tbody>
</table>

Based upon your vaccine platform, develop your preferred and minimal shelf life and stability characteristics. Indicate whether your vaccine will require preservatives, vaccine vial monitors or refrigeration.
TPP – Element 10
Product stability and storage

“There are few immunization issues more important than the appropriate storage and handling of vaccines.”


Vaccine Storage and Handling chapter from WHO/PAHO
https://www.paho.org/immunization/toolkit/resources/partner-pubs/ebook/Chapter5-Vaccine-Storage-and-Handling.pdf?ua=1

Vaccine Vial Monitor

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Explanation</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔️</td>
<td>The inner square is lighter than the outer circle. If the expiry date has not passed, USE the vaccine.</td>
<td>I</td>
</tr>
<tr>
<td>✔️</td>
<td>As time passes the inner square is still lighter than the outer circle. If the expiry date has not passed, USE the vaccine.</td>
<td>II</td>
</tr>
<tr>
<td>✗</td>
<td>Discard point: the color of the inner square matches that of the outer circle. DO NOT USE the vaccine.</td>
<td>III</td>
</tr>
<tr>
<td>✗</td>
<td>Beyond the discard point: inner square is darker than the outer circle. DO NOT USE the vaccine.</td>
<td>IV</td>
</tr>
</tbody>
</table>

From WHO/PAHO

TPP – Element 11

Co-administration with other vaccines

Interference with COVID-19 vaccine or the other vaccines

<table>
<thead>
<tr>
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<th>Critical or Minimal</th>
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</thead>
<tbody>
<tr>
<td>Can be given with other vaccines without affecting immunogenicity, safety or efficacy of the vaccines.</td>
<td>Must be used as a stand alone vaccine.</td>
</tr>
</tbody>
</table>

Based upon your vaccine platform, consider whether your vaccine might interfere with: Team 1- pediatric vaccines; Team 2 – adult vaccines; Team 3 – vaccines for the elderly. You may consider all three groups if you wish.
TPP – Element 12
Presentation
Liquid/lyophilized, mono-dose/multi-dose, dosage volume

<table>
<thead>
<tr>
<th>Preferred</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Liquid product in mono-dose or multidose (10-20) presentations. Maximal dosage volume 0.5mL.</td>
<td>Liquid or lyophilized product, mono or multidose, diluent provided. Dosage 0.5mL.</td>
</tr>
</tbody>
</table>

Based upon your vaccine platform, determine likely presentation characteristics. If proposing multi-dose vials describe how the vaccine will be formulated, managed and discarded in compliance with WHO’s multi-dose vial policy.
TPP – Element 13

Production

Number of doses of vaccine to be produced annually.

<table>
<thead>
<tr>
<th>Preferred</th>
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</tr>
</thead>
<tbody>
<tr>
<td>9 billion doses</td>
<td>350 million doses</td>
</tr>
</tbody>
</table>

Describe whether your vaccine platform allows for high, medium or low yield production based on manufacturing of the vaccine and the delivery system.
TPP – Element 14

Registration and Prequalification

Type of license- e.g. is it experimental

<table>
<thead>
<tr>
<th>WHO</th>
<th>US FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO prequalified and/or meets criteria for EUAL (Emergency Use Assessment &amp; Listing Procedure).</td>
<td>Emergency Use Authorization, Expanded Access Program.</td>
</tr>
</tbody>
</table>

Briefly outline steps for seeking approval of your vaccine through the WHO EUAL process or the FDA Emergency Use Authorization or Expanded Access Program process.
TPP – Element 15

Post-marketing Surveillance

Monitoring safety, effectiveness, herd immunity, potential emergency of vaccine resistant mutants

<table>
<thead>
<tr>
<th>WHO and National Regulatory Authorities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-marketing surveillance will include assessment of serious adverse effects, effectiveness and emergence of vaccine resistant SARS-CoV-2 mutants in accordance with national regulatory authorities and the WHO prequalification requirements.</td>
</tr>
</tbody>
</table>

Dr. LaRussa will determine the assignment.
WHO PPCs and TPPs

PPCs and TPPs shape vaccine product development

Although not formal WHO guidelines, PPC and TPP documents have oversight from WHO’s Product Development for Vaccines Advisory Committee, which in turn informs WHO’s Strategic Advisory Group of Experts on Immunization (SAGE) on the status of vaccine development. However, a policy recommendation for vaccine use will ultimately depend on a multitude of factors in addition to product specific attributes, including affordability, cost-effectiveness and the programmatic considerations such as feasibility of implementation and anticipated coverage. Broader perspectives such as equity and community acceptability are also important for health policy.

https://www.who.int/immunization/research/ppc-tpp/en/