Development of a Target Product Profile (TTP)

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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.

https://www.who.int/immunization_standards/vaccine_quality/priority_pq_vaccines_2018_2020/en/

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

- TPPs provide technical guidance as to WHO's criteria in response x 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?

Preferred	Critical or Minimal
Immunization protects against COVID-19 infection.	Immunization reduces the severity of COVID-19 disease.

Develop and defend three distinct minimal indications.

TPP - Element 2

Target population

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

Preferred	Critical or Minimal
All ages and medical profiles.	Adults including the elderly.

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?

Preferred	Critical or Minimal
None.	Immune compromised patients.

Develop and defend three contraindications that you think might pose safety concerns as regards **your** vaccine.

TPP - Element 4

Safety/Reactogenicity

Adverse events (AEs)

Preferred	Critical or Minimal
Mild, transient AEs No serious AEs.	Safety and reactogenicity profile whereby vaccine benefits outweigh safety risks.

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?

Preferred	Critical or Minimal
> 70% efficacy (on population basis, including the elderly).	> 70% efficacy (population basis) and >50% efficacy in the elderly.

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

TPP - Element 6

Dose regimen

Single/multiple dose, time between doses, booster requirements

Preferred	Critical or Minimal
Single-dose regimen.	No more than two dose regimen one month apart.

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

Preferred	Critical or Minimal
Lifetime.	Confers protection for at least 6 months.

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

Preferred	Critical or Minimal
Oral.	Injectable.

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

Preferred	Critical or Minimal
Multivalent.	Monovalent.

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

Preferred	Critical or Minimal
Shelf life > 24 months at -20 °C. Stability > 6 months at 2-8°C.	Shelf life > 12 months at -20 °C. Stability >8 hours at 2-8°C.

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. ”

https://blogs.unicef.org/blog/getting-children-immunized-going-the-extra-mile-in-car/

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

Symbol	Explanation	Stage
✓	The inner square is lighter than the outer circle. If the expiry date has not passed, **USE** the vaccine.	I
✓	As time passes the inner square is still lighter than the outer circle. If the expiry date has not passed, **USE** the vaccine.	II
✗	**Discard point:** the color of the inner square matches that of the outer circle. **DO NOT** USE the vaccine.	III
✗	Beyond the discard point: inner square is darker than the outer circle. **DO NOT** USE the vaccine.	IV

From WHO (www.who.int).

https://s3.amazonaws.com/gpei-tk/reference_links/en/Pakist_Guide_Book_for_AICs.pdf

TPP – Element 11

Co-administration with other vaccines

Interference with COVID-19 vaccine or the other vaccines

Preferred	Critical or Minimal
Can be given with other vaccines without affecting immunogenicity, safety or efficacy of the vaccines.	Must be used as a stand alone vaccine.

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

Preferred	Critical or Minimal
Liquid product in mono-dose or multidose (10-20) presentations. Maximal dosage volume 0.5mL.	Liquid or lyophilized product, mono or multidose, diluent provided. Dosage 0.5mL.

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.

Preferred	Critical or Minimal
9 billion doses	350 million doses

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

WHO	US FDA
WHO prequalified and/or meets criteria for EUAL (Emergency Use Assessment & Listing Procedure).	Emergency Use Authorization, Expanded Access Program.

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

WHO and National Regulatory Authorities
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.

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/