Process for prioritization and current recommendations for the evaluation of candidate vaccines

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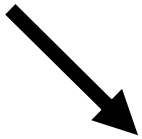


1 Prioritization

Independent expert process to prioritize candidate vaccines to enter WHO-sponsored clinical trial

A process for prioritization of candidate vaccines by an independent **WHO Technical Advisory Group on candidate vaccine prioritization** (**TAG-CVP**). This includes ongoing review of emerging information.

2 Availability

Agreement on availability and access to candidate vaccines

Decisions will be informed by outcomes of the prioritization process; consensus on minimum number of candidate doses required for research during outbreaks and that need to be available at any time point.

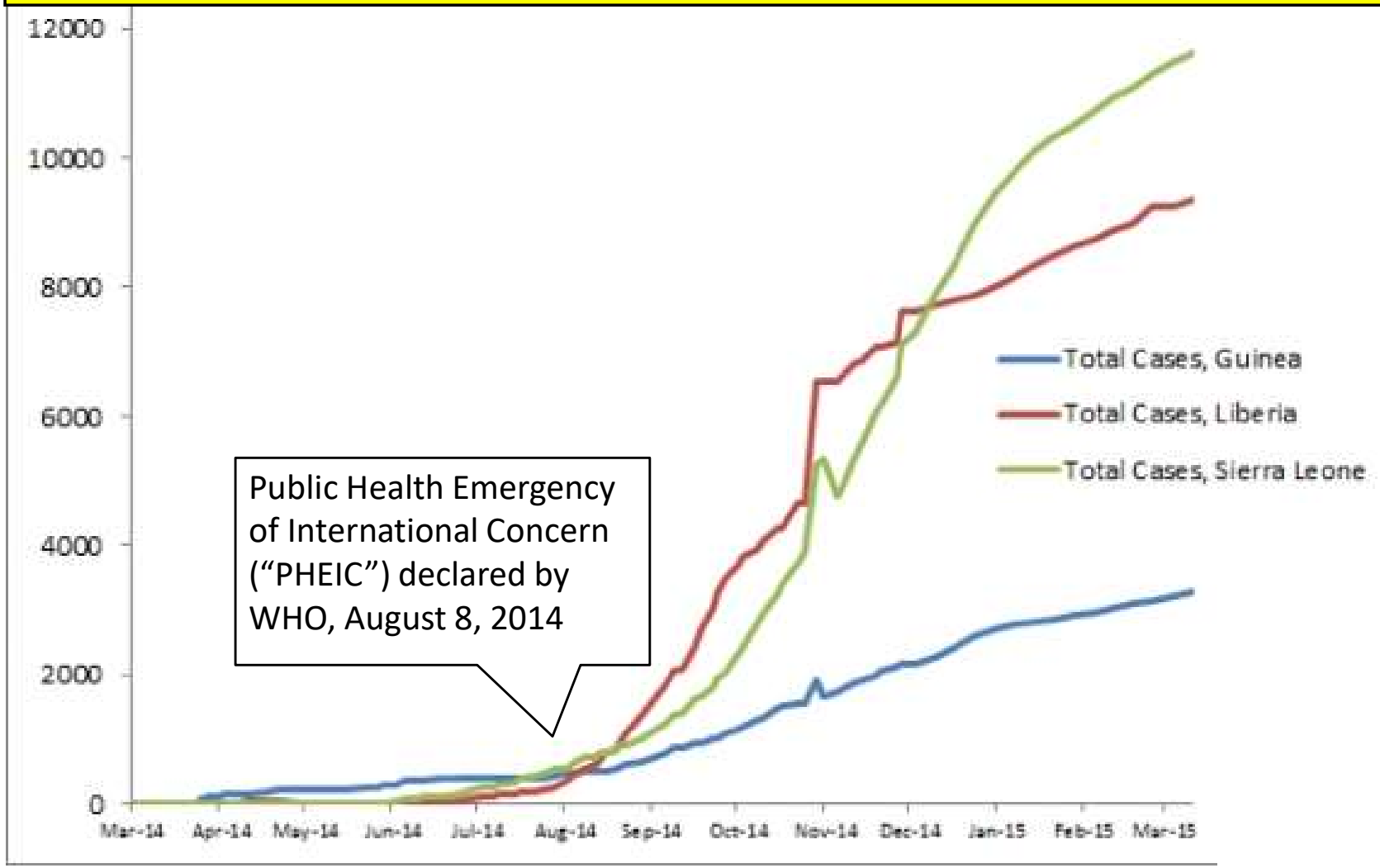
3 Clinical trials*

Standardized platforms to scale clinical trials equitably

** includes expanded access*

This emerges from a collaborative multilateral approach in which the Ministries of Health are at the core of all research efforts.

WHO Ebola case counts, West Africa, March 2014 - March 2015



CVD

Examples when multiple vaccine candidates had to be considered in the response to PHEICs or to outbreaks that had potential to progress to a PHEIC

***Orthoebolavirus zairense* – West Africa outbreak 2014 (PHEIC)**

- VSV-vectored vaccine expressing glycoprotein
- ChAd3-vectored vaccine expressing glycoprotein
- Ad26-based vaccine expressing glycoprotein
- MVA-BN Filo (as a heterologous booster)

Orthoebolavirus sudanense – Outbreaks in Uganda, Sept 2022 to January 2023

- VSV-vectored vaccine expressing sudanense glycoprotein
- ChAd3-vectored vaccine expressing sudanense glycoprotein
- ChAdOx1-vectored vaccine expressing marburgense glycoprotein

Orthomarburgvirus marburgense – Outbreaks in Equatorial Guinea and Tanzania 2023

- Two VSV-vectored vaccines expressing marburgense glycoprotein
- ChAd3-vectored vaccine expressing marburgense glycoprotein
- ChAdOx1-vectored vaccine expressing marburgense glycoprotein

High-risk populations for Filovirus disease and strategies to protect them with vaccine

	Reaching the target persons	Regimen & onset of protection	Duration of protection needed	Relative no. of doses needed	Vaccination strategy
Health care workers (HCWs)	Easy	Single-dose, rapid onset	Long-term (May need 2 doses; 2nd with heterologous vaccine)	Modest	All HCWs, prophylactic
Family members, Social contacts	Difficult	Single-dose, rapid onset	Can be relatively short	Large	Rings around cases
Funeral rite performers	Variable	Single-dose, rapid onset	Ideally, long-term	Moderate	Aim for all

Characteristics of an "ideal" Filovirus vaccine

- **Safe and effective in all ages and hosts** including infants, elderly, immunocompromised & pregnant women
- **High efficacy & effectiveness** in all ages and host groups
- **Direct protection –** early onset (~1 week) & long-lived (life-long)
- **Single-dose**
- **Administered without a needle** (oral, i.n., skin patch)
- **No cold chain required**

- Vaccinated persons do not shed the pathogen following exposure
- **Indirect protection** follows high (or moderate) coverage
- **Amenable to LARGE-SCALE ECONOMICAL manufacture**
- Indelible marker denoting vaccination (e.g., smallpox or BCG scar)
- Can be co-administered with other vaccines, if data are available

Safety: Animal models; early human clinical trials with the candidate vaccine. Data from clinical trials or post-licensure assessments of other vaccines based on the same platform (e.g., live vector; RNA vaccine; protein plus adjuvant)

Potential for efficacy: Known efficacy with the same vaccine platform against a different pathogen; immunogenicity documented in Phase 1 or 2 clinical trials with the specific vaccine candidate. Rapidity of onset of immune response; potential for interference from prior naturally-acquired or vaccine-induced antibodies to the vaccine antigen or platform; challenge data in animal models (sometimes extra consideration for NHP data); less emphasis on small animal models; cross-protection against different strains of the pathogen.

Availability (Supply): Delivery timeline for product to be ready for use in the trial having successfully completed all release tests, some stability data, and long-term storage temperature, potential for scale-up, and commitment by the manufacturer to take the product to licensure. Affordability (cost of goods plus).

Ease of administration and implementation: Route of administration (parenteral, oral, intranasal), number of doses needed, pacing between doses, cold chain requirements, presentation of the vaccine, need to reconstitute vaccine with diluent prior to injection

WHO TAG-CVP Members and their Expertise

Working Group Member	Votes	Institution	Expertise*
Dr. Sergio de Andrade Nishioka	Yes	Fundação Oswaldo Cruz (Fiocruz), Brasil	**Regulatory sciences; clinical trials, epidemiology**
Dr. Sue-Nie Park	Yes	Korea Univ. Medical Complex	**Regulatory sciences; microbiology**
Dr. Junzhi Wang	Yes	Nat. Inst. for Food & Drug Control, China	**Analysis of biologics; Regulatory sciences;**
Prof Dani Cohen	Yes	Sch of Pub Hlth, Tel Aviv Univ., Israel	**Vaccine trials; clin. immunology; seroepidemiology;**
Ms Teuila Pati McDonald	Yes	EPI Coordinator, MoH, Samoa	**EPI; mass immunization; cold chain management**
Dr. Sudhanshu Vrati	Yes	Reg Ctr for Biotechnology, India	**Virology; molecular virology;**
Dr Subhash Kapre	Yes	InventVax & Inventprise, USA	**Vaccine manufacturing; vaccine formulations**
To be filled ^	Yes		**Vaccine safety; Pharmacovigilance;**
Prof. César Muñoz-Fontela**	No	German Ctr for Infect. Res. Germany	**Animal models; immunology**
Dr Simon Funnell**	No	Public Health England, UK	**Animal models; immunology**
Prof Miles Carroll@	No	Oxford, UK	
Prof. Elizabeth Miller (Rapporteur)	No	London Sch Hyg Trop Med, UK	**Epidemiology, clinical trials, vaccinology**
Prof Myron M Levine (Chair)	‡	CVD, Univ. of Maryland, USA	**Vaccine development; clinical trials, infect. dis.**
* Expertise in relation to Terms of Reference; ^ To be filled after Dr. Rebecca Chandler moved to CEPI; ** Leaders of WHO animal models consortium; ‡ If necessary, but not routinely @ For discussions on filovirus vaccines			
WHO Secretariat: Ximena Riveros Balta, Dr Ana Maria Henao Restrepo; Philip Krause			

Vaccines are placed into Baskets based on clinical data. Candidates can be moved from Basket #3 to Basket #2 to Basket #1 as new data were generated and shared

Basket #1

Vaccine candidates of interest supported by sufficient preclinical and Phase 1 & 2 clinical safety and immunogenicity data to allow progression to a Phase 3 trial

Basket #2

Vaccine candidates of interest supported by preclinical and Phase 1 clinical safety and immunogenicity data to allow progression to a Phase 3 trial, **contingent on adequate Phase 2 data**

Basket #3

Vaccine constructs of interest with supportive preclinical data and awaiting initiation of a Phase 1 trial, or the Phase 1 trial is only recently underway

TAG-CVP OVERALL VACCINE SCORES SUMMARY SHEET (without option for "bonus points") Vaccine being scored: __XXXXXXXXXXXXX_____							
TAG-CVP member Evaluation	**Safety profile [scoring weight, 25 points)**	**Potential for efficacy (based on immunogenicity & animal; models) [scoring weight, 25 points]**	**Vaccine stability [scoring weight, 10 points]**	**Potential for mass vaccine delivery [scoring weight, 15 points]**	**Vaccine availability (supply) (manufacturing) [scoring weight, 25 points]**	**Total composite score (of a possible 100)**	**Vaccine should enter a WHO-sponsored trial (Yes or No)**
Scoring experts							
1							
2							
3							
4							
5							
6							
7							
8							
					MEAN		

OVERALL VACCINE SCORES SUMMARY SHEET (with option for "bonus points")

WHO-sponsored Vaccine Trial – TAG-Candidate Vaccine Prioritization

Vaccine being scored _____

TAG-CVP member evaluations	Safety profile [scoring weight, 20 points)	Potential for efficacy (*based on immuno-genicity*) [scoring weight, 20 points]	Vaccine stability [scoring weight, 10 points]	Potential for mass vaccine implementation (delivery) [scoring weight, 15 points]	Vaccine availability (supply, ease of manufacture) [scoring weight, 20 points]	Composite score of a possible 85 points	TOTAL SCORE WITH BONUS POINTS (UP TO 15)	VACCINE SHOULD ENTER A TRIAL (Y OR N)
Scoring experts								
1								
2								
3								
4								
5								
6								
7								
8								
Reasons for adding bonus points:								

Characteristics of three live vector-based vaccines to prevent *Sudan* disease (Data available at the time of review by the WHO TAG-CVP, October 13 through November 8, 2022)			
	IAVI	**Sabin Vaccine Ins.**	**Oxford University**
Type of live vector	Replicating	Non-replicating	Non-replicating
Live vector	VSV	ChAd3	ChadOx1
Heterologous antigens expressed	*Sudan* gp	*Sudan* gp	*Sudan & Zaire* gps
Route of administration	i.m.	i.m.	i.m.
Licensed vaccines with this live vector	Yes	No	Yes
Concerning post-licensure safety signals	No	Not relevant	Yes
Safety data of live vector in pregnant women	Yes	?	Yes
NHP protection data against Sudan	Yes	Yes	No
Immune Correlate of Protection vs Sudan	Yes	Yes	No
Phase 1 human clinical safety/immunogenicity with Sudan vaccine candidate	No	Yes	Yes
Phase 2 human clinical safety/immunogenicity with Sudan vaccine candidate	No	Yes	Yes
Human efficacy data against Sudan ebolavirus	No	No	No

THANK YOU