SINGLE SHIELD PRIZE

Desired Product Attributes

Single-administration pandemic influenza A(H5N1) vaccine

The following Desired Product Attributes describe product requirements and target nonclinical metrics aligned with approved two-dose pandemic influenza vaccines. These attributes will inform evaluation of submissions to the Single Shield Prize.

Important note: This document is subject to change and may be updated or further refined. The most current version will be linked on the Single Shield Prize website; the date in the document footer indicates when it was last updated.

Attribute	Minimal/Threshold	Optimal
1. Nonclinical Efficacy (Biological Performance)		
[A.] Immunogenicity Read out: Immunogenicity should be assessed at standardized time points following vaccination (baseline, Day 14, 21, 60, 90, 180) Unless otherwise specified, immunogenicity data should be generated using qualified, fit-for-purpose assays. Applicants should report quantitative results such as GMTs, geometric mean fold rise, responder rates, and measures of variability (e.g., 95% confidence intervals or standard deviations), as appropriate for the study design.		
HAI response (primary endpoint for HA-based vaccines)	• 70% of vaccinated animals (n≥10) achieve ≥ 4-fold rise in vaccine-induced HAI Ab responses by Day 21 against the homologous H5N1 strain following a single administration.	• 90% of vaccinated animals (n≥10) achieve ≥ 16-fold rise in HAI Ab response by Day 14 against the homologous H5N1 strain following a single administration.
Neutralizing Ab (Virus neutralization/microneutralization assay (MN))	• 70% of vaccinated animals (n≥10) achieve ≥ 4-fold rise **AND** a titer of ≥ 1:80 from baseline following a single administration.	• 90% of vaccinated animals (n≥10) achieve ≥ 8-fold rise **AND** a titer of ≥ 1:160 from baseline following a single administration.
Cellular immunity	*No minimal/threshold defined*	• Detectable antigen-specific cellular immune responses following a single administration. ≥2-fold increase in antigen-specific $CD4^+$ and/or $CD8^+$ T cells compared with comparator or baseline in ≥70% of animals when compared to naive animals/control

Attribute	Minimal/Threshold	Optimal
Breadth (heterologous)	*No minimal/threshold defined*	• Demonstrate functional Ab responses against the homologous H5N1 strain and detectable cross-reactive activity against at least one antigenically distinct H5 virus • Demonstrate broad cross-reactive Ab responses against representative H5 clades/subclades with supporting functional neutralization data, where available.
Fc Effector Function (ADCC)	*No minimal/threshold defined*	>75-90% of vaccinated animals demonstrate a statistically significant increase over baseline in at least one Fc-mediated effector function (such as ADCC, ADCP, complement deposition, or Fcγ-receptor activation) and is associated with enhanced protection.
[B.] Ferret Challenge Model Gold Standard for PanFlu (Read out: Viral load, survival, clinical disease, pathology, breadth of protection and durability)		
Survival	≥70% survival after a validated lethal homologous strain challenge	≥90% survival (preferably 100%) after a validated lethal homologous strain challenge
Viral load reduction	≥2 log reduction of infectious-virus titer relative to controls in a prespecified respiratory compartment and time point	≥3 log reduction or 100% clearance of the virus within 5 days (as indicated by nasal wash, nasal turbinates specimens) with virus below detection in the LRT
Clinical disease	≤20% weight loss; timely recovery; reduced disease illness following homologous viral challenge	• ≤10% weight loss; minimal or no fever; timely recovery and sustained protection following homologous viral challenge
Lung pathology	Reduction in pulmonary inflammation and gross lung lesions compared to control animals	No or Minimal lung pathology with preservation of lung structure, near complete LRT protection

Attribute	Minimal/Threshold	Optimal
Viral shedding	*No minimal/threshold defined*	• Reduction in peak infectious nasal wash titer, shedding duration, and/or shedding AUC relative to controls; trend toward accelerated viral clearance compared to controls • Infectious virus below detection by approximately Day 5, preferably earlier, in the majority of animals
Transmission	*No minimal/threshold defined*	Reducing viral load / likelihood of infection to naïve, co-housed ferrets
[C.] Durability		
Durability of Immune Markers	• Following a single administration, ≥70% of vaccinated animals retain a mechanism-relevant immune response (e.g., HAI, MN, NAI) throughout at least 4 months. • The group response should remain above baseline and retain measurable functional activity against the homologous virus.	• ≥90% of vaccinated animals, for at least ≥6 months, retain activity against the prospectively defined panel of antigenically distinct viruses, and show evidence of durable antigen-specific memory
Durability of Protection	Protective efficacy against mortality and reduced disease severity/lung viral titers maintained for 4-6 months; protection from mortality or severe disease and reduction in lower respiratory viral burden relative to controls	Protection against mortality and reduced disease severity/lung viral titers maintained for ≥6 months or the longest scientifically appropriate interval supported by the model with ≥ 90% survival or near complete protection from severe disease, minimal lower respiratory pathology, and protection against an antigenically distinct heterologous challenge virus.
[D.] Nonclinical safety		
Nonclinical safety	Vaccines should be acceptably tolerated at the intended dose and at an appropriate dose margin with no meaningful vaccine-related safety findings in animal studies	Acceptable safety profile at a multiple of intended clinical dose with no serious or clinically meaningful local or systemic toxicity; supports advancing toward IND-enabling studies; no evidence of enhanced disease following homologous or heterologous virus challenge.
2. Route of Administration & Regimen		

Attribute	Minimal/Threshold	Optimal
Dosing/Regimen	single dose vs. placebo	
Route	Intramuscular, intradermal, transdermal, subcutaneous	
Dose optimization	Demonstrate reproducible immunogenicity, protection and acceptable tolerability using a feasible/minimally effective antigen dose	Demonstrate durable immunogenicity, protection and acceptable tolerability using a feasible/minimally effective antigen dose and/or dose-sparing capacity
Time to protection	Provides protection against homologous viral challenge no later than Day 21.	Protective immunity by Day 14 or earlier and sustained protection against homologous viral challenge
3. Formulation and Delivery Performance Demonstrated controlled Ag availability while maintaining structural integrity and biological potency. (Criteria are specific for the single administration candidate at this early development stage, and should not be considered as ultimate product targets)		
Stability	Demonstrate stability for >3–6 months under intended storage conditions while maintaining predefined quality attributes (e.g., identity, structural integrity, purity, and potency).	Demonstrate stability for ≥6 months under intended storage conditions while maintaining predefined quality attributes, with evidence of acceptable shipping/temperature-excursion tolerance and a credible path toward a ≥12-month shelf life.
Platform	Platform supports protective immunity after one admin and has a credible path to scalable GMP manufacture, analytical control, safety evaluation, and incorporation of a pandemic antigen without fundamental redesign.	Mature or well-characterized plug-and-play platform supporting rapid, broad, durable immunity, rapid antigen substitution, scalable multi-site manufacturing, established analytical and regulatory leverage, enhanced GC/Tfh or other mechanistic response where linked to breadth or durability.
Antigen-adjuvant compatibility (If applicable)	Antigen and adjuvant should demonstrate physicochemical compatibility; with no meaningful loss of antigen and adjuvant potency, and preservation of structural, conformational, and biological integrity and stability during proposed storage and duration of clinical trial and/or in-use period.	
4. CMC and Analytical (Nonclinical Requirements)		
Identity	Confirm the sequence, antigenic and structural identity of the specific active ingredient or construct (drug substance or drug product) using appropriate analytical and orthogonal methods	

Attribute	Minimal/Threshold	Optimal
Potency	A qualified, quantitative, platform-appropriate potency assay that retains drug substance (DS) or drug product (DP) biological potency (at least 80% of reference or initial potency and is within predefined product specifications) throughout the intended shelf life	Demonstrate the retention of drug substance and drug product biological potency (at least 90% of the reference or initial potency, and within set product rules) during the whole shelf life, using qualified, quantitative, and stability-indicating assays that show consistency between batches with different test/orthogonal methods.
Manufacturability	The manufacturing process should be compatible with scalable GMP production and should be capable of producing toxicology and initial clinical lots with acceptable lot-to-lot DS/DP yield, quality, potency and product consistency.	