GLOBAL HEALTH PRESS

STEPS OF VACCINE DEVELOPMENT

Question	Action	Issues
1. Is there an unmet medical need?	Fully describe the epidemiology and the burden of disease, globally and locally	Most countries have no suitable, let alone complete epidemio-logical data
2. What are the platform options (recombinant protein, mRNA, live virus/bacterium,...) for a vaccine candidate	Is production at large scale feasible	No company owns the full spectrum of platforms.
3. What is the target product profile (TPP) of the vaccine to be developed (*see the TPP table below*)	Include Platform, vaccine antigen, schedule, safety, efficacy,... see example below	"Living document"; may require adaptation during development; discontinue if key characteristics fail.
4. What is the feasibility and probability of success?	• Check if large scale production is possible • Is there a pathway for a license? • Are sufficient resources available (skilled, knowledgeable, expert staff, factory, > 1 bn US $ spending„ at risk".	• Manufacturing facilities should be in place before Phase 3 trials. • A Phase 3 study may be unethical if a vaccine is already available. • Expect the risk of failure to be approximately 90%.
5. Which preclinical work is needed?	• Define vaccine antigen: • Develop CMC= chemistry, manufacturing, controls • Animal studies on immunogenicity and safety	• Follow GLP, GMP, BSL-2,3, or 4 standards as appropriate
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7. Is a license granted?	• Document safety and impact in phase 4 study post licensure and regular safety follow-up	• Requires millions of vaccinated subjects to detect rare AEs. • Check requirements for use in children
8. What are requirements for vaccine recommendations by NITAGs?	• Document : • national burden of disease; • Health economics (HE) • Impact / benefit	• Formal assessment of vaccine if used in local health system; vaccine acceptance by population?
9. Will the vaccine be reimbursed?	• Get HE data; • Describe individual vs. population benefit	• Reimbursement in some countries comes with NITAG; in other countries separate process
10. What is best practice (benefit to individual subjects at risk)?	• Get recommendations from Scientific societies looking at the benefit for individual (risk) patients	• May be only a fraction of the population; may not be reimbursed (e.g. travel vaccines)
11. Will patients be willing to use the vaccine?	• Check cultural and religious concerns • Assess local vaccine access and vaccine hesitancy	• e.g. HPV in the USA or Halal production for Muslims; safety profile
12. Start with the end in mind— address all 12 points above before deciding to proceed.	• Make full plan and including building a factory / the factories with the start of the project.	• A substantial level of resources is required, including both manpower and financial investment.

Vaccine-Development in Short

Is There a Medical Need? Is There a Vaccine Candidate?

License	**Data Required** • Pre-Clinical research, CMC • Clinical studies: Efficacy, safety, reactogenicity
Recommendation	SCIENCE | FINANCING | ACCEPTANCE | CO-OPERATION
Reimbursement	• Health economics
Best Practice	• Scientific Societies: Data as; benefit for individual patient or selected population?
Patient Preference	• All above; cultural & individual beliefs, values
Real Vaccine Use	• All of the above, vaccine access; vaccine hesitancy;

Population Based / Individual Protection

Target Product Profile (TPP): Example for a next pandemic influenza vaccine (influenza A)

Composition/Platform	mRNA
Strain coverage	**HxNy t.b.d. - based on actual risk situation**
Indication	**Prevention of current pandemic influenza as of age 6 months**
Dosing	**2 + 1 (3 weeks and 6 months apart)**
Contraindication	**Allergy or serious AE after previous mRNA vaccine**
Immunogenicity	**(18-60 years) SCR ≥ 40%; SPR ≥70%; GMT ≥2.5; ≥60years ≥ 30%; 60%; 2.0**
Efficacy/ Effectiveness	**≥60%; 95%CI and LBCO t.b.d.; immunogenicity surrogates as above**
Duration of protection	**≥12 months**
Co-Administration	**None**
Reactogenicity	**Non-inferior to other mRNA vaccine**
Safety, special warnings	**Non-inferior to licensed mRNA vaccine**
Vaccination Goal	**Individual and population protection against. severe pandemic influenza (hospitalization; death), outbreak control**
Presentation, shelf life	**MDV and single dose; shelf life up to 24 months at 2-6°C; 1 day at room temperature**

Footnote

To grant children equal access to vaccine protection as compared to adults, licensing authorities usually require a PIP or an iPSP to be submitted early during the development (EMA; FDA):

1. **PIP (Paediatric Investigation Plan):** EU-required development plan describing how a medicine or vaccine will be studied in children, to generate the data needed for paediatric authorisation. Mandatory to be submitted to authorities before submission of marketing authorization.
2. **iPSP (initial Pediatric Study Plan):** US FDA-required plan outlining the proposed paediatric studies (designs, age groups, timelines) to evaluate safety and efficacy in children for a new drug or biologic, including vaccines. Must be submitted no later than 60 days after end-of-phase-2 meeting).