Scientific strategies from recent outbreaks to help us prepare for Pathogen X

How to better anticipate the desired effect of vaccines during outbreaks?

(What research data are needed to decide on optimal use of vaccines, beyond COVID-19?)

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Timelines for the malaria vaccine RTS,S (Mosquirix) from concept to the point of consideration for global policy recommendation

https://www.sciencedirect.com/science/article/pii/S0264410X21013955?via%3Dihub
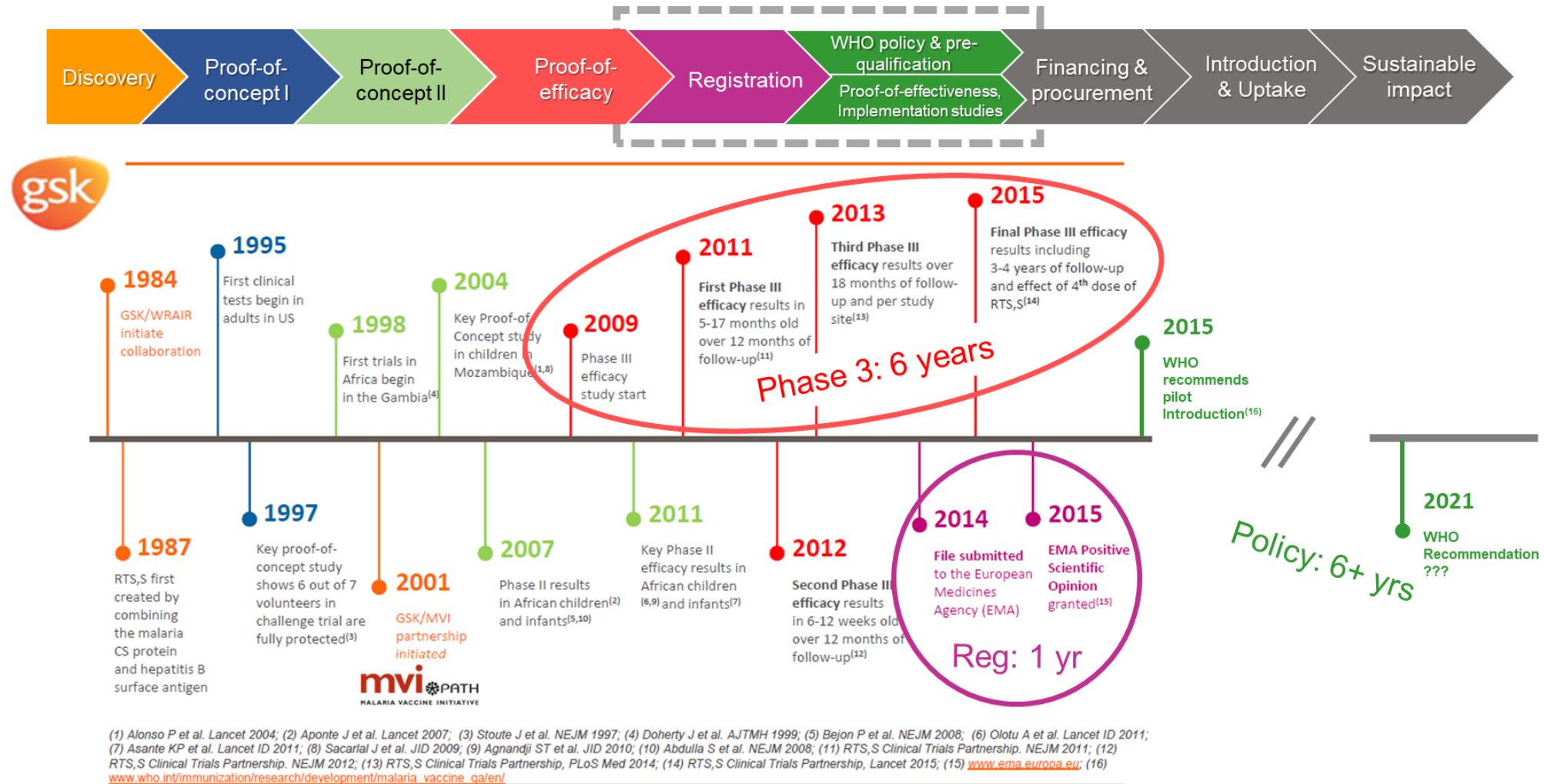
Malaria Vaccine Implementation Programme
Framework for Policy Decision

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SAGE

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Framework for Policy Decision for RTS,S

- MPAC and SAGE requested data be collected through the pilot implementations to answer questions on feasibility, safety, impact to inform a policy decision on wider use of RTS,S

- Framework for Policy Decision aims to describe how data will inform policy at the end of the pilots in 2022

- Also, will describe how data could inform
  1. Expansion of vaccinations into pilot comparator areas
  2. Broader country-wide implementation prior to 2022[1] should emerging findings show:
     - Concerns about safety "resolved"
     - Implementation data "favorable"
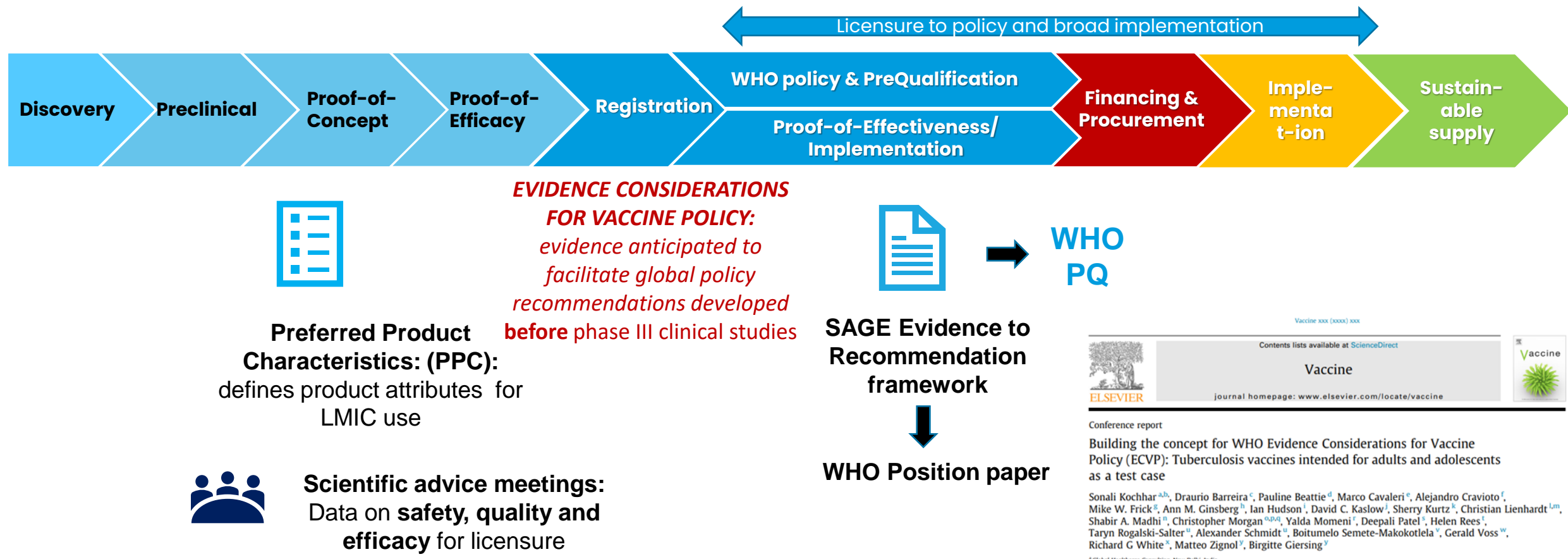   - Fourth dose coverage "high"

Press conference October 2021

Context of COVID-19 response, and lessons learned to better prepare to respond to future pandemics

- Acceleration of the development and evaluation of candidate vaccines followed by expedited regulatory approval (e.g. US Food and Drug Administration (FDA) emergency use authorization (EUA), European Medicines Agency (EMA) conditional marketing authorization, WHO Emergency Use Listing Procedure (EUL)) and subsequent licensure

- Early deployment of scarce doses of vaccines (under accelerated review and approval) for priority populations required for public health benefits

- Limited data and evidence available to inform and support global policy decision-making

- Important to align the clinical trial and observational data or evidence anticipated to be needed for policy decisions for new vaccine for pandemics

- Enable planning for critical data collection along with the accelerated clinical trials to ensure rapid policy formulation and introduction of the new vaccines

Context for the need for evidence considerations for Vaccine Policy (ECVP)

Licensure to policy and broad implementation

| Discovery | Preclinical | Proof-of-Concept | Proof-of-Efficacy | Registration | WHO policy & PreQualification / Proof-of-Effectiveness/ Implementation | Financing & Procurement | Implementa-t-ion | Sustain-able supply |

Preferred Product Characteristics: (PPC): defines product attributes for LMIC use

Scientific advice meetings: Data on **safety, quality and efficacy** for licensure

EVIDENCE CONSIDERATIONS FOR VACCINE POLICY: *evidence anticipated to facilitate global policy recommendations developed* **before** *phase III clinical studies*

SAGE Evidence to Recommendation framework

WHO Position paper

WHO PQ

https://www.sciencedirect.com/science/article/pii/S0264410X21013955?via%3Dihub

What are these gaps in the existing guidance to navigate the end-to-end process?

PPC parameters TB vaccines (adols & adults)	WHO Policy Recommendation parameters	Gavi Vaccine Investment Strategy (VIS) parameters
Indication for use, Target population	Recommendation(s) for use (Burden / recommended targeted risk population(s) by epi setting(s); other populations (permissive /contraindicated); geographies (regional, national, subnational), etc.)	
Immunogenicity Efficacy and proposed endpoints Durability of protection Safety	Benefits (pre-clinical and clinical; direct: effectiveness / preventable disease, and duration of protection; indirect: herd effect; etc.) Harm (pre-clinical and clinical; safety/ tolerability; benefit-harm-acceptance assessment; etc.)	**Health impact** Broader health system benefits
Dose schedule Co-administration	Feasibility (implementation considerations: regimen, route, setting(s); storage, delivery, etc.) Resource Use (Costs: illness; product & implementation; Cost-effectiveness; Supply and wastage: vaccine & delivery considerations; etc.)	Implementation feasibility
'Dosage, regimen, and cost of goods should be amenable to affordable supply. Favorable cost-effectiveness should be established, and price should not be a barrier to access, including in low- and middle-income countries.'	Values & Preferences (related to intervention & comparative health outcomes) Equity (Vaccine access; health, social, economic security, human rights/civil liberties, etc.) Acceptability (by stakeholders; affordability, etc.)	Vaccine cost **Value for money** Operational cost **Equity & social protection impact** **Economic impact** Additional implementation costs Global health security impact Gavi comparative advantage

Source: WHO Preferred Product Characteristics for New Tuberculosis Vaccines

Source: SAGE Guidelines development recommendations

Source: Gavi Vaccine Investment Strategy

Strategic intent for Evidence Considerations for Vaccine Policy (ECVP) process and guidance

- Tool to facilitate **early and ongoing communication** between vaccine developers, regulators, policymakers, funders, public health authorities, researchers and technical experts at the national, regional and global level to **mutually outline** the anticipated data and evidence

- The ECVP should be available *before* **the design of pivotal licensure trials,** to be incorporated into trial designs and strategic vaccine development work planning

- For vaccine developers, **greater clarity on anticipated expectations for policy** will increase the likelihood that studies will meet requirements to generate optimal policies

- For new vaccines for priority diseases, the WHO ECVP aims to provide early information on the **clinical trial and observational data, or evidence** anticipated to be needed for WHO global, regional and country-level policy making, program decisions and program implementation

- Does **not preclude or supersede the independent SAGE** recommendations required for all vaccines seeking WHO policy recommendation. However, they will likely catalyse earlier formal discussions with SAGE on the anticipated evidence needs for future policy deliberations

- The ECVP will be **a living document** that is updated as new information becomes available; it will likely replace the WHO PPC and may serve as a helpful starting point for a vaccine specific SAGE WG.

Structure of the ECVP guidance

The ECVP is based on SAGE's **Evidence to Recommendation** framework and includes six tables to describe the following parameters:

- Table 1: Vaccine Product Related Parameters

- Table 2: Regulatory Strategy Considerations for Initial Licensure

- Table 3: Vaccine Delivery related Parameters for the Priority Populations

- Table 4: Vaccination of Specific Populations

- Table 5: Implementation Considerations

- Table 6: Engagement and potential timelines or triggers

Each section identifies:

o   **High Priority** parameters in red: expected to be critical for SAGE and other policy bodies at the regional and country level;

o   **Medium Priority** parameters in blue: for which data and evidence are likely to be beneficial for policy recommendation.

➢ *Prioritization of parameters can be adapted as needed*

Vaccine related and delivery parameters included in the ECVP (red are critical; blue are beneficial)

Section 1: Vaccine related parameters
- Disease indication
- Priority target population/s
- Target countries
- Duration of protection at time of conditional approval and/or licensure
- Duration of protection (as part of effectiveness studies)
- Schedule (for primary series and booster)
- Route of administration
- Co-administration with other vaccines
- Measure of efficacy
- Efficacy endpoints in the clinical trial
  - Primary endpoints
  - Secondary endpoints
- Safety/reactogenicity

- Measure of Effectiveness
- Measure of efficacy/ effectiveness against VOC/ bacterial antigenic variation
- Measure of Immunogenicity

Section 3: Vaccine related parameters
- Vaccine delivery strategy/s for the primary target population
- Vaccine thermostability and storage temperature requirements
- Presentation

Section 5: Implementation related parameters included in the ECVP

- Provides information on the **type of data that could inform policy, financing and introduction decisions** by multiple actors, including policy-makers at the national, regional and global levels, as well as global financing agencies such as Gavi, civil society organisations and implementation partners.

- **Intended to serve as a starting point to catalyse dialogue with regard to refining the data needs and expectations from different stakeholders depending on their specific contexts and policy scenarios.**

- Several parameters will form part of the **Gavi vaccine investment strategy (VIS)** and likely needed for Gavi financing and initial policy introduction in Gavi-supported countries.

- Overarching activities related to implementation should include development of **communication strategies** to facilitate vaccine acceptability, build awareness, and generate demand. This requires generation of a **robust communications and community engagement plan/program,** vaccine-related events (VRE) response plan, and supporting materials which are updated throughout the development process.

- Issues and myths on the disease and vaccination need to be identified and addressed, prior to and during vaccination campaigns.

Section 5: Implementation related parameters included in the ECVP (red are critical; blue are beneficial)

- Feasibility *(i.e., practicality of vaccine implementation, including in high burden countries (HBCs))*
- Values and preferences of the target populations for vaccine *(i.e., the likely acceptability of the vaccine)*
- Demand potential *(i.e., visibility into future uptake and market size, including for HBCs, that can inform market shaping discussions with stakeholders including donors, industry partners, and vaccine purchasers)*
- Health Impact *(i.e., the benefit of vaccination to the vaccinated individuals, and to the wider population)*
- Economic impact *(i.e., contribution of vaccine introduction to micro- and macro-economic benefits per country)*
- Value for money *(i.e., estimates on likely utility derived from budget spent in the target populations)*
- Economic evaluation/Alternative interventions *(i.e., Comparison of the cost and benefits, also relative to alternatives)*
- Equity and social protection impact *(i.e., prioritizing the needs and rights of the most vulnerable, and ensuring equitable benefit from vaccines)*
- Access and affordability *(i.e., ensuring that the vaccine will be made broadly and equitably available at an affordable price)*
- Global health security impact *(i.e., the potential benefit of the vaccine in averting bio-security risks)*

Does the ECVP framework have applicability to better prepare for Pathogen X?

ECVP is a new tool that can:

➢ **Enable planning for critical data collection along with the accelerated clinical trials to ensure rapid policy formulation and introduction of the new vaccines**

➢ **Facilitate early discussion/alignment on the clinical trial/observational data and evidence anticipated for policy decisions for new pandemic vaccines**

A pathogen X ECVP would need to be developed by a WHO expert working group

- Generic ECVP framework developed and reviewed by SAGE; was published on the WHO website and can be adapted to different vaccines/diseases: https://www.who.int/publications/m/item/who-evidence-considerations-for-vaccine-policy-development-%28ecvp%29

- An **exemplar ECVP for TB vaccines for adults and adolescents has been drafted** by an expert WG, including RITAG chairs and SAGE members. Draft completed; public consultation will begin in September.

Acknowledgements – the WHO ECVP working group

- **WHO secretariat:** Birgitte Giersing & Dereck Tait (consultant)
- **ECVP working group chairs:** Sonali Kochhar & Helen Rees
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- Alexander Schmidt - GMRI
- Marta Tufet/Cate Bennett - Gavi
- Susan Wang – US CDC
- Charlie Weller – Wellcome Trust

- SAGE Members and Secretariat