

SAVAC – The Strep A Vaccine Global Consortium

Development Strategy Outline

8 May 2020

1. MISSION

The SAVAC **mission** is to ensure that safe, effective and affordable Strep A vaccines are available and implemented to decrease the burden of Strep A disease in the most in need.

- SAVAC is aligned to the WHO Strep A Vaccine Research and Development Roadmap, whose vision is: “A safe, globally effective and affordable Strep A vaccine is needed to prevent and potentially eliminate acute Strep A infections (pharyngitis, skin infections, cellulitis, invasive disease) and associated antibiotic use, immune-mediated sequelae (kidney disease, rheumatic fever and rheumatic heart disease) and associated mortality.”
- SAVAC aims to represent the international Strep A vaccine community with a central networking and connecting role.
- SAVAC has a role in identifying and filling research and development gaps for Strep A vaccines broadly, including advocacy/awareness, epidemiology/burden, pipeline, correlates, and funding

2. A 5-YEAR STRATEGY 2019-2024

SAVAC has a broader vision and strategy beyond the 2-year horizon of funding from the Wellcome Trust – a strategy that will take the Strep A field further along the current R&D Roadmap with alignment to the WHO Preferred Product Characteristics guidance and the WHO-endorsed Full Value of Vaccines Assessment (FVVA) evaluation approach (formerly called Full Public Value of Vaccines).

The goal of SAVAC is to reduce the burden of Strep A infection / Strep A-infection-associated diseases through the development and use of safe, effective and affordable Strep A vaccines. To accomplish this goal, SAVAC will pursue a strategy based on the following:

ADVOCACY AND COMMUNICATION. The foundation of this strategy is communication – SAVAC must make Strep A a larger Global Health priority among funders and countries. It will make use of the World Health Assembly resolution calling for a reduction in Strep A burden, highlighting the role that vaccines can play as a cost-effective solution to this problem. Although the Wellcome Trust funding does not specifically fund advocacy *per se*, SAVAC will retain communication, advocacy and awareness-raising as a critical element of its work, and seek resources from other sources to amplify these efforts. This includes development and maintenance of a website where up-to-date Strep A related news / research may be easily referenced, with a particular focus on Strep A vaccines, and where a clear and informative summary of Strep A as a global problem can be easily accessed. The website will link to available news, resources, advocacy, and social media to enhance the visibility and improve appreciation of the Strep A problem.

COORDINATION. The Strep A field is small, so that, to the extent possible, SAVAC will ensure that its efforts and resources will be coordinated to avoid redundancy within the SAVAC community and with other Strep A activities.

FUNDING. Strep A is underfunded relative to disease burden. SAVAC will;

- Seek additional funding for SAVAC activities including Communication/Advocacy and the work of other Working Groups.
- Encourage funding agencies and industry to increase investment in Strep A vaccine development and more broadly in Strep A research.

Strep A should also be recognized as a poverty-related disease and as pathogen highly relevant for antimicrobial resistance (AMR) in order to qualify for funding by the European Union, EDCTP and AMR biomedical research programs.

SCIENCE. Strep A vaccine development should be grounded in science, mindful of ethical and safety requirements. This includes knowledge of burden, pathogenesis, immunity, auto-immunity, vaccine development, correlates of risk and immune protection, and safety. Of these, only the vaccine safety workstream is supported by the initial funding from the Wellcome Trust, but all workstreams are essential. SAVAC will retain them as critical elements, seeking funding for them where possible.

VACCINE SUPPLY AND ACCESS. The common goal of Strep A vaccine development is to reduce the broad Strep A disease burden, and so vaccine developers must be mindful not only of the science but of the downstream elements of vaccine development – manufacturing and supply, demand, cost, policy, and financing. The Consortium will help, through the FVVA, to identify, anticipate and de-risk issues that might impede the efficient adoption of effective Strep A vaccines, aligned with the WHO vision for the future of vaccine life course programs with coverage and equity as central considerations.

2.1 Implementation of the 5-year strategy

In its first five years, SAVAC aims to ensure that the following key milestones are achieved by its partners or other relevant organizations:

- Work in concert with other initiatives (e.g., Coalition to Advance New Vaccines Against Group A Streptococcus (CANVAS) initiative, the Australian Strep A Vaccine Initiative (ASAVI)), to maximize respective impacts and reduce the duplication.
- Develop the FVVA for Strep A including the broadest synthesis of the value of a Strep A vaccine across different stakeholders (section 3.2.4.1)
- Identify critical gaps in understanding of Strep A disease burden and identified funded strategies to target them;
- Develop a consensus statement on safety requirements for testing of Strep A vaccine candidates and engaged regulators accordingly;
- Delineate the methodology to identify immune correlates of risk and protection and initiated preliminary work;
- Assess a short list of vaccine manufacturers;
- Achieve critical momentum in advocacy as a core function with communication and advocacy plans in place;
- A defined regulatory, policy and financing decision pathway including WHO pre-qualification and through SAGE and Gavi; and
- Funding mechanisms for access to Strep A vaccines for middle-income countries as well as Gavi-eligible low-income countries

Ultimately, SAVAC partners will have implemented the following:

- Preparedness activities in countries in Africa and Asia in anticipation of Phase II and III trials
- Integrated Product Development Plans (IPDPs) and Life Cycle Management Plan (LCMP) for one or more vaccine candidates
- Progressed at least two vaccine candidates through Phase II trials
- Progressed at least one vaccine candidate through Phase IIb/III

3. THE 2-YEAR STRATEGY (CURRENT WELLCOME TRUST FUNDING)

The current Wellcome Trust funding is considered as a first step of a longer-term strategy described above. The funding covers 2 years with a possible 12-month no-cost extension for a total budget of US \$2.2 million.

3.1 Role of the SAVAC Executive Committee (EC)

There is no Strep A vaccine development activity in major multinational vaccine companies or developing country vaccine manufacturers at this current time. Endorsement of WHO-sponsored consensus documents on a Roadmap for Strep A vaccine R&D and a Preferred Product Characteristics document are initial steps, but a truly global Consortium is needed to fill the remaining gaps and to move the Strep A vaccine agenda beyond the consensus documents to realize Strep A vaccine development. SAVAC will bring together, inform, and organize those parties interested in furthering Strep A vaccine R&D, with the aim of promoting a more focused and efficient use of resources to accelerate vaccine licensure, uptake and use.

Members of the SAVAC Executive Committee will be responsible for different work streams (1. Vaccine safety; 2. Epidemiology; 3. Vaccine landscape; 4. Correlates of protection) and teams of EC members will join different efforts as necessary. The proposed consortium will provide leadership and bring focus to the development of Strep A vaccines.

The key areas under the responsibility of the EC include:

- Advocacy;
- Coordination of Working Groups in the four workstream areas outlined above;
- Communication including website;
- Engaging consultants in a strategic manner;
- Organization of strategic Consultations/Conferences; and
- Secretariat, Telecommunications and Travel.

3.2 Implementation plan

3.2.1 SAVAC Executive Committee (EC)

SAVAC will organize periodic teleconferences and at least three meetings for the interaction between working group and Technical Advisory Committee that provides guidance on the development of the FVVA work so that updates are shared and technical support is provided.

The SAVAC Executive Committee Charter (see separate document) has been developed to describe *modus operandi* (frequency of calls, one mid-summer, then every other month starting in September 2019, agenda and minutes templates, roles and responsibilities, creation of SharePoint for EC members)

3.2.2 Communication strategy

The EC will position SAVAC as the focal point global efforts related to Strep A vaccines. Clear messaging and a tiered communication strategy is therefore crucial. A coordinated, strategic and carefully timed approach to the announcement of SAVAC and Strep A vaccine development efforts is necessary. In addition, securing funding for this activity is also a priority.

The communication strategy will be tailored to the various stakeholders. A broader process will then need to be put in place to:

- Identify global, regional and country-specific stakeholders to be targeted;
- State the purpose of the communication for each stakeholder;
- Identify preferred interlocutors to convey the messages to the targeted audience;
- Develop messages for the targeted audience;
- Develop timing of communication and preferred communication support to be used; and
- Ensure that the communications host organization has the capacity to maintain up-to-date communications, including agreed messaging, and acting as a singular point of contact for the Global Strep A community

Stakeholders will include (at a minimum):

- Scientific community
- Communities affected by Strep A
- Broader public
- Donors
- Developing Country Vaccine Manufacturers (DCVM)
- Health Authorities in both HICs and LMICs
- WHO, SAGE, PDVAC
- Gavi

3.2.3 Communication action plan

A timed approach will be developed as follows:

- Development of a communication strategy and specific action plan;
- Creation of a SAVAC Website (IVI);
- Official launch;
- Stakeholder meeting in association with the Global Vaccine and Immunization Forum (GVIRF) in Seoul;
- Plan for a meeting in the 2nd year of the grant as a close-out of initial Wellcome Trust funding, and with a view to next steps of the 5-year strategic plan;
- Seek additional funding for regional advocacy meetings in Africa and Asia-Pacific; and
- Use the email listings from key meetings (Seoul, London, Lancefield Society)

3.2.4 Alignments with WHO Strep A Research and Development Roadmap

Group A Strep Research and Development Roadmap (and Preferred Product Characteristics) documents were published by WHO in 2018, with members of SAVAC EC as key authors (Vekemans et al. Clin Infect Dis 2019).

Follow-up actions were identified during the WHO Consultation on Strep A Vaccines, May 2018. Particular areas requiring attention in order to facilitate vaccine development were identified. These areas are encompassed in the SAVAC strategic plan.

3.2.4.1 Activities funded under current grant

Full Value of Vaccines Assessment (FVVA)

The WHO template for the FVVA will be adapted for Strep A vaccines. The FVVA for Strep A will contain the broadest synthesis of the value of a Strep A vaccine across different stakeholders (normative, research, manufacturing, state-level policy, implementation). It will contain information from the business case and the investment cases.

The key elements of the FVVA were outlined and prioritized during the FVVA Working Group meeting held at TKI, Perth, March 8, 2019.

Safety

SAVAC will gather experts (including on regulatory matters) to review what we know, what we would like to know, and what data to collect and for how long about Strep A vaccine safety to guide vaccine design and clinical trial design (e.g., long-term safety assessment, cardio assessment, immediate immune reactions triggered by the vaccine in Step A naïve and immune individuals). This expert review will fill a key gap for the field, providing guidance for vaccine developers.

3.2.4.2 Activities unfunded under current grant

Advocacy (See 3.2.2)

While not funded under the current grant, advocacy remains a core function of SAVAC. Funding should be secured as an early priority. As outlined above, advocacy needs to target multiple levels, with different approaches. The SAVAC website has been developed (<https://savac.ivi.int>)

Epidemiology, disease burden, and prevention

While not funded under the current grant, a key activity of SAVAC will be to re-establish case definitions for Strep A disease entities (with review of previously developed case definitions within the collaborative framework of NIH, US CDC and WHO). Furthermore, a gap analysis of burden of disease data by disease type, region and country will provide a framework for further funding applications to address key missing areas of data. There will be an opportunity to intersect and potentially leverage off disease burden work being undertaken as part of the FVVA.

Correlates of protection

While not funded under the current grant, a key activity of SAVAC will be to advocate for further work in standardizing immune correlates of risk and protection and providing technical advice to any efforts toward this goal.

Vaccine landscape

While not funded under the current grant, SAVAC will maintain an up-to-date vaccine landscape analysis of any vaccine candidates in pre-clinical and clinical development.