



## **MEDIA RELEASE**

### **UPDATE ON THE SAHPRA REVIEW OF THE SPUTNIK V VACCINE**

#### **Embargo: Immediate release**

**Pretoria, 18 October 2021** – SAHPRA has been engaged in a rolling review of the data for the Sputnik V COVID-19 vaccine since the initial application was submitted on 23 February 2021. This vaccine was developed by the Gamaleya Research Institute of Epidemiology and Microbiology in the Russian Federation. The locally-licensed applicant is Lamar International Pty (Ltd).

The Sputnik V vaccine combines two separate adenovirus-vectored constructs, one relying on the Adenovirus Type 26 (Ad26) and the other on Adenovirus Type 5 (Ad5), as the delivery vehicles for the antigen.

Concerns have been raised about the safety of Ad5-vectored vaccines in populations at risk for HIV infection. One of the challenges faced by such vaccines is the presence of pre-existing Ad-specific neutralising antibodies (NAbs) in the general population.

The safety of adenovirus vaccine vectors has been evaluated in a number of studies. In particular, the results of the STEP trial (which primarily recruited men who have sex with men in the Americas)<sup>1</sup> and the PHAMBILI trial (which recruited heterosexual men and women in South Africa)<sup>2</sup> were considered. Both clinical trials were designed to administer three doses of an Ad5-vectored vaccine encoding the HIV gag, pol and nef proteins. In both the STEP clinical and PHAMBILI trials, administration of an Ad5-vectored vaccine was associated with enhanced susceptibility/acquisition of HIV in men. The STEP trial was stopped in September 2007 due to lack of efficacy, but evidence quickly emerged of an enhanced risk of HIV infection in a particular subgroup of participants (uncircumcised men with high titers of pre-existing antibodies to Ad5). Over extended follow-up, the increased risk of HIV among vaccine recipients became statistically significant when the entire trial population was analysed.<sup>3</sup> The STEP trial results led to the early cessation of the PHAMBILI

trial. Although the initial results from PHAMBILI trial did not show enhanced HIV risk, this risk was confirmed after extended follow up.<sup>4</sup>

During the assessment of the application for approval of the Sputnik V vaccine, SAHPRA reviewed the outcomes of the STEP and PHAMBILI trials in detail, as well as the arguments advanced in a commentary in Lancet in 2020, by Buchbinder *et al.*<sup>5</sup> In particular, this commentary pointed to confirmatory data from a non-human primate challenge study: “infecting rhesus macaques with Ad5 and then immunising them with a replication-incompetent Simian immunodeficiency virus (SIV) vaccine based on Ad5 increased the risk of SIV acquisition from low-dose SIV penile challenge”.<sup>6</sup>

SAHPRA therefore requested the applicant to provide data demonstrating the safety of the Sputnik V vaccine in settings of high HIV prevalence and incidence. The applicant was not able to adequately address SAHPRA’s request.

In addition, SAHPRA held a consultation meeting with expert committees, including leading members of the local and international scientific community, on this matter.

To date, the Sputnik V COVID-19 vaccine has not received Emergency Use Listing by the World Health Organization (WHO). The most recent WHO update indicates that the process is “On hold, awaiting completion of rolling submission”.<sup>7</sup> A further note states: “Anticipated date will be set once all data is submitted and follow-up of inspection observations completed”. Recent media coverage has confirmed that there is ongoing engagement between WHO and the Russian authorities.<sup>8</sup>

Following the consultation with local and international scientific experts and after considering all the available data, including review of the dossier submitted by Lamar International (Pty) Ltd, SAHPRA resolved that:

1. The Section 21 application for Sputnik V by Lamar international Pty (Ltd) not be approved at this time. SAHPRA is concerned that use of the Sputnik V vaccine in South African, a setting of a high HIV prevalence and incidence, may increase the risk of vaccinated males acquiring HIV.
2. The rolling review of the Sputnik V vaccine will, however, remain open for submission of relevant safety data in support of the application.

SAHPRA notes media reports that applications for the approval of the Ad26-vectored component only (denoted as Sputnik Light) are expected to be submitted to a number of national medicines regulatory authorities. SAHPRA has not yet received an application for Sputnik Light.

**Issued by:**

Dr Boitumelo Semete

**CEO**

**Boitumelo.semete@sahpra.org.za**

**For further enquiries /information contact:**

**Media contact:**

**Ms Nthabi Moloji**

Mobile: 078 125 2060 / 082 407 8854

E-mail: [Nthabi.moloji@sahpra.org.za](mailto:Nthabi.moloji@sahpra.org.za)

**Mr Yuven Gounden**

066 1202 669

[yuveng@sahpra.org.za](mailto:yuveng@sahpra.org.za)

[media@sahpra.org.za](mailto:media@sahpra.org.za)

**About SAHPRA:**

SAHPRA is tasked with regulating (monitoring, evaluating, investigating, inspecting and registering) all health products. This includes clinical trials, complementary medicines, medical devices and in-vitro diagnostics (IVDs). Furthermore, SAHPRA has the added responsibility of overseeing radiation control in South Africa. SAHPRA's mandate is outlined in the Medicines and Related Substances Act (Act No 101 of 1965 as amended) as well as the Hazardous Substances Act (Act No 15 of 1973).

SAHPRA has three pillars to ensure that medicines, medical devices and IVDs meet the requisite standards to protect the health and well-being of all who reside in South Africa:

- Safety
- Efficacy
- Quality

It is these three pillars that define the ethos of SAHPRA.

---

<sup>1</sup> Buchbinder SP, Mehrotra DV, Duerr A, *et al.* Efficacy assessment of a cell-mediated immunity HIV-1 vaccine (the Step Study): a double-blind, randomised, placebo-controlled, test-of-concept trial. *Lancet.* 2008; 372: 1881-1893.

---

<sup>2</sup> Gray GE, Allen M, Moodie Z, *et al.* Safety and efficacy of the HVTN 503/Phambili study of a clade-B-based HIV-1 vaccine in South Africa: a double-blind, randomised, placebo-controlled test-of-concept phase 2b study. *Lancet Infect Dis.* 2011; 11: 507-515

<sup>3</sup> Duerr A, Huang Y, Buchbinder S, *et al.* Extended follow-up confirms early vaccine-enhanced risk of HIV acquisition and demonstrates waning effect over time among participants in a randomized trial of recombinant adenovirus HIV vaccine (Step Study). *J Infect Dis.* 2012; 206: 258-266

<sup>4</sup> Moodie Z, Metch B, Bekker LG, *et al.* Continued follow-up of Phambili phase 2b randomized HIV-1 vaccine trial participants supports increased HIV-1 acquisition among vaccinated men. *PLoS One.* 2015; 10:e0137666

<sup>5</sup> Buchbinder SP, McElrath MJ, Dieffenbach C, Corey L. Use of adenovirus type-5 vectored vaccines: a cautionary tale. *Lancet* 2020; 10260: e68-e69.

<sup>6</sup> Qureshi H, Ma ZM, Huang Y, *et al.* Low-dose penile SIVmac251 exposure of rhesus macaques infected with adenovirus type 5 (Ad5) and then immunized with a replication-defective Ad5-based SIV gag/pol/nef vaccine recapitulates the results of the phase IIb Step trial of a similar HIV-1 vaccine. *J Virol.* 2012; 86: 2239-2250.

<sup>7</sup> Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process (29 September 2021).

[https://extranet.who.int/pqweb/sites/default/files/documents/Status\\_COVID\\_VAX\\_29Sept2021\\_0.pdf](https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_29Sept2021_0.pdf)

<sup>8</sup> Anon. WHO keeps Sputnik V's EUL process on hold over missing data. *Pharmaceutical Technology*, 14 October 2021. <https://www.pharmaceutical-technology.com/news/who-sputnik-v-eul-process-on-hold/>