## CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

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# **COVID-19 vaccination policies** and the new challenges of international travel

International travel is rebounding as coronavirus disease 2019 (COVID-19) vaccinations continue and more countries are opting for 'living with COVID' in the hopes of moving from a pandemic footing toward an endemic one. Such travel remains far from risk-free, however, given the existence of asymptomatic carriers and the emergence of new severe acute respiratory syndrome coronavirus 2 variants. To protect their residents, most countries have instituted policies requiring incoming travelers to be fully vaccinated according to their own policies and to show proof of a negative COVID test [1,2].

This has raised new challenges for everyone who wants to travel internationally, especially for those who have received vaccines not yet approved by the World Health Organization (WHO) and other regulatory agencies like the United States Food and Drug Administration and the European Medicines Agency. Residents of many low-to-middle income countries do not have access to some vaccines approved by these entities. This generates clear inequalities in international travel policies around the world.

The case of individuals vaccinated with Gam-COVID-Vac is an example. On February 2, 2021, the first study on the vaccine, produced by the Gamaleya Institute in Russia, reported on the safety and efficacy of this rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 jab (Gam-COVID-Vac or Sputnik V). The efficacy was 91.6%, similar to the mRNA vaccines BNT162b2 (BNT, Pfizer; Pfizer, New York, NY, USA) and mRNA-1273 (Moderna, Cambridge, MA, USA), and superior to the adenoviral vaccines ChAdOx1 nCoV-19 (AZD1222; AstraZeneca, Cambridge, UK) and Ad.26. COV2 (J&J/Janssen; Johnson & Johnson, New Brunswick, NJ, USA) [3,4].

Many countries as well as the WHO, have not approved vaccination with Gam-CO-VID-Vac waiting for reliable independent validation of its efficacy [5]. Yet, given the scarcity of WHO-approved vaccines, this vaccine has been used in at least 75 countries in Asia, Africa, and Latin America [6]. Consequently, many persons vaccinated with the Gam-COVID-Vac from these countries have experienced restrictions in their international movements.

Beginning in November 2021, all travelers to the United States were required to show proof of being fully vaccinated as well as a negative COVID-19 test. Only WHO-approved vaccines were accepted, leaving persons who have had the Gam-COVID-Vac not considered fully vaccinated [7,8] and consequently unable to enter the United States. This complex situation also applies to those who got other COVID vaccines not approved by the WHO, including Cansino (CanSinoBIO, Tianjin, China), Novavax (produced in India), EpiVacCorona (VECTOR Center of Virology, Koltsovo, Russia), Abdala (Center

for Genetic Engineering and Biotechnology, Havana, Cuba), Soberana (Finlay Institute, Havana, Cuba), and others.

The implication is that travelers from countries where non-WHO-approved vaccines are the only ones that are widely available will have to find a way to obtain a WHO-approved vaccine for traveling to the United States and some European countries. For example, travelers who have received the twodose schedule of Gam-COVID-Vac will also be required to get two additional doses of any mRNA vaccine, two doses of the AZD1222 vaccine, or a single dose of the J&J vaccine.

This is problematic because mixing anti-covid vaccines is mostly recommended by the WHO in case of vaccine shortages [9]. Requiring aspiring travelers to mix jabs, despite not recommending it in other cases, raises ethical questions regarding their justification and complicates monitoring in postvaccine pharmacovigilance protocols.

Inconsistencies between countries in their policies and reporting requirements also impose unnecessary burdens upon travelers, especially those from low-to-middle income countries. Some countries, including many high-income countries, require unvaccinated or not fully vaccinated travelers to follow measures like frequent testing and reporting, passenger locator forms, and quarantines. Some use official lists of "green," "red," "orange," and "scarlet red" countries, changing vaccination and testing requirements according to COVID epidemiology indicators in the country of origin, banning travelers from regions of high risk for new and emerging strains of coronavirus such as the Omicron variant [10,11].

Indeed, many new restrictions have been implemented across the world to avoid the spread of this variant [12]. Early epidemiological data suggests that Omicron may present mainly mild symptoms. If it does not overwhelm hospitals as the Delta variant did, the new travel bans and changes in vaccination requirements to travel may not end up being necessary. Regardless of whether or not the new policies are actually necessary, they nevertheless create inconveniences for travelers especially from low to middle-income countries who possess less widely-accepted documentation of their vaccination status.

In order to end the pandemic and normalize international travel, it should be a priority to solve the gap between highincome countries and many low to middle-income countries in relation to access to COVID vaccines. Overall, ethical questions remain about the ethics of COVID-19 travel rules and the restrictions based on the vaccination status of international travelers. If some vaccines cannot be approved because they lack independently validated data on efficacy, then studies to produce the evidence needed to establish efficacy and safety should be expedited through international collaboration to harmonize travel policies around the world.

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