INSIGHTS FROM

MEDICC

Cuba's COVID-19 Vaccine Enterprise: Report from a High-Level Fact-Finding Delegation to Cuba

EXECUTIVE SUMMARY

Executive Summary

In June 2022 an international delegation of scientists from the United States, the Caribbean and Africa traveled to Havana, Cuba for a three-day fact-finding mission to better understand Cuba's COVID-19 vaccine development and vaccination efforts. It was the first time in five years that a scientific delegation with significant US presence had engaged in discussions with medical researchers in Cuba. It also included African and Caribbean members to ensure there was a diversity of scientific and public health perspectives. Together, delegation members represented a broad range of expertise in public health systems, infectious diseases, biotechnology, and vaccine development.

The visit was organized by MEDICC (Medical Education Cooperation with Cuba), a US-based non-profit that promotes health-related dialogue and collaboration. Since 1997, MEDICC has facilitated exchanges between Cuban and US health professionals, scholars, policymakers, foundations, students, and leaders of medically underserved communities. Delegation organization and travel were supported in part by a grant from the Open Society Foundations.

During our three days in Havana, MEDICC delegation members met with experts involved in the production and deployment of Cuba's COVID-19 vaccines. We also visited three vaccine production facilities, met with Cuban health professionals who led the country's national COVID-19 adult and pediatric vaccination campaigns, and visited a local elementary school where children and teachers described their experiences with vaccination efforts.

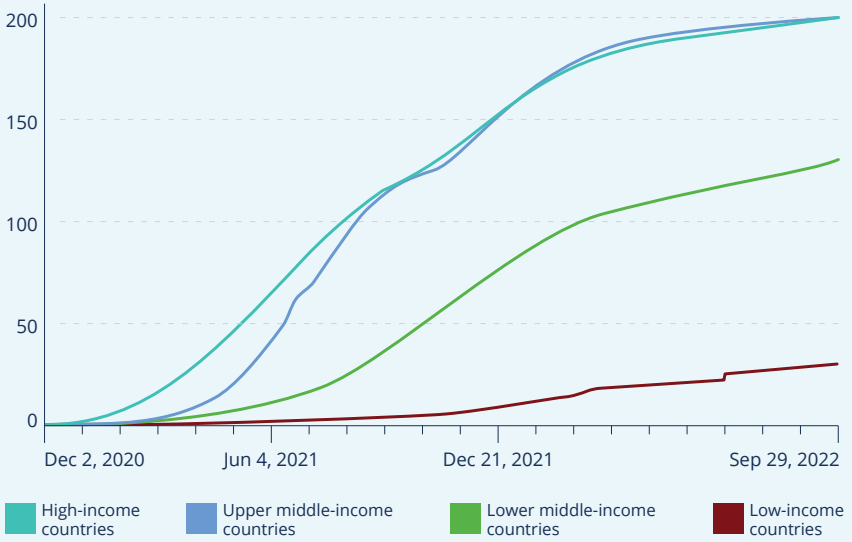
The purpose of the fact-finding mission was three-fold: first, we wanted to learn how and why a relatively small country of some 11 million people—one facing considerable economic hardships—had developed, manufactured and deployed its own vaccines, which were shown to have over 95% efficacy in preventing severe disease and death. Second, we wanted to understand Cuba's vaccine rollout strategy and preliminary results. Third, we wanted to explore Cuba's approach to science in the context of public health, with a focus on how Cuba's COVID-19 vaccine development effort and vaccination model could reveal opportunities to reduce global inequities in access to vaccines and other health innovations—especially given the country's existing network of international partnerships.

When we visited in mid-2022, globally there were daily tallies of some 843,000 new confirmed COVID-19 cases and 1874 deaths per day, with only 60% of the global population fully vaccinated.[1,2] In contrast, Cuba was reporting fewer than 20 new infections daily and zero deaths,[3] and 90% of the population, including 97.5% of children over the age of 2, had been fully immunized with the Cuban-developed vaccines. This compared to August of 2021, prior to vaccination, when infections in Cuba peaked at 10,000 a day and deaths at 100.[4]

The delegation was mindful of predictions that the world is perilously close to the next pandemic, with crossover zoonotic infections—which already account for 75% of emerging infectious diseases—on the rise amidst advancing climate change.[5] We were also alarmed by the inequitable vaccine access that has prolonged the pandemic to now—and how it highlights a broader failure of today's surge of biomedical innovation to reach billions of people in low- and middle-income countries.[6]

Worldwide COVID-19 Doses Administered per 100 People, By Income Group

All doses, including boosters, are counted individually



Source: Official data collated by Our World in Data, World Bank

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It is important to note that the MEDICC delegation was not functioning as a regulatory review or certification body. Likewise, it was outside of its scope to seek independent verification of the data presented regarding COVID-19 vaccines, vaccination coverage and voluntary vaccination compliance or their role in Cuba's overall pandemic response strategy. Rather, we sought to engage in frank, open and direct exchanges with Cuban scientists and regulatory, industry and public health experts—without involvement by high-level government officials—an aim that was fulfilled.

The following summary is based on our site visits, extensive discussions between delegation members and our Cuban peers, and relevant documents in the public record. A more detailed exploration, including technical aspects of Cuba's COVID-19 vaccines, plus extensive data from clinical trials and vaccine rollout, can be found in the full Technical Report.

Cuba COVID-19 Vaccine Timeline

- **March 2020:** Cuba initiates COVID-19 vaccine development effort.
- **July 9, 2021:** Abdala vaccine receives Emergency Use Authorization (EUA) for use in adults.
- **August 20, 2021:** SOBERANA 02 and SOBERANA Plus vaccines receive EUA for use in adults.
- **September 3, 2021:** SOBERANA 02 and SOBERANA Plus receive EUA for use in the pediatric population.
- **October 27, 2021:** Abdala receives EUA for use in the pediatric population.

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Cuba's COVID-19 Vaccines

Concerned about the potential to procure vaccines from global suppliers, Cuban health officials decided in March of 2020 to pursue their own COVID-19 vaccines. They ultimately developed, manufactured and used two COVID-19 vaccine regimens.

One vaccine is called Abdala. It utilizes three doses of the same formulation administered intramuscularly 14 days apart. It was developed by Cuba's Genetic Engineering and Biotechnology Center. It is based on technology similar to that employed by the Center for its hepatitis B vaccine, Heberbiovac. That vaccine has been used in Cuba since 1992 and was approved in 2001 by the World Health Organization (WHO) for international use.

Cuba's other COVID-19 vaccine regimen involves two doses of a vaccine called SOBERANA 02 followed by one dose of a formulation known as SOBERANA Plus. Each is administered intramuscularly 28 days apart. The SOBERANA vaccines were developed by Cuba's Finlay Vaccine Institute. SOBERANA 02 is what is known as a conjugate vaccine. It is based on technologies developed in the 1980s that have produced vaccines now in use globally that are known to be safe and especially effective for producing a strong immune response in children.

Both the Abdala and SOBERANA vaccines generate immunity with a 'spike' protein isolated from the SARS-CoV-2 virus. The spike protein is what the virus uses to penetrate human cells. Many vaccines in use globally—including those available in the United States and Europe—rely on some aspect of the spike protein to generate immunity. Also, like those vaccines, clinical trials assessing their efficacy were conducted before the arrival of the omicron lineage of immune-escaping variants.

Evidence of efficacy, Abdala vaccine: Data presented from a phase 3 clinical trial indicated the vaccine's efficacy was 92.28% for preventing symptomatic disease, 100% for preventing severe disease and death, and had a good safety profile with no reports of severe adverse events.

Evidence of efficacy, SOBERANA vaccines: Data presented from a phase 3 clinical trial showed the SOBERANA regimen's efficacy was 92% for preventing symptomatic disease and 100% for preventing severe disease and death, and had a good safety profile with no reports of severe adverse events.

Vaccine Regulatory Review and Emergency Use Authorization

Review of Cuba's COVID-19 vaccines—from pre-clinical development through phase 3 clinical trials—was conducted by the country's regulatory authority, the Center for State Control of Medicines and Medical Devices (CECMED). Since 2011, the Center has retained certification as a Level 4 National Regulatory Authority of Reference from WHO and the Pan American Health Organization (PAHO).

In the summer of 2021, CECMED granted emergency use authorizations (EUA) allowing the Abdala and SOBERANA vaccines to be administered to adults. In the fall of 2021, after additional trials were conducted in children, the agency granted emergency use authorization for vaccination of Cuba's pediatric population (aged 2 to 18 years).

Cuba's COVID-19 Vaccination Strategy and Results

Cuba's Ministry of Public Health formulated a multi-phase strategy for achieving rapid coverage with Cuba's COVID-19 vaccines via the country's universal public health system, relying mainly on its neighborhood-based primary health care professionals and facilities. Rollout began with a series of targeted efforts to vaccinate essential health workers and scientists along with people in high-risk groups and those living in territories with particularly high infection rates. Cuba then proceeded to mass vaccination focused on adults and, later, children and adolescents aged 2–18 years. Thus, Cuba became the first country to vaccinate children as young as two years old.

Subsequent booster vaccination efforts for adult and pediatric populations were implemented via the same multi-phase approach used in the initial vaccine rollout.

Cuban health officials credited past investments in nationwide primary healthcare infrastructure—including some 11,000 neighborhood family doctor-and-nurse offices and nearly 500 community clinics—with facilitating rapid immunization of the general population. At the peak of the campaign, Cuban health professionals were administering 300,000 COVID-19 vaccine doses per day.

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COVID-19 Cases and Deaths by Month Cuba, 2021-2022

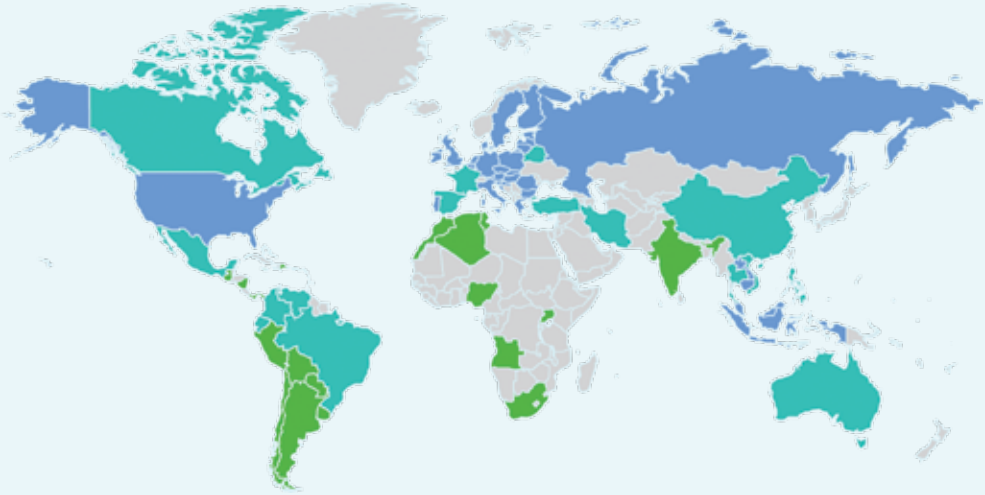
Source: I Morales, Ministry of Public Health, Havana

Cuba's Biotech Sector: Foundation for COVID-19 Vaccine Development

As has been documented elsewhere and confirmed by our visit, Cuba's COVID-19 vaccine development was rooted in a decades-long effort by the Cuban government to create a biotech R&D sector, which began in 1981. Today, Cuba's biotech industry includes 32 research and development institutes and manufacturing entities operating under the umbrella of the state-owned conglomerate **BioCubaFarma**. Their collective mandate is to develop products that address health problems in Cuba and, once domestic needs are met, to engage in export and partnerships to make them available in other countries.[7] BioCubaFarma companies export products to some 40 countries in the Americas, Africa, Europe, Asia and the Middle East and are involved in product development partnerships in the USA, France, Iran, China and Viet Nam, among others.

Prior to embarking on the COVID-19 vaccine effort, the two institutions that led the work already had an international reputation for developing safe, effective vaccines. This includes a recombinant hepatitis B vaccine approved for use in Cuba since 1992; another against Haemophilus influenza type b (Hib), in use in Cuba since 2003; and the world's first effective vaccine against a deadly form of meningococcal meningitis caused by serogroup B meningococcus (MenB), in use in Cuba since 1989.[8,9] Additionally, BioCubaFarma companies produce 8 of the 11 pediatric vaccines administered through the country's national immunization program. (*See full **Technical Report** for peer-reviewed content on Cuban biotech products.*)

Cuban Biotech in the World, 2021



Exports	Business Modalities		Exports & Business Modalities
Angola	Armenia	Laos	Australia
Algeria	Austria	Latvia	Belarus
Argentina	Belgium	Lithuania	Brazil
Bolivia	Brunei	Luxembourg	Canada
Chile	Bulgaria	Malaysia	China
Dominican Republic	Cambodia	Malta	Colombia
Guatemala	Croatia	Myanmar	Ecuador
India	Cyprus	Netherlands	France
Jamaica	Czechia	Poland	Iran
Morocco	Denmark	Portugal	Mexico
Nicaragua	Estonia	Republic of Korea	Philippines
Nigeria	Finland	Romania	Serbia
Panama	Germany	Russia	Singapore
Paraguay	Greece	Slovakia	Spain
Peru	Hungary	Slovenia	Thailand
St. Vincent & the Grenadines	Indonesia	Sweden	Turkey
South Africa	Ireland	United Kingdom	Venezuela
Tunisia	Italy	USA	Viet Nam
Uganda	Kazakhstan		
Uruguay	Kyrgyzstan		

Source: BioCubaFarma, Havana, 2022

Potential for International Collaboration

A new high-tech manufacturing facility at the Mariel Biotech Industrial Complex, coupled with the plants producing the SOBERANA vaccines, boosts minimum production capacities to some 15 million doses monthly, according to Cuban vaccine producers. Cuba's trade and technology transfer agreements, its joint ventures and related commercial partnerships—particularly, but not exclusively, with other developing countries—indicate that Cuba's COVID-19 vaccines could be exported to countries of the Global South. While global supplies of existing formulations of COVID-19 vaccines rose substantially in 2022, less clear is the availability of boosters that could help maintain protection. And equitable access, regardless of supply, remains a goal rather than a reality.

As of September 2022, Cuba's COVID-19 vaccines had received emergency use authorizations from several countries that have also signed commercial contracts, including Mexico, Iran, Viet Nam, St. Vincent & the Grenadines, Belarus and Venezuela. Abdala was being considered for Emergency Use Listing (EUL) by WHO, and the SOBERANAs were expected to follow suit. Cuban health professionals also have expressed consistent interest in collaborating with other health systems. Their input could be particularly valuable for developing strategies to achieve high rates of vaccination compliance, as well as rapid and equitable vaccine rollout—including for children—during public health emergencies.

Meanwhile, we also learned about international partnerships with public and private sectors for developing a number of other advanced health innovations—and efforts in Cuba to increase production capacity for therapies to treat a range of infectious and non-communicable diseases. For example, Cuba's Molecular Immunology Center is partnering with the Roswell Park Comprehensive Cancer Center in Buffalo, NY, to test a Cuban biotech treatment targeting certain types of lung as well as head and neck cancers.[10]

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Summary of Findings and Recommendations

The following is a synthesis of the delegation's findings and related recommendations that emerged from our site visits, discussions with Cuban scientists and public health experts, and relevant documents in the public record.

FINDING: In a difficult social and economic environment, Cuban scientists developed, tested and manufactured two safe and highly efficacious COVID-19 vaccine regimens and used them to vaccinate more than 90% of the population. This achievement demonstrates product development and public health capabilities urgently needed in the developing world. For example, the Abdala and SOBERANA vaccines utilize technologies that require only household refrigeration, important for low-resource settings. Cuba also has increased its capacity to manufacture vaccines and other advanced biologics targeting both infectious and non-communicable diseases. Meanwhile, Cuba's biotech sector embraces a strong public health mission. It has tight linkages to a nationwide primary healthcare system, which provides access to its innovations via a comprehensive network of health professionals and community clinics.

RECOMMENDATION: External economic barriers that hamper development, production, use, or cost recovery for Cuba's biotech and pharmaceutical products or international collaboration with Cuba's research institutions, biotech firms and public health professionals should be removed, to aid in the global fight against existing and emerging threats and support equitable access to medical innovations. The pandemic we still fight today has been greatly prolonged by shocking inequities in access to vaccines and treatments. This same disparity will impede efforts to address the next pandemic, just as it has affected fights against a number of diseases in the past. It is also impeding efforts to reduce the growing global burden of non-communicable diseases.

Cuba alone cannot close this gap, but it could be making a much greater contribution. However, current restrictions on trade and investment with Cuba are severely limiting efforts to take advantage of Cuba's considerable biotech R&D capabilities. Despite these impediments, Cuban biotech companies and research institutions have managed to establish a network of global partnerships. It includes at least one US partner and a number of institutions in Africa, Latin America and the Caribbean, and Asia. These should serve as frameworks for wider engagement with Cuba as a full partner for improving access to medical innovation, as can decades of WHO/PAHO and UNICEF partnerships with Cuba. Newer multilateral mechanisms such as the Coalition for Epidemic Preparedness Innovations (CEPI) and recent summits on global health security should be informed by Cuban expertise and experience. We also urge the new Financial Intermediary Fund for Pandemic Prevention, Preparedness and Response, hosted by the World Bank, to include Cuban vaccine developers in considerations by implementing entities.

FINDING: Cuba's COVID-19 vaccination rate in children and adolescents 2–18 years old (97.5%) is far greater and was achieved far earlier than any country in the world. Cuba conducted pediatric clinical trials to assess safety and efficacy in children and adolescents and sought high coverage rates once immunizations began as a way to both protect youngsters and limit infections in the broader population. In general, children often serve as vectors for accelerating the spread of infectious diseases to populations that are more at risk, such as the elderly.

RECOMMENDATION: Cuba's high pediatric coverage merits immediate international assessment for its potential to help blunt transmission rates in the general population, especially with new variants that partially escape immunity provided by vaccines or prior infections. Given the relatively low pediatric coverage with COVID-19 vaccines in most countries, there is a paucity of data available internationally to assess how high coverage might impact disease transmission in other populations. An international research collaboration with Cuban scientists and public health professionals can help answer that question.

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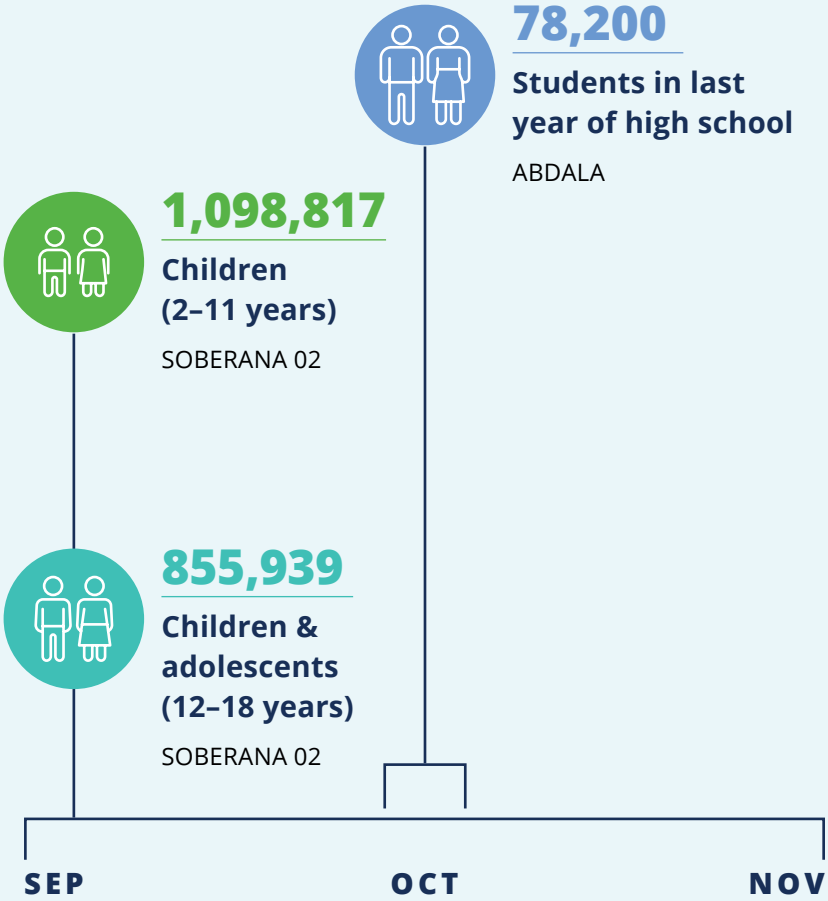
Cuba: COVID-19 Vaccination in Pediatric Ages, 2021



Source: I Morales, Ministry of Public Health, Havana

FINDING: Cuban health authorities are exploring the potential of the SOBERANA Plus vaccine to serve as a universal booster, regardless of the initial vaccine series, and to boost protection provided by prior infection.[11]

RECOMMENDATION: International partnerships should explore whether SOBERNA Plus, either in its current form or modified to target new variants, can serve as a universal booster to support efforts globally to maintain protection against COVID-19. The vaccine utilizes a well-established technology that could enable rapid scale-up of production—inside or outside Cuba—and the ability to adjust the formulation to target new variants of concern. Also worthy of study is Cuba's experience using SOBERANA Plus to boost immunity in COVID-19 convalescent patients.

FINDING: Lag in publishing peer-reviewed phase 3 results has likely delayed global access to Cuba's COVID-19 vaccines. Cuban scientists were working in very challenging conditions and were rightly focused on readying vaccines for domestic use. But peer-reviewed evidence is particularly important for the global scientific community and is considered by WHO for its emergency use approval, a crucial benchmark for guiding vaccine procurement for low-income countries.

RECOMMENDATION: Cuban researchers should be encouraged to publish their results more quickly and more frequently in international peer-reviewed journals. While the dearth of publications from low- and middle-income country scientists in peer-reviewed journals is well established, Cuban scientists' track record in biotech and public health appears to position them well to confront this obstacle. We encourage primarily English-language journals to extend support and mentoring where possible—and in all cases to give due consideration to Cuban research, especially given its potential contribution to health needs in the Global South.

As previously noted, the delegation was not intended to provide formal vetting or certification of vaccine safety and efficacy, or to verify vaccination coverage or compliance. That said, Cuba has a well-documented international reputation for developing safe, effective vaccines, and delegation members found the science presented on the country's COVID-19 vaccines to be compelling and convincing.

Like the Cuban scientists we met, we share a commitment to promoting scientific collaborations that seek to address the global gap in access to high-impact health innovations and interventions, a long-term disparity magnified by the pandemic. Our delegation and our Cuban colleagues benefited from open, transparent scientific engagement, a prerequisite for the bilateral and multilateral collaboration urgently needed today to effectively prevent and address global health emergencies.

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*(See Appendix A in the **Technical Report** for full bios.)*

Footnotes and References

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The full Technical Report from this fact-finding delegation includes detailed findings and recommendations, a list of Cuban scientists participating in our discussions, and links to peer-reviewed content on the Cuban COVID-19 vaccines.

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Disclosures

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