

INSIGHTS FROM



Cuba's COVID-19 Vaccine Enterprise:

Report from a High-Level Fact-Finding Delegation to Cuba



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Context for the Delegation's Visit to Cuba

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. The delegation was comprised of experts in public health, infectious diseases, biotechnology, and vaccine research and development. The purpose of the fact-finding mission was three-fold: first, to learn how and why a relatively small country of some 11 million people—one facing considerable economic hardships—chose to develop, manufacture and deploy its own vaccines; second, to understand the country's strategy for vaccine rollout and its preliminary results; and third, to explore Cuba's approach to science in the context of public health, with implications for what a safe, effective Cuban vaccine might have for COVID-19 vaccine equity—particularly for the most vulnerable in the Global South.

When we visited in mid-2022, COVID-19 infections were spiking around the world with the appearance of new immune-evasive variants. At that time, there were over 843,000 new confirmed COVID-19 cases and 1874 deaths per day worldwide, with only 60% of the global population fully vaccinated and much lower rates in low-income countries.^{1,2} In contrast, Cuba reported fewer than 20 new infections daily and zero deaths,³ while 90% of the population, including 97.5% of children over the age of 2, were vaccinated with vaccines developed and produced on the island. Our delegation was tasked with examining the science, manufacturing processes, regulatory mechanisms and vaccination strategy. All of those are credited with shifting the pandemic burden in Cuba from a peak of some 10,000 new infections and almost 100 deaths reported daily in August of 2021, just as a nationwide vaccination campaign was launched,⁴ to the lower levels reported in June 2022.

The Cuban vaccines used nationwide—Abdala, SOBERANA 02 and SOBERANA Plus—were developed and underwent clinical trials between spring 2020 and spring 2021. Both Abdala and the SOBERANA regimes are protein sub-unit vaccines that generate immunity via the SARS-CoV-2 spike protein. Following analyses of results from pre-clinical studies and phase 1, 2 and interim results from phase 3 trials, **all three received emergency use authorization (EUA) for use in adults from Cuba's national regulatory authority**

(NRA), the Center for State Control of Medicines and Medical Devices (CECMED), in the summer of 2021. EUA for use in Cuba's pediatric population was authorized in fall 2021 after examining results from phase 1 and 2 clinical trials in children, and phase 3 results from clinical trials in young adults—known as immunobridging:⁵

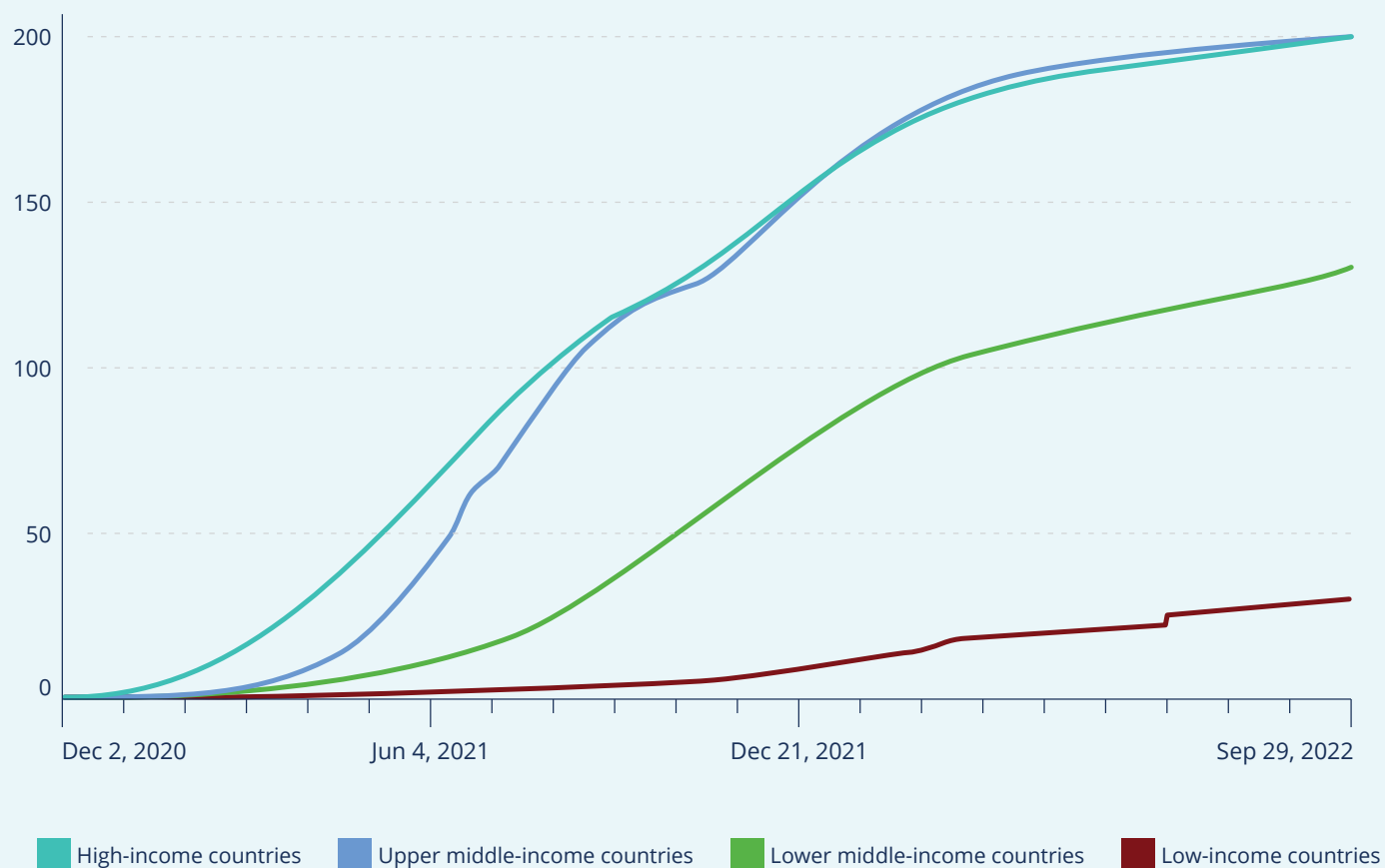
- **July 9, 2021:** Abdala vaccine receives EUA for use in adult population
- **August 20, 2021:** SOBERANA 02 and SOBERANA Plus vaccines receive EUA for use in adult population
- **September 3, 2021:** SOBERANA 02 and SOBERANA Plus receive EUA for use in pediatric population
- **October 27, 2021:** Abdala receives EUA for use in pediatric population

At this writing, Cuba's COVID-19 vaccines have received EUAs from several countries that have also signed commercial contracts, including Mexico, Iran, Viet Nam, St. Vincent & the Grenadines, Belarus and Venezuela. Abdala is currently being considered for Emergency Use Listing (EUL) by the World Health Organization (WHO), and the dossier for the SOBERANAs has been prepared for submission. An exploratory study has also been completed of SOBERANA Plus to assess its reactogenicity and immunogenicity in 30 Italian volunteers previously vaccinated with Pfizer, Moderna, AstraZeneca or Johnson & Johnson vaccines; [clinical trials for SOBERANA Plus use as a universal booster are ongoing](#). At the time of our fact-finding mission, certain data on safety and efficacy of the Cuban COVID-19 vaccines had yet to be published in peer-reviewed journals, a process important to the scientific community and WHO evaluation. (See *Appendix C for updated publications list*.)

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.⁶ Even as the specter of COVID-19 appeared to wane, we were also alarmed by the inequitable vaccine distribution that continues to threaten entire continents, countries and communities.⁷

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

The MEDICC Delegation and Its Unique Mission

This fact-finding trip to learn more about the island's COVID-19 vaccines was the first time in five years a scientific delegation with significant US presence had engaged in discussions with scientists in Cuba. African and Caribbean members of the delegation offered developing-country scientific perspectives, and together, delegation members represented a broad range of expertise. *(See Appendix A for the list of delegation members issuing this report; see Appendix B for the list of participating Cuban scientists and their institutional affiliations.)*

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 organizing and travel were supported in part by a grant from the Open Society Foundations.

It is important to note that the MEDICC delegation was not functioning as a regulatory, certification or scientific review body. Likewise, it was out of its scope to seek independent verification of the data presented regarding COVID-19 vaccines, vaccination coverage and voluntary vaccination compliance. Nor did the group intend to perform a rigorous evaluation of Cuba's national, multisector pandemic response strategy that incorporated the vaccine initiatives. 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.

During our three days in Havana, MEDICC delegation members met with experts involved in the science, clinical trials, regulatory processes, production, and public health vaccination campaigns for Cuba's COVID-19 vaccines. Specifically, we met with directors of Cuba's national regulatory authority, CECMED, that regulates all biotech products developed and used in Cuba. We received detailed

briefings from scientists at the institutions that led the country's COVID-19 vaccine development (the [Finlay Vaccine Institute](#) and the [Genetic Engineering and Biotechnology Center](#), CIGB), as well as from those responsible for conducting clinical trials (the [Pedro Kourí Tropical Medicine Institute](#) and [Hematology and Immunology Institute](#)). We also visited three vaccine production facilities, including a new one at the Mariel Biotech Industrial Complex west of Havana, which was being equipped to expand production of the Abdala vaccine, as well as other vaccines and biotech products for diseases prioritized by Cuba's national health system. Finally, our delegation 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.

Delegation discussions covered many aspects of the country's COVID-19 vaccine development and immunization experience. Key areas we examined were:

- Cuba's experience with novel vaccine development and production as part of its broader biotechnology sector, in existence since the 1980s.
- The rationale behind Cuba's decision early in the pandemic to embark on independent COVID-19 vaccine development and production.
- The regulatory process utilized to grant Emergency Use Authorization for Cuba's COVID-19 vaccines.
- The Cuban COVID-19 vaccine technologies and studies undertaken to establish safety and efficacy of their vaccine candidates.
- The strategy that leveraged Cuba's universal public health system to achieve widespread COVID-19 vaccine coverage, including vaccination of children as young as two years old, the world's first country to do so.⁸

Cuban Vaccine Development and Biotechnology: 1981–2022

As has been documented elsewhere and confirmed by our visit, Cuba's COVID-19 vaccine development capacity is rooted in a decades-long effort by the Cuban government to create a biotech R&D sector, which began in 1981 with the opening of the Biological Research Center (CIB), just five years after the first biotech company opened its doors in the USA; that year, CIB produced Cuba's first biotech product, human leukocyte interferon alfa.¹ Today, Cuba's biotech industry includes 32 research and development institutes and manufacturing entities. They operate under the umbrella of the state-owned conglomerate **BioCubaFarma**, with a collective mandate to develop pharmaceuticals and products to address health problems in Cuba first. Marketing these products abroad proceeds once domestic needs are met, fueling the centers with new resources, in what scientists term a 'closed-loop approach'.²

BioCubaFarma officials reported that their companies have a portfolio of over 900 products, including novel therapies and vaccines, biosimilars, diagnostic tests and reagents, medical technologies, and agriculture and animal health products. They noted that consortium members have joint ventures, licensing, co-development and/or commercial representation agreements in more than 40 countries, including Spain, France, Germany, Brazil, Russia, China, India, the United States, Iran and South Africa.

For example, between 2016 and 2018, joint trials were conducted in the United States between the Roswell Park Comprehensive Cancer Center and Cuba's Molecular Immunology Center (CIM) to test CIMA-vax-EGF, a CIM-developed therapeutic vaccine designed to halt the advance of lung cancer and thus extend survival times for patients. Phase 1 trial results were published in the peer-reviewed journal **Frontiers in Oncology** shortly after our visit.³ In Iran, a manufacturing plant was opened in May 2022 to begin producing SOBERANA 02 under the name PastoCoVac, after Iran's Pasteur Institute ran its own clinical trials on the vaccine from

Cuba's Finlay Vaccine Institute. Technology transfer agreements between Cuba and Brazil began in 2004 with institutions from the two countries pursuing joint biotechnology projects, including the production of recombinant erythropoietin and pegylated interferon. Technology transfer of the Finlay Vaccine Institute's meningitis AC vaccine enabled scale-up in Brazil for export to halt a vast disease outbreak in Africa (at the request of WHO).¹

Prior to embarking on the COVID-19 vaccine effort, the two institutions involved in creating Abdala and SOBERANA—CIGB and IFV—already had an international reputation for developing safe, effective vaccines, including 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). Additionally, BioCubaFarma companies were producing 8 of the 11 vaccines administered through the country's national childhood immunization program.

The basic technology used in the Abdala vaccine is similar to that used for CIGB's hepatitis B vaccine, Heberbiovac. Another CIGB product for treating chronic hepatitis B infections, HeberNasvac, is a therapeutic intranasal hepatitis B vaccine that received regulatory approval in 2015; CIGB scientists used HeberNasvac as a model for developing the Mambisa nasally-administered COVID-19 vaccine candidate. At the time of our visit, Mambisa was being tested as a potential booster for people who had received Abdala—the first to begin clinical trials in humans for a COVID-19 booster administered nasally.

Developed by IFV and CIGB scientists, Cuba's *Haemophilus influenza* type b or Hib (which, despite its name, is a bacterial disease, not a form of flu) vaccine, Quimi-Hib, is a conjugate vaccine; it received WHO approval for international use in 2010.^{4,5}

IFV is perhaps best known for its pioneering work in 1989 to develop the world's first effective vaccine against meningitis produced by serogroup B meningococcus, a rare but often deadly disease.⁶ The Institute also developed biosimilars' vaccines against typhoid fever and leptospirosis, a bacterial disease that poses a risk of kidney damage and brain inflammation. IFV's SOBERANA vaccine regimen was based in part on the Institute's previous experience with conjugate vaccine technology—both Quimi-Hib and Quimi-Vio, the latter a Cuban vaccine against *Streptococcus pneumoniae* causing pneumococcal disease, are conjugate vaccines.

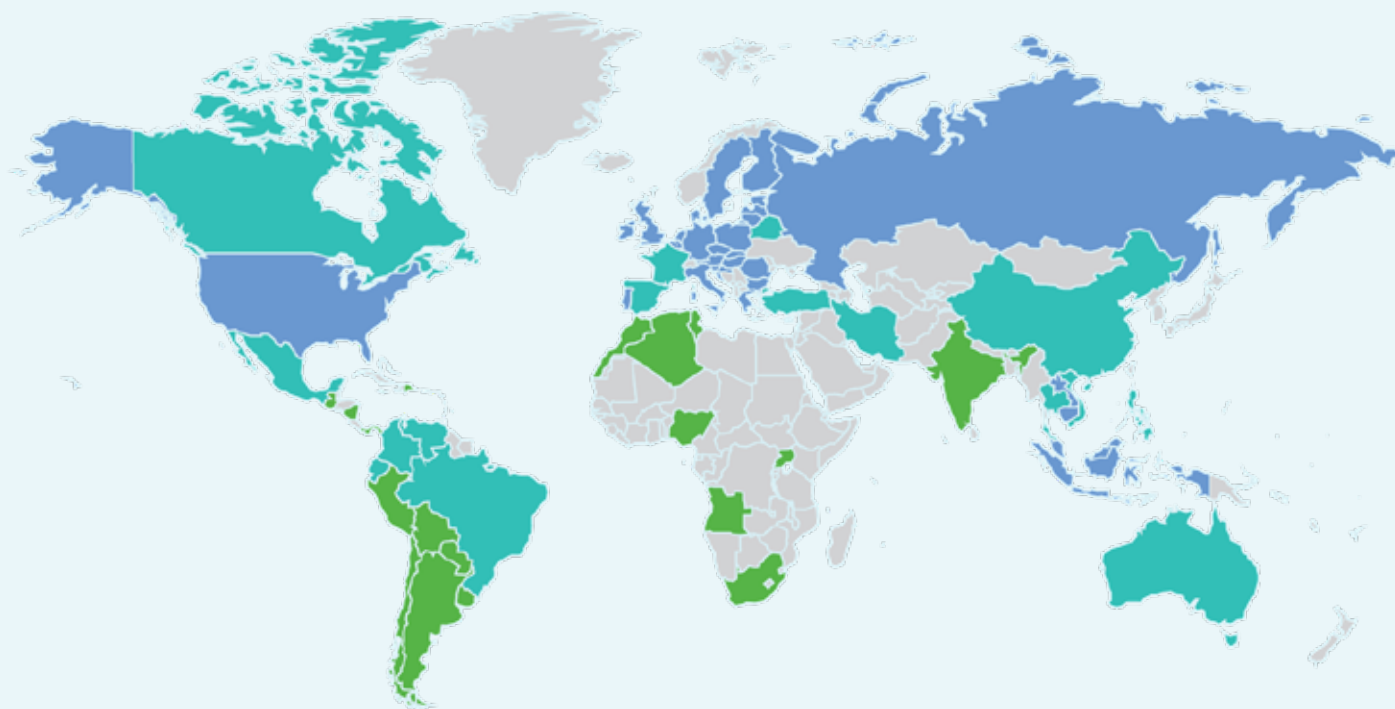
In addition to highlighting the country's vaccine research and novel products development capacities, BioCubaFarma directors pointed to investments in advanced biotech manufacturing, exemplified by the Mariel Biotech Industrial Complex west of Havana

that the delegation visited. Such investments also include a growing capacity to manufacture monoclonal antibodies for use in both vaccines and biological therapies, infrastructure that is often lacking outside wealthy countries. For example, CIM has developed a monoclonal antibody called Itolizumab used to fight damaging inflammatory responses in diseases like rheumatoid arthritis. During the pandemic, Cuban regulators noted that they granted EUA to prescribe Itolizumab for treating the dangerous and potentially fatal inflammatory immune reaction occurring in COVID-19 infections, dubbed the 'cytokine storm'. (See *Appendix C for publications*.) Several members of the MEDICC delegation visited a manufacturing facility operated by the Center that, during the pandemic, had pivoted from producing monoclonal antibodies to producing viral proteins in mammalian cell cultures for the SOBERANA vaccines.

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Cuban Biotech in the World, 2021



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

Source: BioCubaFarma, Havana, 2022

Pivoting for the Pandemic: Why, How and Which Vaccines?

An important area of inquiry for the MEDICC delegation was why, given Cuba's limited resources, officials made the potentially risky decision to invest in an independent COVID-19 vaccine development program. This approach contrasted with decisions by many low- and middle-income countries that sought vaccines via the COVID-19 Vaccines Global Access program called COVAX. This is an international effort co-led by the Coalition for Epidemic Preparedness—along with Gavi, the Vaccine Alliance and WHO—that has helped some low- and middle-income countries acquire affordable vaccines, although not supplying the quantities or guaranteeing the accessibility originally hoped for.⁹

An Early Decision to Develop COVID-19 Vaccines Domestically

Cuban experts meeting with the MEDICC delegation cited three key reasons the country decided in March 2020 to place its bets on a domestic COVID-19 vaccine program.

- **Cuban scientists and health officials were confident in their abilities to domestically produce safe, effective vaccines and rapidly deploy them across the Cuban population.** Cuban scientists from BioCubaFarma (the umbrella, state-owned conglomerate responsible for biotech and pharma, see Sidebar) said they were relatively confident that their decades of experience in vaccines provided a strong foundation for developing effective ones for COVID-19. In addition, they believed Cuba's track record of supplying safe, effective childhood vaccines had earned public trust in domestically-produced vaccines—and this trust would facilitate public compliance with COVID-19 vaccination campaigns.
- **They foresaw a long wait for Cuba to be able to access other vaccines, particularly given that it was not one of the poorest countries singled out for free vaccines by COVAX.** When Cuban scientists began their COVID-19 program, the global scramble for vaccines had just started, later including full-blown hoarding by some wealthy countries. Even in a best-case scenario, Cuban health officials told us, they believed that it would take a long time for the world's major vaccine developers to meet global demand, and certainly to do so equitably. They also noted that requisites for COVAX eligibility precluded Cuba from receiving sufficient vaccines within a practical timeframe, even if it paid millions to purchase them.¹⁰

- **Producing vaccines domestically was the only cost-effective and sure way to achieve high levels of coverage.**

Cuban health officials said they were concerned that the combined impact of US sanctions and the loss of tourist revenue during the pandemic would make it difficult to purchase enough vaccines (at prices yet unclear) on the international market or through COVAX to cover their whole population. In addition to vaccinating adults, Cuban health officials also believed early on that their vaccination efforts would have to extend to millions of children in order to stem the pandemic.

Why Cuba Developed Various Vaccine Candidates and Decided to Use Two Vaccines

Cuban researchers at Finlay and CIGB began working simultaneously on various vaccine candidates, realizing that not all would make the final cut of success in human trials. Finally, as we learned, they moved forward with two different COVID-19 vaccine regimens utilizing two different technologies that require separate manufacturing processes: the SOBERANAs and Abdala. These vaccines also require different immunization schedules in terms of the number of days between doses. According to our discussions with Cuban scientists and public health officials over the course of our visit, several factors seem to have driven the decision to use both vaccines.

One factor was the pace of development. The Abdala vaccine advanced faster than the SOBERANA vaccines, in part because it relied on simpler manufacturing technologies. Secondly, production capacities by individual manufacturers likely also influenced the decision since existing facilities could not guarantee a sufficient volume of one vaccine at a single production plant. Ultimately, Abdala became a more practical option to halt the rapid surge of the delta variant in 2021, due to the shorter time between doses, enabling full vaccination faster. When it came time to vaccinate children, however, the SOBERANA vaccines appeared as a first choice, given that they were based on conjugate vaccine technologies that have been used for decades in Cuba for childhood immunizations.

Regulatory Oversight: Cuba's National Regulatory Authority

Central to Cuba's COVID-19 vaccine development program was regulatory oversight of biotech products by its national regulatory authority (NRA), the Center for State Control of Medicines and Medical Devices (CECMED).

Established in 1989, we learned that the Center provides regulatory reviews and approvals of all medicines, biopharmaceuticals, vaccines and medical devices produced in Cuba or imported for use in the country's health system. A presentation by the CECMED director noted that the Pan-American Health Organization (PAHO) certified the agency as a Collaborating Center for Regulation of Health Technologies and a Regional Reference National Regulatory Authority. The director also explained that CECMED has retained PAHO/WHO certification as a Level 4 National Regulatory Authority of Reference since 2011 (requiring PAHO/WHO evaluation and certification of: regulatory system; registration and marketing; vigilance; market surveillance and control; licensing establishments; regulatory inspection; laboratory testing; clinical trials oversight; and lot release).¹¹

As was the case for NRAs worldwide that were overseeing other COVID-19 vaccine development efforts, CECMED regulators were in uncharted waters due to the need to rapidly expedite complex regulatory reviews—with far less personnel and fewer resources than their US and European counterparts. Worldwide and in Cuba, regulators were challenged to accelerate reviews without sacrificing scientific rigor.

For example, in times of global health emergencies, vaccine developers may employ adaptive trial designs with overlapping phases (seamless trials) for generating initial data on vaccine safety and immune response. Immediate continuation from one phase to another requires having sufficient data from the initial phase to justify moving to the next, and only if the trial design elements overlap.¹²

At the time of our visit, 13 temporary modifications to regulatory processes or procedures had been made during the pandemic, including permissions for seamless trials. Regulatory officials also reported they were able to accelerate reviews of the Abdala and SOBERANA vaccines because both relied on technology platforms utilized in previously approved Cuban-developed vaccines and were manufactured in facilities already certified by CECMED.

CECMED regulators said coordination among the national regulatory authority, Cuba's biotech companies and its national health system helped expedite regulatory reviews while attending to evidence of safety and efficacy. They noted that this coordinated, streamlined approach was buttressed by an Innovation Committee—comprised of regulatory officials, researchers, physicians in various clinical specialties, epidemiologists, virologists and directors of relevant national programs like maternal-child health—established by the Ministry of Public Health. The Committee met regularly to discuss all aspects of the country's efforts to prevent and treat COVID-19 infections. CECMED's director explained that such coordination enabled regulatory questions to be answered more quickly and discussed more thoroughly, and for changes to be enacted faster when required in clinical trials organization.

Cuban regulatory officials said they hoped to emerge from the pandemic with a well-established process for conducting regulatory reviews in the context of health emergencies. CECMED's director also said the next step for her agency was to become a **WHO Listed Authority**, the highest WHO level reserved for the world's most trusted NRAs, whose opinions are relied upon internationally.

Cuba's COVID-19 Vaccines: Science, Clinical Trials and Emergency Use Authorization

During the three-day fact-finding trip, one group met with scientists at meetings hosted by CIGB, where the Abdala vaccine was developed; a second group was hosted at IFV for similar briefings on the SOBERANAs vaccines developed there.

Scientists at both institutions explained that before proceeding with clinical testing, all trials for COVID-19 vaccine candidates were reviewed and approved by CECMED and clinical sites inspected and certified for adherence to international good clinical practices (GCPs). The trials were conducted by external institutions (i.e., not by those producing the vaccines); their progress and how they were conducted were monitored by external ethics research committees; and adherence to GCPs were analyzed by Cuba's National Clinical Trials Coordinating Center. Researchers noted that, in addition to specific inclusion/exclusion criteria, trial participation required participants' written informed consent.

Trials involving pediatric groups 2–18 years old required written informed consent from the child's parents or legal guardians; volunteers 12 years and older also had to provide written consent. (A complete list of clinical trial sites, study purpose, design, inclusion/exclusion criteria, formulations, technical and ethical considerations, and funding for each trial is available at the [Cuban Public Registry of Clinical Trials](#), a WHO Primary Registry.)

In addition to the three vaccine formulations later authorized for use, our delegation received brief information about three innovative Cuban biopharmaceuticals—Nasalferon, Itolizumab and Jusvinza—that were repurposed to treat COVID-19 and received CECMED emergency use authorization for expanded-access use. We were told that another COVID-19 vaccine candidate, Mambisa, was still in clinical trials, and scientists emphasized its potential as a nasal-spray vaccine.

The Abdala Vaccine

Developed by CIGB, Abdala is a protein sub-unit vaccine that relies on vaccine technology similar to that used by the Center for its hepatitis B vaccine, Heberbiovac, included in Cuba's childhood vaccination program since 1992 and [WHO-approved for use internationally since 2001](#). The goal with Abdala, according to developers, was to generate immunity with the receptor binding domain (RBD) portion of the SARS-CoV-2 spike protein. The virus employs the spike protein to penetrate cells; Abdala generates antibodies that interfere with this process. Many COVID-19 vaccines in use globally—including those available in the United States and Europe—rely on some aspect of the spike protein to generate immunity. Like the hepatitis B vaccine, Abdala relies on a recombinant viral protein produced in *Pichia pastoris* yeast and then formulated with an aluminum hydroxide-based adjuvant. (An adjuvant is a substance intended to help a vaccine generate a strong immune response.) Abdala is administered intramuscularly in three doses 14 days apart.

Below, we summarize the information received about Abdala's clinical trials and their results:

Clinical Trials in Adults

From December 2020 through February 2021, Abdala underwent randomized, double-blind, placebo-controlled

phase 1/2 trials to test the vaccine candidate's safety and immunogenicity. The combined (or seamless) trial design was authorized by CECMED and conducted at the Saturnino Lora Provincial Clinical-Surgical Teaching Hospital in Santiago de Cuba in the eastern part of the country. Phase 1 studied 132 healthy participants 19–54 years old; Phase 2 studied 660 healthy participants 19–80 years old.¹³

After CECMED approval, phase 3 multicenter, randomized, double-blind and placebo-controlled clinical trials began in March 2021 with 48,290 healthy volunteers 19–80 years old. The trials were designed to test Abdala's safety, immunogenicity and efficacy and conducted through early June 2021 at 18 certified clinical trial sites in the eastern provinces of Santiago de Cuba, Granma and Guantánamo. Results from this phase 3 trial, announced on June 21, 2021, showed vaccine efficacy at 92.28% against symptomatic infection, 100% against severe disease and 100% against death.

Post-vaccination surveillance data revealed about 16,000 adverse events, divided almost equally between recipients of the placebo and actual vaccine. Scientists involved with the trial said the adverse events were mainly mild issues, such as pain at the injection site; there were no serious adverse events with a clear link to the vaccine. Phase 3 Abdala clinical trials occurred before emergence of the omicron variant, and results were available as a preprint at the time of the MEDICC delegation

visit. (See Appendix C: A phase 3, randomized, double-blind, placebo-controlled clinical trial for adult evaluation of the efficacy and safety of a SARS-CoV-2 recombinant spike RBD protein vaccine, in medRxiv.)

Clinical Trials in Children and Adolescents

A combined phase 1/2 trial ('[Ismaelillo Clinical Trial](#)') was conducted in 592 healthy pediatric volunteers 3-18 years old at 11 certified clinical trial sites in Camagüey province in central Cuba from July through October, 2021. This was a multi-center, randomized, double-blind trial. In late 2021, a similar, second phase 2 trial ('Meñique Clinical Trial') was conducted in 703 healthy pediatric volunteers 3-18 years old. The objective of these trials was to assess safety and immunogenicity, as well as to compare these results to adult cohorts receiving the same vaccine regimens.

The SOBERANA Vaccines

The SOBERANA vaccine relies on a three-dose regimen, combining two different vaccines to generate protection (known as a heterologous regimen). The first two doses are with the SOBERANA 02 vaccine, the third with SOBERANA Plus. They are administered via intramuscular injection 28 days apart. The viral proteins used in the SOBERANA vaccines are produced in mammalian cells. The technology required to manufacture vaccine proteins in mammalian cells makes production of the SOBERANAs somewhat longer and more expensive.

Finlay scientists noted that the SOBERANA 02 vaccine is based on conjugate vaccine technologies developed in the 1980s that are now utilized in vaccines globally. For this vaccine, Finlay researchers linked (conjugated) the RBD portion of the SARS-CoV-2 spike protein with a protein (tetanus toxoid) taken from the tetanus bacterium (*Clostridium tetani*). Scientists have found that, with conjugate vaccines in general, linking a protein isolated from a disease pathogen to one from an unrelated virus or bacteria is a safe and effective way to elicit a strongly protective immune response, involving helper T cells.

Our delegation learned that scientists decided to consider a third dose because results from early clinical testing indicated two doses of SOBERANA 02 were not producing sufficiently high titers of neutralizing antibodies. What's more, early results indicated that use of SOBERANA Plus as a third dose produced results superior to a third dose with SOBERANA 02 in terms of neutralizing antibodies.

Principal investigators reported 99% of trial participants 3-18 years old experienced high seroconversion levels of RBD antibodies following the full, three-dose Abdala vaccination regimen. They also presented adverse event data to our delegation: 32% of participants in the Ismaelillo trial experienced at least one adverse event (causally related or not) after the three-dose regimen; total number of adverse events was 413. The most common were pain and redness at injection site, headache, sleepiness and fever, with lower frequencies of adverse events in the 3–11-year-old age group. No vaccine-related serious events were observed. CIGB scientists opted not to conduct phase 3 pediatric trials due to ethical considerations around using a pediatric placebo control group, and instead used phase 1, 2 and immunobridging results for requesting EUA (see below, as the same strategy was applied for the SOBERANAs).

SOBERANA Plus is not a conjugate vaccine. Instead, it relies on vaccine technology like that used for Abdala. However, Finlay scientists noted that SOBERANA Plus utilizes a slightly different version of the RBD protein (called a dimeric protein) that they viewed as well-suited for boosting immunity provided by vaccination or prior infection. This protein was then formulated with an aluminum hydroxide-based adjuvant to amplify its immune-generating potential.

Data presented by principal investigators showed 92% efficacy of the SOBERANA regimen for preventing symptomatic disease and 100% effective for preventing severe disease and death.

Clinical Trials in Adults

Two phase 3 trials of the SOBERANA vaccine regimen were conducted in adult populations. Both were performed in the spring of 2021: one in Cuba, (before detection of the omicron variant on the island in December 2021) involving

44,031 healthy volunteers 19–80 years old and another in Iran in partnership with the Pasteur Institute there, involving nearly 24,000 participants in a similar age range.

For the Cuban trial, researchers described random assignment of 44,031 participants into three groups: one received two doses of SOBERANA 02; the second received the full regimen—two doses of SOBERANA 02 followed by a single dose of SOBERANA Plus; the third group received a placebo. All doses were administered 28 days apart. This trial was conducted during circulation of beta and delta variants in Cuba.

Data presented by principal investigators showed 92% efficacy of the SOBERANA regimen for preventing symptomatic disease and 100% effective for preventing severe disease and death. Reported efficacy of the two-dose regimen was significantly lower than the three-dose combination: 69.7% against symptomatic COVID-19 and 74.9% against severe disease. (The small number of deaths—2 in vaccinated and 3 in the placebo group—precluded a point estimate of vaccine efficacy for preventing this outcome.)

The clinical trials demonstrated safety of the SOBERANA vaccines and used WHO definitions for adverse events. Reported adverse events included some level of pain or swelling at the injection site, headache or fatigue—all mainly after the first dose. These events were more common in the vaccinated group compared to placebo group. There were isolated reports of systemic adverse events including dengue infection, hypertension and erythema multiforme, but no reports of severe or potentially life-threatening events involving any of the volunteers.

Peer-reviewed safety and immunogenicity results from open-label parallel phase 1 and 2a trials for SOBERANA 02 in homologous or heterologous regimens were published in the journal *Vaccine* shortly after our fact-finding mission.¹⁴ Included in this manuscript are in vitro results indicating a strong T-cell response induced by SOBERANA 02 which could be instrumental in protecting against immune-evading variants. The journal *Med* later published safety and immunogenicity results for a phase 2b placebo-control trial, reaffirming selection of the heterologous regimen.¹⁵ Phase 3 results presented to the delegation had been submitted for publication but, at the time of our meetings, had not yet appeared in a peer-reviewed journal.

The phase 3 trials in Iran were randomized, double-blind and placebo-controlled and involved nearly 24,000 healthy participants 18–80 years old. This was a multi-center trial conducted in eight cities throughout the country; the first cohort (n = 17,972) received a two-dose regimen of SOBERANA 02, 28 days apart, while the second cohort (n = 5,987) received an additional dose of SOBERANA Plus on day 56. This trial was

conducted during exclusive circulation of the delta variant.

The Iranian trial reported 51% efficacy against symptomatic disease in trial participants who received the two-dose SOBERANA 02 regimen and 65% efficacy in the group that received the heterologous regimen (SOBERANA 02 and SOBERANA Plus). The two-dose regimen showed 80% efficacy against severe disease, which jumped to 96.5% with the three-dose regimen. There was one COVID-related death observed in the placebo group.

Clinical Trials in Children and Adolescents

An open-label combined phase 1/2 trial was conducted at the Juan Manuel Márquez Pediatric Teaching Hospital in Havana in the summer of 2021 involving 350 children and adolescents 3–18 years old. The purpose of the trial was to assess safety, reactogenicity and immunogenicity using the heterologous SOBERANA regimen in healthy children and compare these results to phase 3 trial results in healthy young adults, in whom the SOBERANA vaccines had already demonstrated significant protection.

Results of this pediatric trial, available as a preprint, revealed the regimen was safe and generated a strong immune response, demonstrating non-inferiority to that obtained in young adults.

Cuban researchers opted not to conduct phase 3 pediatric trials due to ethical considerations around using a pediatric placebo control group, and instead used phase 1/2 pediatric results and those from phase 3 in young adults to request emergency use authorization. This process, known as immunobridging, has also been recommended by the US Food and Drug Administration when evaluating COVID-19 vaccines for children.¹⁶

Clinical Trials in COVID-19 Convalescents

SOBERANA Plus underwent phase 1 and 2 clinical trials in Havana during the spring of 2021 for use in convalescent adults 19–80 years old, its results published.¹⁷

A second open-label phase 1/2 trial with 518 COVID-19 convalescent volunteers 2–18 years old was conducted at the Juan Manuel Márquez Pediatric Teaching Hospital in Havana and the Paquito González Cueto University Pediatric Hospital in Cienfuegos. These participants received a single dose of SOBERANA Plus with the objective of measuring safety, reactogenicity and immunogenicity in children 2–18 years old previously infected with symptomatic or asymptomatic COVID-19. These results, also published, were compared to those of convalescent adults 19–29 years old and to healthy (non-convalescent) children 3–18 years old.¹⁸

Public Health Strategy for Vaccinating Cuba's Population Against COVID-19

Cuba's Ministry of Public Health formulated a strategy aimed at achieving rapid vaccination for the vast majority of the Cuban population. This relied on domestically produced vaccines that could be stored at household refrigerator temperatures and thus distributed across the island for use in the universal health system's primary health care centers. In a presentation to the MEDICC delegation, ministry analysts described a multi-phase rollout of the Abdala and SOBERANA vaccines, including an intervention study and public health intervention, accompanied by a large cohort study in Havana; mass vaccination of adults, and children 2-18 years old; and booster regimens for adults and pediatric populations.

Cuban public health experts credited past investments in nationwide primary healthcare infrastructure—including neighborhood family doctor-and-nurse offices acting as primary care providers and nearly 500 community clinics—with facilitating rapid immunization of the general population in the context of a universal health system. They also noted that Cubans of different skin colors experience similar rates of various co-morbidities, such as hypertension, and that basic COVID-19 assessments by both phenotype and skin color did not reveal differences in rates of disease incidence or adverse events post-vaccination. We did not receive such information concerning socio-economic status.

The mass vaccination campaign utilized 120,000 health workers, who administered vaccines through 11,000 vaccination centers. For the pediatric population, vaccinations were administered either at these centers (for younger children) or at schools certified as vaccination centers. Officials reported that, at the peak of the campaign, Cuban health professionals were administering 300,000 COVID-19 vaccine doses per day.

Cuban protocols called for each person vaccinated to be checked by a health professional, typically, the individual's primary care provider, before they were immunized and evaluated again one hour after, as well as stocking vaccination centers with medications to address adverse events. Vaccines were taken to people who were unable to leave their homes.

Intervention Study

In March 2021 based on safety results demonstrated in phase 2 trials,^{13,14} CECMED approved intervention studies to further evaluate the Abdala and SOBERANA vaccines in high-risk groups for symptomatic COVID-19 infection, severe disease and death and to record adverse events. The cohort was comprised of 164,000 essential workers in the country's health facilities and biotech industry. Most of that group, about 140,000, were frontline health workers. The remainder were involved in product development in BioCubaFarma research and manufacturing enterprises.

The Abdala study included 120,000 volunteers from Havana, Santiago de Cuba, Granma and Guantánamo provinces, who received 3 doses of the vaccine beginning in late March 2021. The remainder of the cohort—in Havana—received two doses of SOBERANA 02, followed by SOBERANA Plus.

Public Health Intervention

Utilizing an approach commonly used in clinical vaccine trials, Cuban scientists undertook an interim analysis (with a data cutoff date 14 days after the third dose) of the Abdala phase 3 trial that provided preliminary evidence of the vaccine's safety and efficacy. In May 2021, these results were presented to the Ministry of Public Health. In consultation with the Innovation Committee, the Ministry decided to move forward with a public health intervention to vaccinate a large number of people with Abdala (and later, SOBERANA) in areas where the caseload was increasing most rapidly.¹⁹ This decision, based on a risk-benefit analysis made in consultation with the Innovation Committee, was taken within the legal framework of Public Health Law #41, which permits such actions in health emergencies.²⁰ The emergency at hand was a sharp rise of delta variant cases and deaths in certain territories.²¹ Ultimately some 3 million Cubans were vaccinated in various municipalities of Havana, Matanzas, Ciego de Ávila and Santiago de Cuba provinces—regions that were experiencing the sharpest surge of infections.

At the time, neither Abdala nor the SOBERANA had received emergency use authorization, and public health officials we spoke with noted that they had been criticized in the international media for this public health intervention. However, they maintained that the subsequent drop in cases and deaths vindicated their decision.

On July 9, 2021, CECMED granted EUA for Abdala for the country's adult population based on interim phase 3 trial results, data from the intervention study mentioned above (unpublished) and 'real world effectiveness' evidence from the public health intervention. This permitted deployment of the vaccine in the mass vaccination campaign for Cuba's adult population.

Mass Vaccination: Adult and Pediatric Populations

Vaccination of Cuba's adult population began in July 2021 with the three-dose Abdala regimen. Analysis of previous results and surveillance for adverse effects continued in post-marketing studies. Researchers presented data from a study conducted in Havana of 1.35 million Cubans who received the Abdala vaccine from July 9 through August 31, 2021. That analysis focused on protection against severe disease and death; effectiveness for both outcomes in those fully vaccinated was over 98%. When the delegation visited, the study was available as a preprint, later published.²²

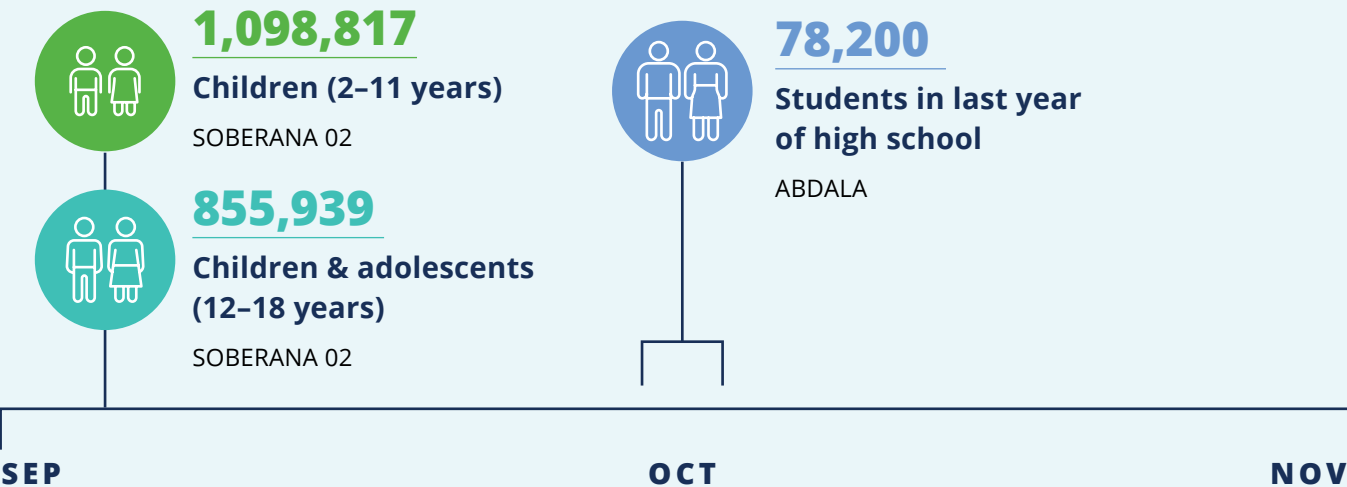
On August 20, 2021, SOBERANA 02 and SOBERANA Plus also received EUA from CECMED for use in Cuba's adult population based on interim phase 3 results.

On September 3, 2021, the SOBERANA vaccine regimen received EUA from CECMED for pediatric immunizations for children aged two and over. In reviewing EUA for the SOBERANA regimen in children and adolescents, CECMED considered the phase 1/2 safety and immunogenicity results in pediatric volunteers and efficacy data from phase 3 trials with young adults using the same heterologous schedule. Additionally, based on phase 1/2 results from the pediatric trials in Havana and Camagüey and comparisons to young adult trial results mentioned above, CECMED granted Abdala EUA for use in pediatric populations on October 27, 2021.

The pediatric vaccination campaign was rolled out as follows: some 78,000 students in their last year of high school received the Abdala vaccine beginning in October 2021; almost 856,000 children and adolescents 12-18 years old and just over 1 million children 2-11 years old, received the SOBERANA regimen between September and November. Health officials presenting to the delegation reported that from September through November 2021, approximately 2 million Cuban children and adolescents 2-18 years old were vaccinated with Abdala and the SOBERANA vaccines.

Our delegation learned that **by June 2022 when we visited, 97.5% of the pediatric population was fully vaccinated** (some 200,000 infants under 2 years old were ineligible for vaccination). Of vaccinated children, 0.01% reported adverse events, none life-threatening.

Cuba: COVID-19 Vaccination in Pediatric Ages, 2021



Source: I Morales, Ministry of Public Health, Havana

Booster Strategy and Rollout

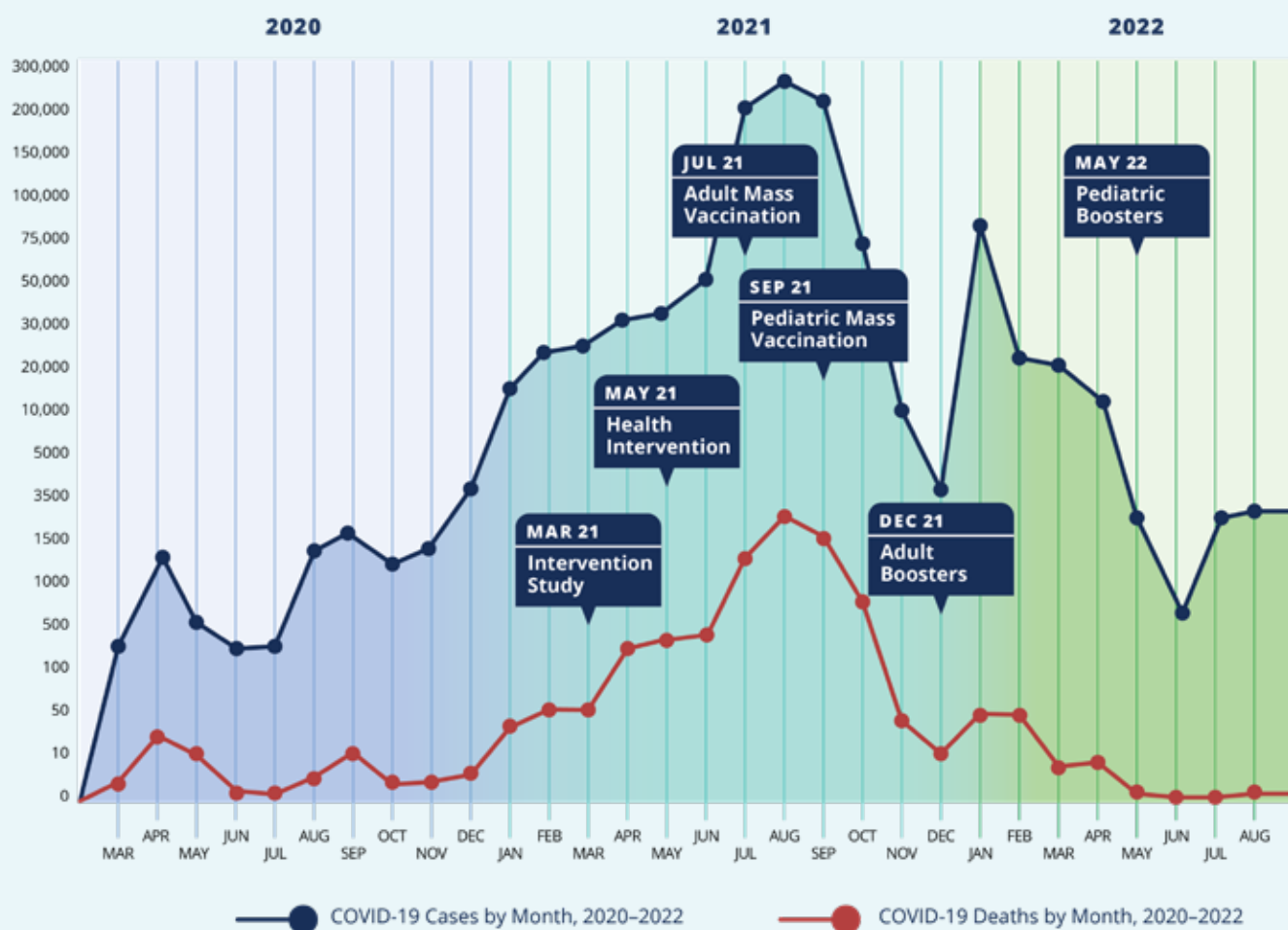
In our meetings, Cuban public health officials explained that the booster strategy was a phased approach like that used in the earlier rollout: first, frontline health workers and scientists, followed by high-risk groups and territories, and finally, adults 19 years and older and the pediatric population 12-18 years old. Use of the Abdala and SOBERANA vaccines as boosters was included in the designs of CECMED-approved clinical trials.

Cuban health officials recommend SOBERANA Plus as a booster for COVID-19 convalescent adults 19 years and older, COVID-19 convalescent children and adolescents, and as a universal booster (see below) for those vaccinated with

any other COVID-19 vaccine. Both Abdala and SOBERANA Plus are recommended as boosters three months after completing the initial immunization series, while SOBERANA Plus is recommended for COVID-19 convalescents two months after infection.

Cuba began applying boosters in the adult population in December 2021; pediatric boosters in children and adolescents aged 12–18 years, in May 2022. A few months after our fact-finding trip, it was reported that Cuba started applying boosters in children aged 2–11 years in Cienfuegos province, later extended to the rest of the country.²³

COVID-19 Cases and Deaths by Month, Cuba, 2020–2022



Source: I Morales, Ministry of Public Health, Cuba

Delving Deeper: Delegation Discussions with Cuban Vaccine Scientists

The comprehensive presentations from IFV and CIGB scientists, principal investigators, Cuban regulators and public health specialists sparked extensive discussions with our delegation. Key issues covered included: potential vaccine effectiveness against omicron variants; immunity duration and booster strategy; the possibility for SOBERANA Plus to serve as a universal booster; the role of primary healthcare systems in health emergencies; reporting adverse events; vaccination compliance; and funding for vaccine R&D in Cuba.

Preliminary Evidence of Effectiveness Against Omicron Variant

At the time of the delegation's visit, surveillance data indicated that Cuba had yet to be challenged by the omicron BA.4 and BA.5 subvariants causing a significant spike in cases elsewhere in the world. However, the original omicron strain already had moved through the Americas, and delegation members asked for insights into potential effectiveness of the Cuban COVID-19 vaccines against it.

IFV researchers responded with preliminary data from an unpublished study in children and adolescents 2–18 years old, comparing pre-immunization infection rates during the delta wave in the summer of 2021 with those post-immunization during the first omicron wave in early 2022. These data showed that infection rates fell from 40 per 1000 during delta (pre-vaccination) to 8.6 per 1000 during omicron (post-vaccination). Meanwhile, infection rates in unvaccinated children under 2 fell only modestly, from 56 to 39 per 1000. Finlay scientists concluded that the sharp reduction in the vaccinated group could provide preliminary evidence of the vaccine's potential to protect against the omicron variant.

Finlay scientists indicated that they focused on pediatric infection rates because they are interested in whether high vaccination coverage in this group could help blunt the nationwide impact from variants like omicron that better evade vaccine-acquired immunity. They noted that Portugal experienced high omicron breakthrough infection rates

despite high vaccination rates in adults and pointed out that Portugal did not have similar vaccination rates in children and adolescents. An important issue is whether children and adolescents play such a large role in disease transmission across populations that high vaccine coverage in this group could reduce the overall impact of immune-evading variants. For example, there was discussion about whether vaccination of older children contributed to the modest drop in COVID-19 infections in children under 2 years old (delta vs. omicron) who had not been vaccinated.

Immunity Duration and Booster Strategy

As mentioned, at the time of the delegation's visit, boosters were already being administered to Cubans 12 years of age and older who had received the full schedule of either SOBERANA or Abdala vaccines. Delegation members were presented findings (unpublished) indicating that the level of neutralizing antibodies generated by both vaccines had dropped six months post-vaccination. Discussion centered on whether this loss in quantity also indicated the same degree of loss in quality of antibody protection—in other words, whether there still was enough to provide at least a modest level of protection. In this regard, Cuban scientists provided intriguing data on B- and T-cell immunological memory response that warrant further study.

Health officials noted that at the time of our visit, some 67% of the Cuban population had received at least one booster. They indicated that either Abdala or SOBERANA Plus can be used as a booster, regardless of the vaccine originally applied—including mRNA or others.

CIGB scientists reported unpublished data from a study in 1083 adults indicating that a fourth dose of Abdala administered six months after primary vaccination restored protection to earlier levels. They also shared data from the pediatric Ismaelillo trial showing that neutralizing antibodies dropped after 7.5 months in the 3–11-year-old age group and after 8 months in the 12–18-year-old age group. Cuban health officials now recommend a second booster for adults aged 50 years and over.

Investigating SOBERANA Plus as a Universal COVID-19 Booster

IFV researchers presented data regarding their ongoing efforts to evaluate SOBERANA Plus as a universal booster for elevating immune response in two different populations: people who were previously infected, but not vaccinated; and people who were vaccinated with one of the many COVID-19 vaccines currently administered around the world.

They presented peer-reviewed results from a phase 2 trial published in June 2022 in the journal *Lancet Respiratory Medicine* that found previously infected (but not yet vaccinated) people who received a single dose of SOBERANA Plus experienced a 31-fold increase in neutralizing antibodies against the alpha, beta and delta variants of concern.²⁴ The study was conducted before the emergence of omicron.

The Finlay team noted they were evaluating data from a small clinical trial in 30 subjects from Turin, Italy who received SOBERANA Plus after being vaccinated with either the Pfizer, Moderna, AstraZeneca or Johnson & Johnson COVID-19 vaccines. Participants in the SOBERANA Plus Turin trial received one dose of SOBERANA Plus at least three months after completing the full schedule of other vaccines. No serious adverse events were reported. Finlay scientists also referenced ongoing studies involving 100,000 volunteers utilizing SOBERANA Plus as a booster for people who have received China's Sinopharm vaccine, the results of which they plan to submit for peer-reviewed publication.

Adverse Events: Recording and Reporting

A vaccine surveillance and pharmacovigilance expert from Havana's Pedro Kourí Tropical Medical Institute (which led clinical trials of SOBERANA 02 and SOBERANA Plus in Cuba's adult population) explained that adverse events are documented via systematic surveillance of adverse events following immunization (AEFI), a mechanism used in Cuba's national immunization program since 1999.²⁵ With the COVID-19 vaccines, active surveillance was conducted the first hour after vaccination, followed by 15 days of passive surveillance. The latter depended on manual recording of adverse events by health professionals in the primary healthcare system.

Data presented for the Abdala vaccine, for example, showed 5,828 adverse events reported after application of 26,991,674 doses in adults. Of these, 5,769 were mild events; 20 were moderate; and 39 serious—9 related to vaccination and 30 unrelated to vaccination. Additionally, there were 20 adverse events of special interest: 8 facial paralysis events (moderate and recovered) and 12 seizures (moderate).

Similar data was presented for adverse events in Cuba's pediatric population that received the Abdala vaccine from October 2021 through April 2022. In this period, 348,704 doses were applied and 22 AEFI reported; the most common were headache, hypertension, low-grade fever and vomiting. In pregnant women who received Abdala, there were 7 mild and 2 serious AEFI after application of 145,147 doses from July 2021 through April 2022. The two serious events were high blood pressure (not vaccine related) in two women who were then admitted to hospital and stabilized.

Of the nearly 1.9 million children and adolescents who received the SOBERANA regimen, 223 reported an adverse event, or 0.01%, a rate of 10.2×10^5 applied doses. As of this writing, no cases of myocarditis, pericarditis or multisystem inflammatory syndrome have been reported for those who received Abdala or the SOBERANAs. Scientists at the Finlay Vaccine Institute noted that following phase 3 clinical trials for both vaccine lines, youngsters received active follow-up for one year; following mass pediatric vaccination, children and adolescents are followed up by their neighborhood family physicians for at least one year.

Health officials noted that at the time of our visit, some 67% of the Cuban population had received at least one booster.

Vaccination Compliance

Asked about vaccine hesitancy or anti-vaccination sentiments, health officials stated that the decision to receive COVID-19 vaccination (or not) was voluntary and left to individuals. They credited several factors with high rates of compliance, including: long-standing public confidence in childhood vaccines developed by Cuban scientists, administered through the National Immunization Program that reports over 98% vaccination rates,^{26,27} as well as consistent messaging and extensive public information offered by scientists on vaccine safety profiles and efficacy, presented on national prime-time television, in social media and elsewhere, and the relationship of family doctors and nurses to residents in the neighborhoods where they live and serve.

They said that eligible people who chose not to get vaccinated sometimes cited an acute illness or concern about severe co-morbidities.

Funding for Cuba's Vaccine Effort

Funding for a costly undertaking like vaccine development, production, clinical trials and deployment amidst a global pandemic—especially for a tourism-dependent country also under stringent US sanctions—was another line of inquiry of interest to the MEDICC delegation. Although we did not fully discuss this issue, subsequent perusal of public records indicates that financing for development of both

vaccine regimens was provided by Cuba itself, including reallocated funds from the BioCubaFarma conglomerate. For the Abdala clinical trials, funds were provided by CIGB; for the public health interventions using the Abdala vaccine, by CIGB and Cuba's Ministry of Public Health (MINSAP); and for the SOBERANA clinical trials and vaccination campaigns, by IFV and the Cuban Fund for Science and Innovation of the Ministry of Science, Technology and the Environment.

Later, in January 2022, the Central American Bank for Economic Integration provided a €46.7-million credit for the *Project to Strengthen the Cuban Biopharmaceutical Industry to Confront COVID-19 in Cuba and the Region*, to be implemented via the United Nations Development Programme (UNDP). Objectives of the grant include: modernizing manufacturing technology, strengthening production infrastructure, scaling up COVID-19 vaccine innovation, and production and acquisition of personal protective equipment. This followed an initial grant to Cuba in 2020 from the same bank for €935,600 to purchase of RT-PCR tests.²⁸ Vaccine finances have been supplemented by various donations, such as those from MediCuba-Europe, MediCuba-Suiza and the Swiss Agency for Development and Cooperation.²⁹

Funding information, plus clinical trials registration and authorization dates, ethics committees, clinical sites, selection criteria, study design and outcomes for all biopharmaceuticals and medical devices can be accessed at the [Cuban Public Registry of Clinical Trials](#).

Delegation Findings

The MEDICC delegation highlighted the following key observations based on our site visits and information from Cuban scientists and public health experts in Havana in June 2022, as well as documents in the public record:

1. In a difficult socio-economic context, Cuban scientists developed and tested two lines of COVID-19 vaccines, each exhibiting over 95% efficacy rates against severe disease and death, with good safety profiles. This result alone merits attention by the global scientific community to control and prevent pandemics, and to build more equitable in-country capacities for doing so.
2. The two lines of Cuban vaccines (the SOBERANAS and Abdala) rely on classic protein sub-unit technologies that the country's biotech institutions have used previously with success. These vaccines require refrigeration but not deep freeze—an important factor for health systems to carry out mass vaccination in resource-constrained settings.
3. The Cuban vaccines were used to fully vaccinate some 90% of the Cuban population by the time of the delegation's visit, as compared to 60% global rates of vaccination, 54% in lower middle-income countries and 13% in low-income countries.
4. Cuba's vaccination rate in children and adolescents 2–18 years old (97.5%) is the world's highest and may be a factor in controlling infections caused by immune-evasive variants, a line of research worth pursuing.
5. As elsewhere, continued monitoring of Cuban COVID-19 vaccines and their effectiveness against new variants is warranted, as well as duration of immune response. In this context, innovations including SOBERANA Plus as a potential universal booster are intriguing for their possible contribution to pandemic control.
6. Previous biotechnology research, development, production and regulatory experience allowed Cuba's BioCubaFarma centers to quickly pivot towards creating COVID-19 vaccines and to repurpose existing therapies for treating severe infections.
7. Cuba has a robust, well-documented history of international biotech collaboration and technology transfer for health—particularly with other countries of the Global South—which continued through the pandemic.
8. A new high-tech manufacturing plant at the Mariel Biotech Industrial Complex promises to boost Cuba's vaccine manufacturing capacities to at least 15 million doses monthly, a minimum that incorporates production of Abdala at Mariel and the SOBERANAS at their current plants. This would enable Cuban exports to contribute to global COVID-19 vaccine shortfalls, especially if priced affordably for low- and middle-income countries.
9. Lag in publishing peer-reviewed phase 3 results has been disadvantageous to Cuba's COVID-19 vaccine program, likely delaying availability of these vaccines internationally. WHO emergency use listing is vital to such global registration and potential use of the Cuban vaccines.
10. Our delegation and our Cuban colleagues benefited from open, transparent scientific engagement, a prerequisite for the bilateral and multilateral collaboration urgently needed to effectively address global health emergencies.

Recommendations from the Fact-Finding Delegation

1. Multilateral and bilateral mechanisms for health promotion and pandemic prevention should actively engage Cuban scientists in dialogue, academic exchange and joint research. This is our main, overarching recommendation. Current threats to health, alarming global inequities and the specter of recurring pandemics mandate science-based international collaboration and policymaking to protect our populations and our planet. Vital to these efforts are scientists in developing countries such as those in Cuba, who have important contributions to make based on decades of experience and success in disease eradication, and emergency preparedness and response. We learned that dozens of countries and institutions have signed bilateral agreements with Cuban health and biotech sectors, in the USA as well. These should serve as frameworks for research and joint programs to improve population health and equity—in the Americas and beyond. Decades of WHO/PAHO and UNICEF partnerships with Cuba should be leveraged, and newer multilateral mechanisms such as the Coalition for Epidemic Preparedness Innovations (CEPI) and summits on global health security should enlist Cuban expertise and experience to draw lessons from:

- **Key results and prospects for Cuba's COVID-19 vaccines and biotech pharmaceuticals.** Several features of Cuba's protein-based vaccines deserve attention: duration of their immunogenicity, use in pregnant and nursing women, ability to address new variants, and SOBERANA Plus's effectiveness as a universal booster for other internationally available vaccines. In addition, it is important to determine if the types of vaccines developed in Cuba provide any advantages for people with comorbidities and for children; or, due to less stringent storage requirements and affordable pricing, for low- and middle-income countries.
- **Cuba's vaccination strategy and national vaccine rollout, considering its experience rapidly vaccinating 90% of its population, including 97.5% of children and adolescents two years and older.** Two aspects merit immediate attention: Cuba is the only country to have vaccinated such a high percentage of children at such an early age so early in the pandemic, an experience that promises abundant, valuable information on whether pediatric vaccination can help

blunt transmission rates in the general population. Second, the high COVID-19 vaccination rates also speak to how Cuba met the health equity challenge that has plagued so many other nations, where vaccine access and take-up rates have fallen short or been uneven by population subgroups. This in turn relates to vaccine compliance and its relationship to Cuba's universal health system, primary healthcare coverage, public health workforce, public messaging and population health literacy levels—all globally pertinent as even childhood vaccination rates plummet, influenced by vaccine hesitancy and refusal. Several recent studies also have considered the role of primary health care for public education, contact tracing, accessible treatment and vaccine administration. The Cuban experience may be relevant in this regard as well, with its 11,000 family doctor-and-nurse offices and nearly 500 community clinics involved in all these aspects, including vaccination.

- **Health and biotech capacity-building in Cuba, a critical component for other low- and middle-income countries aiming to develop domestic capabilities, build more equitable health systems and contribute to more equitable pharmaceutical access worldwide.** Cuba's pre-existing and integrated vaccine development, manufacturing, regulatory and immunization capabilities enabled rapid vaccine rollout—rare among countries of its size or economy. As we learned, Cuba entered the pandemic with key components of a national biopharmaceutical–public health pandemic response strategy that facilitated a pivot to address COVID-19. The country had cultivated a brain trust of vaccine scientists and a workforce pipeline; built state-of-the-art manufacturing facilities; established a national biomedical regulatory authority that interacts with PAHO/WHO and retains high-level certifications from both; and established a universal health system relying on strong primary care. How did the country accomplish this on a shoestring budget? Does the Cuban experience hold clues to success for other developing countries?
- The scientists we met explained that Cuba's vaccine manufacturing strategy is designed to satisfy domestic need first and consider export thereafter. In this context, Cuba may provide an example of the advantages of local vaccine and biotech manufacturing,

particularly in the face of global shortfalls, hoarding and inequitable access. Additionally, opportunities exist for Cuba to work with the Africa Union/Africa CDC as they pursue establishment of vaccine manufacturing on the continent (see the [Partnerships for Vaccine Manufacturing](#) report and [Now is the Moment to Launch an African Vaccine Industry](#)).

- As the world searches for ‘pancorona’ vaccines to cover a broader range of viruses, it is essential to recall that in most of the world, not only are the current vaccines in short and unequal supply, but few countries actually have the capabilities to produce their own. Cuba’s vaccine development experience stands in sharp contrast.
- **The experience of Cuba’s regulatory authority, contributing to fast-tracking harmonization of regulatory processes in the Americas and globally.** During evaluations to consider emergency use authorization for the country’s COVID-19 vaccines, Cuba’s regulatory authority (a PAHO/WHO-certified Level 4 Regulatory Authority of Reference since 2011) faced challenges common to its counterparts everywhere, particularly how to balance the urgency of product approvals with rigorous evidence review. But it had the additional challenge of assessing products developed by publicly funded/operated institutions subject to clinical trials organized by government-run public health institutions. Regulator independence has long been a subject of concern with research conducted by large, financially flush conglomerates, but the path to authorization through integrated, publicly operated research and regulatory institutions has been less studied. Cuba’s experience provides an opportunity to do just that, advancing criteria for the harmonization process and its ethical underpinnings.
- 2. **External trade and financial barriers that hamper development, production, use or cost recovery for Cuba’s biotech and pharmaceutical products should be removed.** Moreover, we advocate collaboration with Cuba to boost production capacities for its COVID-19 vaccines and other proven biologics, and to advance research and public health initiatives. In this context, we applaud assistance from WHO/PAHO, UNICEF, the European Union and others, and 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 strengthening pandemic preparedness and response.

The Mariel Biotech Industrial Complex—poised to scale up production of at least one COVID-19 vaccine plus other therapeutics—should be supported, as it may also help address global vaccine shortfalls and inequities when coupled with Cuba’s record of collaboration with other developing countries. Havana’s Finlay Vaccine Institute has received good marks on the [Fair Pharma Scorecard](#), and the Cuban health ministry [has gone on record](#) stating that the country’s vaccines will be priced affordably or even provided free for poorer nations. Thus, we commend Cuba’s application to WHO for Abdala emergency use listing and encourage SOBERANA developers to follow suit as soon as possible; if Cuban vaccines ultimately receive such approval, it will open the door to their registration by other countries, especially low- and middle-income nations that often rely on PAHO/WHO-certified findings. In such a context, we encourage Cuban biotech companies to become regional vaccine suppliers.

Our delegation learned that Cuba has established working partnerships with institutions in Africa, the Latin American-Caribbean region and Asia—examples of South-South training, technology transfer and joint venture initiatives that also merit recognition and support.

3. **International partners should invest in modernizing Cuba’s health-sector data systems, to better position the country for the next health emergency and facilitate health research.** Evident in our site visits to CIGB, IFV and the Mariel Biotech Industrial Complex was Cuba’s capacity for biomedical science and innovation, despite the impact of the pandemic, a global recession and US sanctions. Nevertheless, some basic technology is lacking at the local level.

Investing in updated health systems technology would result in more efficient electronic records, promotion of data-sharing and facilitation of more robust epidemiological surveillance, as well as expedited reporting of adverse events and analysis of the pandemic’s macro effects on Cuban population health.

4. Cuban researchers should be encouraged to routinely publish their results more quickly and more frequently in international peer-reviewed journals. This is essential to achieve credibility for their findings, especially for those as important and compelling as we observed during our visit for the COVID-19 vaccines. Cuban scientists completed phase 3 clinical trials of their COVID-19 vaccines a year prior to our fact-finding mission, but these results had yet to be published. Delegation members acknowledged that Cuban scientists were operating in challenging conditions but recognized that the lack of peer-reviewed publication—also considered by WHO for determining emergency use listing—is an obstacle to worldwide accessibility for these vaccines. 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. In this context, we encourage primarily English-language journals to extend support and mentoring where possible, and in all cases, give due consideration to Cuban research. The delegation commends our Cuban peers for providing comprehensive and thought-provoking presentations on all aspects of the country’s COVID-19 vaccine experience: the science involved in developing and testing the vaccines; production processes and facilities used for their manufacture; regulatory protocols employed to provide emergency use authorizations; and the public health strategies Cuba implemented for maximum vaccination coverage in a short period of time. Delegation members also noted the responsiveness and generosity of Cuban experts in providing thoughtful, detailed consideration of our questions and comments.

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 aim to address the global gap in access to high-impact health innovations and interventions, a long-term disparity magnified by the pandemic.

Footnotes and References

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A young child with light brown hair and eyes is wearing a black face mask with white polka dots. They are also wearing a lei made of large white and pink flowers. The child is holding a small, fluffy white dog. The background is a soft-focus outdoor setting with greenery and a wooden fence.

APPENDICES

**A. Delegation Members Issuing
This Report**

B. Cuban Participants

**C. Peer-reviewed publications
on Cuban COVID-19 vaccines
and related topics**

Delegation Members Issuing this Report

Delegation Co-Leaders:

MICHAEL T. OSTERHOLM PHD is Regents Professor, McKnight Presidential Endowed Chair in Public Health, the director of the Center for Infectious Disease Research and Policy (CIDRAP), Distinguished Teaching Professor in the Division of Environmental Health Sciences, School of Public Health, a professor in the Technological Leadership Institute, College of Science and Engineering, and an adjunct professor in the Medical School, all at the University of Minnesota. In November 2020, Dr. Osterholm was appointed to President-elect Joe Biden's 13-member Transition COVID-19 Advisory Board. He is the author of the New York Times best-selling 2017 book, *Deadliest Enemy: Our War Against Killer Germs*, in which he details the most pressing infectious disease threats of our day and lays out a nine-point strategy on how to address them, with preventing a global flu pandemic at the top of the list. In addition, Dr. Osterholm is a member of the National Academy of Medicine (NAM) and the Council of Foreign Relations. He is a frequent consultant to the World Health Organization (WHO), the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Department of Defense, and the CDC. He is a fellow of the American College of Epidemiology and the Infectious Diseases Society of America (IDSA).

CRISTINA RABADÁN-DIEHL PHARM D PHD MPH is Associate Director for Clinical Trials at Westat, a position she assumed in 2018 after a 25-year career at the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services (HHS). She is a Pharmacist, Molecular Biologist and Public Health Professional with vast experience in global health. Dr. Rabadán-Diehl provides leadership and technical expertise in the design and execution of Phase I-Phase IV clinical trials and develops partnerships with domestic and international government and nongovernment stakeholders. She was Director of the Office of the Americas in the Office of Global Affairs, Office of the Secretary, at HHS. In this role, she coordinated U.S. Government (USG) policy and functions related to HHS activities in the Americas region, in collaboration with HHS Divisions such as the NIH, CDC, FDA, and the Administration for Strategic Preparedness and Response (ASPR). During her tenure, she worked closely with PAHO in areas

related to health and research in the Americas and participated in the US response to the Ebola and Zika epidemics. She also served as the HHS Secretary's Representative to the US-Mexico Border Health Commission. As a multidisciplinary scientist, she currently participates in Scientific Review Panels for the NIH and the European Union and serves as a National Advisory Council Member for SAMHSA. Dr. Rabadán-Diehl is an Adjunct Professor at George Washington University, where she teaches Global Health Diplomacy, and a Visiting Professor at the National School of Public Health, Health Institute Carlos III in Spain.

Delegation Members:

JOSHUA ANZINGER, PHD is a Senior Lecturer at the University of the West Indies Department of Microbiology and Consultant Virologist at the University Hospital of the West Indies, both in Kingston, Jamaica. His research interests are primarily in the fields of HIV and arboviruses, and have recently expanded to include SARS-CoV-2 in response to the COVID-19 pandemic. He is Head of the Diagnostic Virology Laboratory at the University of the West Indies, Director of the Global Virus Network Jamaica Affiliate, Member of the Abbott Pandemic Defense Coalition, Member of the PAHO Arbovirus Diagnosis Laboratory Network (RELDA), and Member of the PAHO Caribbean Sub-regional Certification Committee for the Global Eradication of Poliomyelitis.

MARIA ELENA BOTTAZZI PHD is Associate Dean of the National School of Tropical Medicine, Professor of Pediatrics, Molecular Virology & Microbiology, Division Chief of Pediatric Tropical Medicine and Co-director of Texas Children's Center for Vaccine Development at Baylor College of Medicine in Houston, and Distinguished Professor in Biology at Baylor University in Waco. Dr. Bottazzi obtained her bachelor's degree in Microbiology and Clinical Chemistry from the National Autonomous University of Honduras and a doctorate in Molecular Immunology and Experimental Pathology from the University of Florida. Her post-doctoral training in Cellular Biology was completed at University of Miami and Pennsylvania, and afterwards she worked at the George Washington University before relocating to Texas. She is an internationally recognized tropical and emerging

disease vaccinologist, global health advocate and co-creator of a patent-free, open science COVID-19 vaccine technology that led to the development of Corbevax, a COVID-19 vaccine for the world. She pioneers and leads innovative partnerships for the advancement of a robust vaccine development portfolio tackling diseases that disproportionately affect the world's poorest populations, making significant contributions to catalyze policies and disseminate science information to reach a diverse set of audiences. In 2022, alongside vaccine researcher Peter Hotez, she was nominated by Congresswoman Lizzie Fletcher of Texas for the Nobel Peace Prize.

CELIA CHRISTIE-SAMUELS MBBS DM PEDS MPH FAAP FIDSA FRCP(EDIN) is Professor of Paediatrics (Infectious Diseases, Epidemiology and Public Health) at The University of the West Indies (UWI), Mona, Jamaica, on a recent post retirement contract. She is also a consultant paediatrician at the University Hospital of the West Indies and headed their Vaccines Infectious Diseases Centre, along with Jamaica's Perinatal, Paediatric and Adolescent HIV/AIDS Programme. She participated in several international clinical trials, including one that led to approval of a pentavalent vaccine for infant gastroenteritis. She also served on the Anti-infective Drugs Advisory Committee of the US Food and Drug Administration (FDA). She received her undergraduate training in Medicine and Surgery and postgraduate training in Pediatrics at The University of the West Indies (UWI), Mona. She also completed two Post-Doctoral Fellowships in Pediatric Infectious Diseases and in Hospital and Molecular Epidemiology at Yale University and Yale New Haven Hospital, USA and later pursued an MPH degree from Johns Hopkins University. Her work has focused on: HIV/AIDS in women, children and adolescents; implementation of clinical trials of vaccine-preventable diseases; and emerging infectious diseases. She has been recognized with awards including The International Leadership Award from the Elizabeth Glaser Pediatric AIDS Foundation, Excellence in Science Inaugural Stephen Preblud Award from the US CDC (2022), The UWI's Vice Chancellor's Award for Research Excellence (2008), and the Gold Medal for Eminence in Research from the Board of Governors of the Institute of Jamaica (2014). In 2018 she was conferred with the Jamaican national honor of Order of Distinction in the rank of Commander (CD).

NGOZI ERONDU PHD MPH trained as an infectious disease epidemiologist and recently joined the Global Institute for Disease Elimination (GLIDE) as Technical Director. She often provides technical support to the US CDC, WHO and governments across sub-Saharan Africa, the Middle East, and Southeast Asia to strengthen capacities under the International Health Regulations for the control

of infectious diseases such as Ebola, meningitis, malaria, and polio. She also has served in an advisory capacity to the Global Preparedness Monitoring Board, Africa CDC, and the UK Government All-Party Parliamentary Group on Global Health. Dr. Erondu is also a Senior Scholar with the Global Health Policy and Politics Initiative at the O'Neill Institute, Georgetown University Law Center, where she co-chairs the Lancet-O'Neill Commission on Racism and Structural Discrimination in Global Health. She serves as a commissioner on the Lancet Infectious Diseases Commission on Preparedness for Emerging Epidemic Threats. Dr. Erondu is a former Assistant Professor at the London School of Hygiene and Tropical Medicine, where she taught disease outbreak response and epidemiology; an Associate Fellow at Chatham House and the John Hopkins University Emerging Leaders in Biosecurity Programme; and co-editor of the Health Security section for PLOS Global Health.

JEANNE MARRAZZO MD MPH FACP FIDSA holds the C. Glenn Cobbs Endowed Chair and is Professor of Medicine and Director of the Division of Infectious Diseases at the University of Alabama at Birmingham Heersink School of Medicine (UAB). She is a Fellow of the American College of Physicians and of the Infectious Diseases Society of America (IDSA), and was elected Treasurer of the IDSA in 2021, having served on the board since 2018. She was Chair of the American Board of Internal Medicine Council from 2015 to 2018. Dr. Marrazzo has a broad research portfolio that includes the relationships between the vaginal microbiome and female reproductive tract infections, HIV pre-exposure prophylaxis, hormonal contraception, and risk of STI/HIV acquisition. She leads UAB's participation in the RECOVER trial, funded by NIH to study post-acute sequelae of SARS-CoV-2 infection, and a large clinical trial of the meningococcal Group B vaccine rMenB+OMV NZ (Bexsero) to prevent gonococcal infection. She chairs the Biomedical Science Committee of the HIV Prevention Trial Network, the group tasked with integrating the biomedical science agenda across numerous clinical trials of antiretroviral prevention agents. She is also a Co-PI of the NIH-funded Infectious Disease Clinical Research Consortium that leads the Vaccine Treatment and Evaluation Units as well as NIH-funded STI clinical trials. She has been a leading voice in educating colleagues, the community, and the media during the COVID-19 pandemic.

SANDRA MILAN PHD BIO is a Vice President, Project Team Leadership, Molecular Oncology at Genentech's Research and Early Development. She is responsible for leading a group of Project Team Leaders with oversight for programs in cancer. Her group focuses on strategy and implementation of

development programs that have the potential to transform the treatment of cancer. Dr. Milan is responsible for setting multi-molecule, multi-indication franchise strategies and leading teams through significant risk and complexity. Her passion for using science to fight disease and improve patient's lives extends to developing the next generation of leaders. She serves on the Diversity and Inclusion Board of Directors and is a Founder and member of gWISE (Genentech Women in Science and Engineering). Outside of work, Dr. Milan serves on the Board of Directors for UCLA Life Science Division, Chabot Space & Science, and the Chicana Latina Foundation. Dr. Milan received her PhD in Molecular and Cell Biology from UC Berkeley, where she also completed a postdoctoral fellowship. She held a number of leadership roles at Chiron prior to joining Genentech in 2006.

PETER KOJO QUASHIE PHD is a specialist in molecular virology, viral enzymology, antiviral therapeutics and antimicrobial drug mechanism and resistance and Senior Research Fellow and Deputy Director in Charge of Research at the West African Centre for Cell Biology of Infectious Pathogens (WACCBIP), University of Ghana. Dr. Quashie holds a doctorate in Experimental Medicine from McGill University in Canada, backed up by post-doctoral training from the University of Toronto. He is a specialist in antiviral therapeutics with a focus on HIV, Dengue and SARS-CoV-2. He also leads the Quashie Research Group, a subunit of the Virology laboratory at WACCBIP. The group aims to understand and therapeutically target key replicative processes in viruses of pandemic concern. His previous research has spanned the areas of mechanistic enzymology, HIV drug resistance mechanisms, antiviral drug discovery and structural biology of viral proteins. Dr. Quashie coordinates much of WACCBIP's SARS-CoV-2 research initiatives spanning molecular and seroepidemiology studies, host-virus interactions and drug discovery.

THOMAS SCHWAAB MD, PHD is an immunologist and Chief of Strategy, Business Development and Outreach at the Roswell Park Comprehensive Cancer Center in Buffalo, New York, USA. He is also CEO, Global Biotechnology and Cancer Therapeutics (GBCT), CEO, RPCI Oncology, PC; and The Bill and Nancy Gacioch Family Endowed Chair for Translational Research. Dr. Schwaab is an Associate Professor of Oncology and Immunology and joined the Institute's faculty in 2009. In his current role, Dr. Schwaab supervises Roswell's business development and overall strategic development. He assures that business and clinical initiatives are delivered appropriately and support maximal quality, efficiency and effectiveness, and works to continually widen the Institute's scope of operations and growth potential at national and international levels.

DAVID WILLIAMS MA MPH MDIV PHD is the Norman Professor and Chair of the Department of Social and Behavioral Sciences at the Harvard T. H. Chan School of Public Health. He is also a Professor of African and African American Studies at Harvard University. Dr. Williams is an internationally recognized social scientist focused on social influences on health. His research has enhanced our understanding of the complex ways in which socioeconomic status, race, stress, racism, health behavior and religious involvement can affect health. He is the author of more than 500 scientific papers, and he has been invited to keynote scientific conferences in Europe, Africa, Australia, the Middle East, South America, the Caribbean and across the United States. The Everyday Discrimination Scale that he developed is the most widely used measure of discrimination in health studies. Dr. Williams has been elected to the National Academy of Medicine, the American Academy of Arts and Sciences and the National Academy of Sciences. He has been ranked as the Most Cited Black Scholar in the Social Sciences and as one of the World's Most Influential Scientific Minds. His research has been featured in the national print and television media and in his TED Talk.

Appendix B

Cuban Participants in Delegation Discussions

Delegation Co-Leaders:

CATALINA ÁLVAREZ DSC

Managing Director, Biotech Industrial Complex, Genetic Engineering and Biotechnology Center (CIGB Mariel)

VICENTE VÉREZ-BENCOMO DSC

Director, Finlay Vaccine Institute (IFV)

PASTOR CASTELL-FLORIT MD PHD DSC

Director of the National School of Public Health and President of the Council of Scientific Societies in Health

ARTURO CHANG MD MS

Deputy Director, Hematology and Immunology Institute

ERNESTO CHICO PHD

CEO, Innovative Immunotherapy Alliance, Molecular Immunology Center

BELKYS GALINDO PHD

Full professor and senior researcher, Pedro Kourí Tropical Medicine Institute

DAGMAR GARCÍA PHD

Director of Research and Development, Finlay Vaccine Institute (IFV)

GERARDO E. GUILLEN PHD

Director of Biomedical Research, Genetic Engineering and Biotechnology Center (CIGB)

OLGA LIDIA JACOBO MS

Director, Center for State Control of Medicines and Medical Devices (CECMED)

AGUSTÍN LAGE MD PHD DSC

Adviser to the President of BioCubaFarma

MILADYS LIMONTA PHD

COVID-19 Vaccines Project Manager, Genetic Engineering and Biotechnology Center (CIGB)

LISSETTE LOPEZ MD

Head of the National Experts Group in Pediatrics, Ministry of Public Health

PEDRO MÁ-S-BERMEJO MD PHD DSC

Full professor, Pedro Kourí Tropical Medicine Institute

MAYDA MAURI PHD

First Vicepresident, BioCubaFarma

MANUEL MONTANÉ MS

Associate Director, Biotech Industrial Complex (CIGB Mariel)

ILEANA MORALES MD MS

Director of Science and Technological Innovation, Ministry of Public Health

VERENA L. MUZIO PHD DSC

Director of Clinical Research, Genetic Engineering and Biotechnology Center (CIGB)

ROLANDO PÉREZ PHD

Research Director, BioCubaFarma

RINALDO PUGA MD

Cira García Clinic, Principal investigator, SOBERANA pediatric clinical trials

SONIA RESIK MD PHD

Head of Virology Department, Pedro Kourí Tropical Medicine Institute (IPK), principal investigator, ABDALA pediatric clinical trials

MARIA DEL CARMEN RICARDO MD MS

Saturnino Lora hospital, principal investigator, ABDALA clinical trials

BELINDA SÁNCHEZ PHD

Director of Tumor Immunology, Molecular Immunology Center

MARIA EUGENIA TOLEDO-ROMANI PHD

Pedro Kouri Tropical Medicine Institute, principal investigator, SOBERANA clinical trials

YURI VALDÉS

Chemist and Deputy Director, Finlay Vaccine Institute (IFV)

MARILUZ VALDIVIESO MS

Director, Rafael María de Mendive Primary School, Havana

Articles Published by Cuban Scientists on Cuba's COVID-19 Vaccines & Related Topics *(Peer-reviewed unless indicated by PREPRINT)*

Abdala Vaccine

Cuban Abdala vaccine: Effectiveness in preventing severe disease and death from COVID-19 in Havana, Cuba; A cohort study. Pedro I. Más-Bermejo, Félix O. Dickinson-Meneses, Kenia Almenares-Rodríguez, Lizet Sánchez-Valdés, Raúl Guinovart-Díaz, María Vidal-Ledo, et al. *Lancet Reg Health Am*. Volume 16, 2022, 100366, <https://doi.org/10.1016/j.lana.2022.100366>.

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Safety, tolerability, and immunogenicity of a SARS-CoV-2 recombinant spike RBD protein vaccine: A randomised, double-blind, placebo-controlled, phase 1-2 clinical trial (ABDALA Study). Hernández-Bernal F., Ricardo-Cobas M. C., Martín-Bauta Y., Navarro-Rodríguez Z., et al. *EClinicalMedicine* 2022 Apr;46:101383. doi: [10.1016/j.eclinm.2022.101383](https://doi.org/10.1016/j.eclinm.2022.101383). Epub 2022 Apr 9 PMID: 35434578

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Elevated antibody titers in Abdala vaccinees evaluated by Elecsys® anti-SARS-CoV-2 S highly correlate with UMELISA SARS-CoV-2 ANTI RBD, ACE-2 binding inhibition and viral neutralization assays. Lemos-Pérez G., Chávez-Valdés S., González-Formental H., Freyre-Corrales G., et al. *J Biotechnol Biomed* 2022; doi: <https://doi.org/10.26502/jbb.2642-91280055>

An engineered SARS-CoV-2 receptor-binding domain expressed in *Pichia pastoris* as a candidate vaccine antigen. Limonta-Fernández M., Chinea-Santiago G., Martín-Dunn A.M., Gonzalez-Roche D., et al. *New BIOTECHNOLOGY* (2021); doi: <https://doi.org/10.1016/j.nbt.2022.08.002>

Murine monoclonal antibodies against RBD of the SARS-CoV-2 spike protein as useful analytical tools for subunit vaccine development and clinical trials. Blanco OR., Dorta D., Hernández CA., Abreu D., et al. *J Immunol Methods*. 2022 Jan;500:113195. doi: [10.1016/j.jim.2021.113195](https://doi.org/10.1016/j.jim.2021.113195). Epub 2021 Nov 26. PMID: 34843713

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