NVAC NATIONAL VACCINE ADVISORY COMMITTEE

Preparing for COVID-19 Vaccination: Recommendations from the National Vaccine Advisory Committee

Approved December 4, 2020

Over the course of writing this report, COVID-19 illnesses have gone up dramatically, with the Centers for Disease Control and Prevention reporting more than 13 million illnesses and 266,051 deaths in the United States alone in their update on November 30, 2020 at 12:18 PM.[1] Across the globe, we've also experienced incredible loss of human life and illnesses causing a great deal of suffering worldwide as well as remarkable strains on public health and medicine since SARS-CoV-2, the virus that causes COVID-19, was first identified in Wuhan, China, in December 2019.[2]

To lessen the health threat caused by COVID-19, public health and healthcare systems in the United States are planning to implement the largest vaccination campaign since the polio vaccine trials in the 1950s. To support this effort, the National Vaccine Advisory Committee (NVAC) responded to a charge from Admiral Brett P. Giroir, M.D., Assistant Secretary for Health and the Director of the Vaccine Program. On September 23, 2020 Admiral Giroir requested the NVAC make recommendations to: 1) support optimal communications enhancing vaccine uptake, 2) outline approaches for vaccines to prevent COVID-19 in children, and 3) describe lessons learned from the pandemic to develop new and improved vaccines. In addition, the NVAC outlined an approach for vaccinating pregnant women to protect them from COVID-19. These recommendations were added to the response to question 2.

Safe and effective vaccines for COVID-19 have the potential to transform society by reducing death and disease and improving the economic and social consequences caused by the pandemic. In the course of writing this report, several promising announcements have been made by vaccine manufacturers about the safety and efficacy of candidate vaccines and later this month advisory committees and public health agencies will engage in regulatory processes and efforts to eventually provide recommendations for the safe use of effective COVID-19 vaccines in priority populations first and then on a more widespread basis next year.

As the COVID-19 landscape and progress with COVID-19 vaccine efforts continue to evolve, the NVAC has focused on the pandemic and heard expert advice, thoughtfully discussed potential health policy recommendations, and contributed to the development of this report to shape COVID-19 vaccination policy recommendations to the Department of Health and Human

Services. Due to the timing of events, several of these recommendation must start soon in order to advance COVID-19 vaccination efforts.

CHARGE

Admiral Giroir requested responses to the following questions and to provide rationale for the responses.

1. What should HHS do before, during, and after the COVID-19 vaccination campaign to improve the confidence in these vaccines and our nation's immunization system especially within underserved communities, including racial and ethnic minorities?
2. The FDA standards for approval and licensure of vaccines for COVID-19 addresses safety and effectiveness and encourages inclusion of minorities, the elderly, pregnant women, and people with medical comorbidities in clinical trials. In particular, for COVID-19 vaccines, I am interested in the approach the nation should take in regard to vaccination of children, given that there will be relatively little data on children from some of the early clinical trials? As context, the case fatality rate for children under age 18 is .02%. What is the appropriate approach, and timing, of generating the needed data and proceeding to potential childhood vaccination as we move forward?
3. What lessons can we learn from COVID-19 vaccine development more broadly to promote innovation and shorten timelines to increase availability of new vaccines to the American public?

PROCESS

To address this charge in a timely manner, the NVAC met twice during the September 2020 NVAC meeting and discussed potential answers to all three of the questions asked by the Assistant Secretary for Health in the charge. After the meeting, an initial draft of this report was written based on notes from this discussion and shared with the full committee for editing and additional comments. The NVAC met again on October 16, 2020 and heard from several experts on their responses to each question and discussed the merits of their responses. The NVAC also met on December 4, 2020 to hear presentations and discuss the report. Throughout this time period, the NVAC members made revisions to the report and reached consensus over email discussions and through a poll in a review of the draft report that was developed before the vote.

Table 1 lists the experts who presented in support of this report during the last three NVAC meetings.

Table 1. Invited speakers and panel presentations given during the NVAC meetings

Topic	Date	Speakers
Health-In-All Approaches for COVID-19 Vaccination	September 23, 2020	Dr. Kirsten Bibbins-Domingo, University of California, San Francisco Dr. Rebecca Weintraub, Harvard Medical School Dr. Dominic Mack, Morehouse School of Medicine Dr. Oliver Brooks, National Medical Association
Allocation and Prioritization: Considerations and Recommendations for the Distribution of COVID-19 Vaccines	September 23, 2020	Dr. Ezekiel Emanuel, University of Pennsylvania Dr. Sarah Oliver, Centers for Disease Control and Prevention
The Infodemic and COVID-19 Vaccines	September 23, 2020	Dr. Monica Schoch-Spana, Johns Hopkins University Dr. Julia Wu, Harvard Dr. Claire Wardle, First Draft News
Guidance on an Approach for COVID-19 Vaccination in Children	October 16, 2020	Dr. Evan Anderson, Emory University Dr. Barry Bloom, Harvard University Dr. James Campbell, University of Maryland
COVID-19 Vaccine Development Lessons	October 16, 2020	Dr. David Stephens, Emory University; and Dr. Kathleen Neuzil, University of Maryland Dr. Richard Hatchett, Coalition for Epidemic Preparedness Innovations Dr. Karin Bok, National Institutes of Health Dr. Florian Krammer, Mount Sinai
Building Confidence in the Immunization System Before, During and After COVID-19 Vaccine Implementation	October 16, 2020	Dr. Jason Schwartz, Yale University Dr. Efthimios Parasidis, Ohio State University Dr. Linda Fu, George Washington University Dr. Glen Nowak, University of Georgia
Perspective: Why Children Should Eventually Receive Vaccines Against SARS-2 Coronavirus	December 4, 2020	Dr. Stanley Plotkin, University of Pennsylvania (Emeritus)

Topic	Date	Speakers
Approaches to Include Pregnant Women in COVID-19 Clinical Trials	December 4, 2020	Dr. Sascha Ellington, Centers for Disease Control and Prevention Dr. Ruth Faden, Johns Hopkins University Dr. Jeff Roberts, U.S. Food and Drug Administration Dr. Linda Eckert, University of Washington and Representing American College of Obstetricians and Gynecologists Dr. Dana Meaney-Delman, Centers for Disease Control and Prevention Dr. Titi Oduyebo, Centers for Disease Control and Prevention
Vaccine Safety Systems and COVID-19	December 4, 2020	Dr. Peter Marks, U.S. Food and Drug Administration Dr. Arnold Monto, University of Michigan and Representing the Vaccines and Related Biological Products Advisory Committee Dr. Tom Shimabukuro, Centers for Disease Control and Prevention Dr. Sonali Kochhar, University of Washington
Coverage for COVID-19 Vaccines	December 4, 2020	Jeff Wu, Centers for Medicare & Medicaid Services

The recommendations in this report were voted on and approved on December 4, 2020, after committee discussion and public comment.

Recommendations

Question 1: What should HHS do before, during, and after the COVID-19 vaccination campaign to improve the confidence in these vaccines and our nation's immunization system especially within underserved communities, including racial and ethnic minorities?

NVAC approved a letter[3] on September 23, 2020 on the same day Admiral Giroir charged the committee with writing this report to provide recommendations to build confidence in COVID-19 vaccines. The recommendations in this letter support part of NVAC's response to this charge, however, they do not cover all aspects of the first question Admiral Giroir posed to the committee. For example, Recommendation 3 in this letter calls for the prompt creation of a unified, proactive, and highly visible communication structure to reliably inform the public regarding vaccine safety and efficacy. As a variety of approaches will be necessary to engage different communities and audiences, NVAC recommends five other actions and provides

further context in recommendations 1.1 and 1.2 of this report to support advice given in the NVAC letter.

Recommendation 1.1: NVAC recommends the Assistant Secretary for Health coordinate the development of a comprehensive communication plan across the federal government, state and local governments, and with private stakeholders before vaccine licensure and throughout post-licensure implementation. This plan should include a communication campaign to inform stakeholders about available vaccines, vaccination opportunities, and the benefits of vaccination, including relative risks associated with COVID-19 versus vaccination. The campaign and related communication should be evaluated after vaccine implementation and the results presented to NVAC.

The *National Vaccine Plan*[4] describes communication processes and principles, which should be used in the development of COVID-19 vaccination communication efforts. For example, vaccine-related messages and materials, including fact sheets and vaccine information statements[5], should be culturally appropriate and available in multiple languages. Clear, consistent, and accurate messaging is essential for broad acceptance of a novel vaccine, particularly in the current climate of vaccine hesitancy based on misinformation and disinformation. To inform this work, HHS should conduct surveys, focus groups, and other research with various target populations, including communities of color such as African Americans and American Indians and Alaska Natives, frontline workers, and people with chronic conditions, including those living in long-term care facilities.

NVAC recognizes HHS can use effective communication strategies and approaches from previous communication efforts supporting routinely recommended vaccines, new vaccines for other emerging diseases, like the Ebola and H1N1 outbreaks, as well as plans to engage with under-resourced and underserved communities. However, insights gained from communication research should be used to inform an overall communication strategy and the development of targeted messages to clearly articulate an overarching campaign goal and the process to prioritize delivery of vaccines when in limited supply initially, followed by a subsequent stage when the vaccines are available on a more wide-spread basis.

Without a clear strategy to communicate these transitions from limited supply, to more widespread use, the American public may be confused and/or frustrated with the process, which could impact the credibility and success of vaccination efforts. Likewise, this plan should address the likely need for different vaccines and possibly different dosing schedules for various groups. As the safety and efficacy profiles of each vaccine in various target populations is understood, a comprehensive vaccination program should be initiated. The plan should also integrate communication best practices and ensure materials and messages are culturally and linguistically appropriate, available in multiple languages, and comprehended by people with low literacy and numeracy skills.[4]

Engaging trusted local community voices to facilitate effective communications about vaccines is important and requires adequate funding to be successful (e.g., education and training of community leaders, research and evaluation to assess each community's needs, and utilizing paid media in an effective way). Because of the time urgency, this engagement including the necessary financing, needs to begin before the development of the specifics of the final messaging described above. Messaging should be tailored for relevance to the specific locality as soon as possible—as these voices will be critical to the success of this effort.

As noted in the September 23 letter, NVAC urges HHS provide "weekly updates to the media and the public on the status, timeline, and emerging information related to COVID-19 vaccine development, safety processes, approval, and recommendation criteria" to communicate the science and ensure transparency of the vaccine development and licensure process[3]. During later stages, clear and timely information about vaccine safety, availability, and access should be released broadly. Special attention should be made so information is available in under-resourced communities on a wide-spread basis and consistent messaging reaches everyone for which the vaccines are intended at the right times. State and local immunization programs often have close relationships with people in the communities and they should be engaged throughout the process. HHS should use paid media, social media, earned media, and owned media to create an effective media mix.

Recommendation 1.2: NVAC recommends the Assistant Secretary for Health collaborate with CDC, FDA, and others to spearhead the development of an educational or training program for professional and public stakeholders about specific COVID-19 vaccines, the vaccine safety systems, the Countermeasures Injury Compensation Program, how vaccines work, and other specifics that will increase people's willingness to feel confident about taking these vaccines.

Healthcare professionals, especially those on the frontline of vaccine administration, must be highly confident in each vaccine's safety and efficacy in order to recommend, answer questions, and administer COVID-19 vaccines to their patients and be able to competently dispel myths and misconceptions. NVAC proposes a concerted effort to deliver in-depth education that is accurate, accessible, and actionable for professional audiences, including healthcare providers, staff, and public health officials.

Educational trainings should instruct immunization provider teams, including non-clinical workers such as front desk staff and technicians, about each vaccine and how to respond to questions from their patients. Answers to anticipated questions should be prepared ahead of time. Furthermore, this educational program can help reduce administration errors by providing information early about storage and handling. Particularly if more than one vaccine is available and more than one require a two-dose schedule, the importance of using the same vaccine for the series must be emphasized.

Additional educational efforts must also focus on increasing the public's knowledge of vaccines, how vaccines work, and vaccine safety. To this end, HHS should partner with the Department of

Education or other non-profits and professional organizations in science, technology, engineering, and mathematics to develop age-appropriate curricula, training modules, or other educational resources for primary grades, middle school, high school, and college-aged students on vaccines. This curricula may intersect a number of areas including biology, statistics, and communication to build understanding of vaccine science and research as well as support decision-making.

In addition, recognizing the importance of vaccination among communities of color[6], who have suffered the greatest burden of inequity from COVID-19[7], specific educational efforts should be tailored to ethnic and racial minorities, other vaccine-hesitant populations, and people with chronic conditions.

Recommendation 1.3: NVAC advises HHS work with a variety of partners to develop a training program to prepare occupational groups recommended to receive COVID-19 vaccines with operational guidelines for vaccinating their workforce.

This training should cover how specific occupational groups, such as healthcare workers, the prison workforce, teachers, and grocery store employees will have ready access to COVID-19 vaccines as well as address likely challenges in occupational distribution of vaccines so groups work with public health agencies to organizationally prepare for a smooth mass vaccination effort. The scope and importance of this effort requires planning to develop clear sets of roles and responsibilities, operational guidelines, policies, and procedures. Therefore, NVAC suggests HHS work with states, localities, affected industries, and relevant occupational groups to create the program.

Recommendation 1.4: The CDC and local health partners should promote widespread use of Immunization Information Systems (IIS) to improve surveillance, coverage rates, and promote health equity. State or local IISs should have the capacity for real-time tracking of COVID-19 vaccination at the population level, recording data on race, ethnicity and other risk factors (except when data collection poses a barrier to vaccine access or acceptance), identifying gaps in coverage, and providing reminder/recall for series completion.

IIS are databases that participating providers use to record vaccination doses administered, track doses, manage inventory, and help providers target high-risk people and provide them with proof of vaccination. IIS can also track adverse reactions and help others analyze vaccine uptake and study coverage rates. Information from IIS systems should be used to help assess, in real time, the effectiveness of the communication efforts and the need for additional resources and modifications in messaging.

Recommendation 1.5: NVAC recommends the Assistant Secretary for Health convene a meeting to address the need for broad demographic data, data sharing, identify privacy concerns, and outline the technical and operational capabilities of IISs, so public health officials get needed data without concern of data breaches.

Recommendation 1.6: The Assistant Secretary for Health should encourage increased participation of underrepresented groups in phase III vaccine trials.

NVAC suggests the use of tailored communication strategies to recruit clinical trial participants[8] that have not been represented in previous phase III vaccine trials, such as frail older adults, the immunocompromised, and tailored strategies to build on the progress being made enrolling minority participants in the ongoing phase III trials. All clinical trials should reflect the makeup of the U.S. population and inclusive eligibility criteria should increase enrollment of underrepresented populations, as well as those with multiple comorbidities, medically complex patients with underlying health conditions, and other COVID-19 risk factors.

Recommendation 1.7: The Assistant Secretary for Health should work with clinical trial leaders and FDA to develop a clear plan, if and when a safe and effective vaccine is authorized or licensed by the FDA, to balance the scientific need to continue the trials through planned completion to collect and analyze long term safety and efficacy data with the desire of clinical trial participants in placebo groups, especially those in COVID-19 high risk groups to receive the active vaccine.

Question 2: The FDA standards[9] for approval and licensure of vaccines for COVID-19 addresses safety and effectiveness and encourages inclusion of minorities, the elderly, pregnant women, and people with medical comorbidities in clinical trials. In particular, for COVID-19 vaccines, I am interested in the approach the nation should take in regard to vaccination of children, given that there will be relatively little data on children from some of the early clinical trials? As context, the case fatality rate for children under age 18 is .02%. What is the appropriate approach, and timing, of generating the needed data and proceeding to potential childhood vaccination as we move forward?

On September 29, 2020 the American Academy of Pediatrics sent a letter[10] to HHS highlighting the need to include children in SARS-CoV-2 vaccine trials. The NVAC agrees with the need for a safe and effective vaccine for children and adolescents. The NVAC recommends limiting the inclusion of children in randomized clinical trials until safety is established in adults. The NVAC further recommends that protocol development for pediatric trials start now, so they can be initiated quickly after these vaccines are recommended for widespread use in adults. Other considerations regarding pediatric populations include a vaccine's effect on transmission among children and the degree to which asymptomatic children transmit virus.

By continuing to vaccinate healthy adults in clinical trials first, we will learn about potential vaccine side effects or adverse events before their use in children. However, the inclusion of children age 5 years and older in at least one of the vaccine clinical trials, allows the collection of important information that can inform future studies. As in the adult trials, diligent data collection and transparently shared analysis of the results should be focused to minimize safety risks while confirming effectiveness.

In addition to providing recommendations on including children in COVID-19 vaccine clinical trials, the NVAC also decided to provide recommendations on including pregnant women in these trials, as pregnant women have not been recruited yet for COVID-19 clinical trials and preliminary data from CDC suggest that pregnant women may be at increased risk for severe COVID-19 illness.[11] For example CDC reported 27,566 illnesses from COVID-19 in pregnant women with 44 deaths from January 22 to October 20, 2020[12] and increased risk for hospitalization and intensive care unit admission than non-pregnant women.[13] In addition, Hispanic and non-Hispanic black women appear to be disproportionately impacted by a COVID-19 diagnosis when pregnant.[13] Women who test positive for COVID-19 during pregnancy also appear to experience more adverse birth outcomes, such as preterm birth and neonatal intensive care unit admission.[14] These data highlight a need to study immune responses during pregnancy. Safety data is necessary for all vaccines in phase III trials, and these data can inform studies for pregnant women and provide insights in new platforms, such as messenger RNA and viral vector vaccines.

As part of the high-risk population for COVID-19,[13] women of childbearing age will be included in priority groups for COVID-19 vaccines. In the United States, women make up 76% of the healthcare workforce[15] and are also more likely to be health facility service staff,[16] such as cleaners, laundry workers and food service staff who may be more likely to be exposed to the virus and prioritized for vaccination. Additionally, it is likely that some participants will become pregnant during the large phase III clinical trials, allowing researchers to study outcomes for both mother and infant. Moreover, some medications to treat SARS-CoV-2 infections may not be recommended during pregnancy, making safe and effective vaccination even more important.[17]

The likelihood that pregnant women will face severe health consequences, are at risk for infection, and may be more likely to access health services during a pandemic makes inclusion in clinical trials important to understand vaccine safety in all recommended COVID-19 vaccines and to avoid unnecessary risks of off-label use or non-evidence-based vaccination. The American College of Obstetricians and Gynecologists supports inclusion of and diverse outreach to pregnant and lactating women so they can be safely included, and potentially prioritized, in COVID-19 vaccination efforts[18] and for the reasons listed above the NVAC agrees and encourages the enrolling of pregnant women in focused phase II studies to provide results about this special population. Regulatory requirements in the United States have been adjusted to encourage studies of the use of COVID-19 vaccines in pregnant women, including racial and ethnic populations experiencing an unduly higher rate of COVID-19 in their community.[19]

Recommendation 2.1: Due to the relatively low burden of disease in children[20], the NVAC recommends a cautious, deliberative, and phased approach in parallel, but dependent upon sufficient safety and efficacy data first being generated in adults and postmarketing surveillance[21] is in effect.

The NVAC encourages a cautious but deliberate development of a strategy to vaccinate children and a phased approach based in part on what we are learning from adult vaccine and adult vaccine use. The study of the role of children as potential transmitters of COVID-19, and the impact on parents, grandparents, other family members, school teachers, and others in the communities, is ongoing,[22] although research clearly suggests that the rate of infection is higher in older children than it is for those 11 years and under, and the incidence of infection is highest in high school students based on data from 200,000 school students from 47 states.[23] A safe and effective vaccine for children will enable more functional and equitable openings of schools and access to childcare centers across the United States, particularly for those populations who have been disproportionately impacted by COVID-19 disease, including Black, Hispanic, and indigenous peoples. A safe and effective COVID-19 vaccine will also allow for pediatric participation in sports and other settings where children congregate with each other and adults. It is critical to demonstrate that a COVID-19 vaccine is safe and effective for protecting children against the direct burden of COVID-19, including hospitalization and death. Vaccinating children also may play a critical role in developing herd immunity to ultimately defeat this pandemic.

Recommendation 2.2: In terms of data needs, the NVAC suggests further epidemiology and pathogenesis studies to better assess risk, the mechanisms and rates of severe disease in children, as well as the role of children in SARS-CoV-2 transmission before an effective vaccination strategy for children can be implemented.

Pediatric studies should determine direct benefits and risks of vaccines so FDA, CDC, and relevant advisory groups can make decisions about licensing and recommendations, including understanding the immune response and safety concerns in this population, which may differ from adults. The NVAC also urges that clinical trials assess COVID-19 vaccines co-administered with other CDC recommended childhood and adult vaccines to ensure they are compatible to avoid unwanted immunologic and/or safety interactions. Likewise, the results from the clinical trial[24] enrolling children 5 years of age and older can provide an opportunity to investigate safety signals in children from one particular vaccine and specifically look for potential adverse events that may be unique to children.

Recommendation 2.3: The NVAC warns against issuing an Emergency Use Authorization (EUA) for COVID-19 vaccines in children, considering that children typically experience generally mild disease, except for multisystem inflammatory syndrome in children (MIS-C), a rare but serious condition that causes inflammation and various symptoms such as abdominal pain, vomiting, diarrhea, neck pain, rash, tiredness, and bloodshot eyes.[25]

A recent study in New York State found the rate of MIS-C to be relatively low during a period of widespread COVID-19 circulation—with about two per 100,000 people aged younger than 21 years of age.[26] As children may suffer unintended complications or side effects from vaccines, and substantially more data will also be available at least initially, for adults than for children, it would be difficult to recommend a vaccine for children based on an EUA. This aligns with

Recommendation 1 in the letter the NVAC sent to Admiral Giroir on September 23, 2020 to make "safe and effective COVID-19 vaccines available to the public" through the FDA "Biologics License Application (BLA) process and use caution if using expedited processes".[3]

Recommendation 2.4: The Assistant Secretary for Health should work with colleagues in the federal government and industry to review and publish data from all COVID-19 clinical trials, including for women who became pregnant during a clinical trial or were vaccinated before a recommendation was made to vaccinate pregnant women.

Recommendation 2.5: CDC, NIH, and other researchers should continue to study the outcomes of COVID-19 disease and vaccine on pregnancy and publish more evidence about health risks. These studies will provide medical professionals, public health entities and industry with a clearer idea of prevalence and severity of the disease in this population and will support the Advisory Committee on Immunization Practices in making informed recommendations for vaccinating pregnant women against SARS-CoV-2 infections.

Once a COVID-19 vaccine is recommended for use in pregnant women, it should continue to be studied during the postmarketing stage, as are all other recommended vaccines. The NVAC encourages researchers to use these data to further the science around including pregnant and lactating women in vaccine trials.

Recommendation 2.6: COVID-19 vaccine developers should start enrolling pregnant women in phase II clinical trials now using guidance from the Pregnancy Research Ethics for Vaccines, Epidemics, and New Technologies working group.[27]

Question 3: What lessons can we learn from COVID-19 vaccine development more broadly to promote innovation and shorten timelines to increase availability of new vaccines to the American public?

The NVAC believes there are a number of lessons from the development of candidate vaccines that will be applied to future vaccine development and pandemic response, so the world can be better prepared for potential future outbreaks of novel disease. While many lessons from the development of COVID-19 vaccines have yet to be learned and the community will benefit from revisiting this process later in the vaccine development process, the NVAC suggests several recommendations to help support these efforts based on what we know now.

Recommendation 3.1: The NVAC recommends that the federal government assess appropriate levels of future funding, and provide appropriate funding, to mitigate the human and economic burden of future pandemics.

This includes:

1. Enhanced funding for basic research in infectious diseases and vaccine research and development,

2. Enabling manufacturing capacity in the United States to meet surge vaccine demand during a pandemic, in an effort to minimize dependence on other countries,
3. Stockpiling essential ancillary supplies, such as vials, syringes, and cold chain equipment,
4. Establishing access to delivery equipment and infrastructure required for rapid distribution of the vaccines for the entire US population.

It is highly likely that novel pandemics will continue into the future and will become increasingly common because of international travel and population density. The COVID-19 pandemic will allow policymakers to quantify the public health impact and the direct and indirect costs of a modern pandemic and help define an appropriate level of ongoing funding for vaccines as tools against future pandemics.

Recommendation 3.2: The NVAC recommends that the federal government assess the capabilities of the various COVID-19 vaccine platform technologies, including safety, efficacy, dosage regimen, administration, thermostability, and time to make available for broad use.

Investments in the most promising vaccine platforms for future pandemics should be made to improve the product profiles and production of investigational vaccines and define which populations may most benefit from certain platforms. There are multiple vaccine technology platforms being assessed in parallel against COVID-19. This presents a unique opportunity to make comparisons regarding the value of each platform by target population, ease of storage, delivery, administration, and cost. Some platforms may be more useful early in a pandemic, such as those that can produce investigational vaccines rapidly. For example, platforms that avoid the requirement for *ex vivo* cell culture. Platforms that do not require -70°C refrigeration are likely to enhance availability. Other platforms may take longer to produce vaccine candidates for clinical trial study, yet they may be more useful later in a pandemic. For instance these platforms could provide prolonged durable protection, improved effectiveness in special populations, such as the elderly or immune compromised, low reactogenicity, or non-frozen storage requirements.

Recommendation 3.3: The NVAC recommends that the federal government work with non-federal partners to assess the effectiveness of the various private-public partnerships that were formed during the COVID-19 pandemic to identify how these could be improved or maintained on an ongoing basis for vaccine development.

These include partnerships for product development, manufacturing and distribution, such as Operation Warp Speed[28] and U.S.-based clinical trial networks,[29] including the Infectious Diseases Clinical Research Consortium,[30] Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) partnership,[31] and the COVID-19 Prevention Network,[32] as well as international partnerships such as COVAX.[33]

Recommendation 3.4: The NVAC recommends that the FDA and NIH assess the regulatory and clinical trial design lessons learned for COVID-19 vaccine development and apply them to other vaccines.

The lack of harmonization among worldwide regulatory agencies has been an ongoing issue for rapid and efficient vaccine development, and COVID-19 presents an opportunity to improve this. Harmonized clinical trials, such as the World Health Organization's Solidarity Vaccine Trial,[34] may help facilitate stronger evidence to determine the relative effectiveness of candidate vaccines and facilitate comparison of the evidence among these vaccines. Likewise, efforts to compare immune responses of different vaccine candidates can be challenging, given complexities in population biology, protocols, and other factors, which can impact data quality and make immunological comparisons more difficult. The Coalition for Epidemic Preparedness Innovations (CEPI)[35] launched an effort to compare the immunological profile of each COVID-19 vaccine candidate in centralized laboratories to provide robust assays to support regulatory processes and common protocols.

Recommendation 3.5: The NVAC recommends the federal government apply lessons learned from COVID-19 vaccine development to new vaccines against pathogens that are not expected to have pandemic potential but are a high priority for patient health.

The ability of new vaccine platform technologies to rapidly produce clinical candidates, offers an opportunity to reconsider how to develop vaccines of strategic interest and provide funding for foundational research. The demonstration that vaccines could be developed and available in one year given an appropriate level of resources leads to the question of what other vaccines may benefit from lessons learned from COVID-19. This could include vaccines that protect against seasonal or endemic viral infections, antimicrobial-resistant infections or pathogens of interest for biodefense.

Recommendation 3.6: The NVAC recommends the federal government work with global health organizations such as PATH, CEPI, Gavi, the Vaccine Alliance, and the Gates Foundation to ensure that future vaccines against pandemic pathogens can be made readily available at low cost to low- and middle- income countries.

CONCLUSION

The COVID-19 pandemic has created an unprecedented need for safe and effective vaccines, among other valuable public health interventions, to prevent further disease transmission and return society fully to normal activities. Many lessons have already emerged from the pandemic that showcase needs to innovate our processes for developing new and improved vaccines, as well as strengthen vaccine communication efforts and confidence in vaccines. Likewise, as the vaccine development process progresses, planning to include children and pregnant women in vaccination clinical trials poses special considerations. The NVAC reviewed, discussed, and approved the recommendations in this report to help ensure these efforts related to COVID-19 vaccination are successful and that we build on efforts to improve the U.S. vaccination system.

1 Centers for Disease Control and Prevention. United States COVID-19 Cases and Deaths by State. https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days. Accessed December 1, 2020.
2 Centers for Disease Control and Prevention. Coronavirus Disease 2019 (COVID-19) https://www.cdc.gov/coronavirus/2019-ncov/cdcresponse/about-COVID-19.html. Accessed December 1, 2020.
3 National Vaccine Advisory Committee. NVAC Letter to the Assistant Secretary for Health: Recommendations to Build Confidence in COVID-19 Vaccines. https://www.hhs.gov/sites/default/files/nvac_covid-vaccine-development-letter_sept2020.pdf Accessed October 8, 2020.
4 US Department of Health and Human Services. 2010 National Vaccine Plan: protecting the nation's health through immunization. 2010. https://www.hhs.gov/sites/default/files/nvpo/vacc_plan/2010-Plan/nationalvaccineplan.pdf. Accessed October 9, 2019.
5 Centers for Disease Control and Prevention. Vaccine Information Statements (VISs). https://www.cdc.gov/vaccines/hcp/vis/index.html. Accessed October 9, 2019.

6 Centers for Disease Control and Prevention. Health Equity Considerations and Racial and Ethnic Minority Groups. https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html Accessed October 12, 2020.
7 Evans, MK. Covid's Color Line—Infectious Disease, Inequity, and Racial Justice. New England Journal of Medicine. 2020; 383:408-410. DOI: 10.1056/NEJMp2019445.
8 U.S. Department of Health, Food & Drug Administration. Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry. https://www.fda.gov/media/127712/download
9 U.S. Department of Health, Food & Drug Administration. Development and Licensure of Vaccines to Prevent COVID-19: Guidance for Industry. Reviewed June, 2020. https://www.fda.gov/media/139638/download Accessed September 28, 2020.
10 American Academy of Pediatrics. [Letter]. https://downloads.aap.org/DOFA/AAPLettertoHHSandFDAChildreninCOVID19VaccineTrials.pdf. Written September 29, 2020. Accessed October 1, 2020.
11 Khalil, Asma & Kalafat, Erkan & Benlioglu, Can & O'Brien, Pat & Morris, Edward & Draycott, Tim & Thangaratinam, Shakila & Le Doare, Kirsty & Heath, Paul & Ladhani, Shamez & von Dadelszen, Peter & Magee, Laura. (2020). SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. EClinicalMedicine. 25. 100446. 10.1016/j.eclinm.2020.100446.
12 Centers for Disease Control and Prevention. Data on COVID-19 during Pregnancy: Severity of Maternal Illness. https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-populations/pregnancy-data-on-covid-19.html. Accessed October 14, 2020.
13 Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769–775. DOI: http://dx.doi.org/10.15585/mmwr.mm6925a1external icon.

14 Allotey, J., E. Stallings, M. Bonet, M. Yap, S. Chatterjee, T. Kew, L. Debenham, A. C. Llavall, A. Dixit, D. Zhou, R. Balaji, S. I. Lee, X. Qiu, M. Yuan, D. Coomar, M. van Wely, E. van Leeuwen, E. Kostova, H. Kunst, A. Khalil, S. Tiberi, V. Brizuela, N. Broutet, E. Kara, C. R. Kim, A. Thorson, O. T. Oladapo, L. Mofenson, J. Zamora, and S. Thangaratinam. 2020. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: Living systematic review and meta-analysis. BMJ 370:m3320. doi: 10.1136/bmj.m3320.

15 Day JC, Christnacht C. Women hold 76% of all health care jobs, gaining in higher-paying occupations. https://www.census.gov/library/stories/2019/08/your-health-care-in-womens-hands.html.
16 Bureau of Labor Statistics. Labor Force Statistics from the Current Population Survey. https://www.bls.gov/cps/cpsaat18.htm. Accessed October 13, 2020.

17 Favilli, A, Gentili, MM, Raspa, F, Giardina, I, Parazzini, F, Vitagliano, A, Borisova, AV, Gerli, S. Effectiveness and safety of available treatments for COVID-19 during pregnancy: a critical review.J Matern Fetal Neonatal Med. 2020 : 1–14. Published online 2020 Jun 7. doi: 10.1080/14767058.2020.1774875.
18 American College of Obstetricians and Gynecologists. ACOG Statement on COVID-19 and Pregnancy. https://www.acog.org/news/news-releases/2020/06/acog-statement-on-covid-19-and-pregnancy Accessed October 13, 2020.
19 Chen, C. 2020. How—and when—can the coronavirus vaccine become a reality? ProPublica. https://www.propublica.org/article/how-and-when-can-the-coronavirus-vaccine-becomea-reality (accessed September 17, 2020).
20 American Academy of Pediatrics. Children and COVID-19: State-Level Data Report. https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/children-and-covid-19-state-level-data-report/. Accessed October 8, 2020.
21 Centers for Disease Control and Prevention. Vaccine Safety Monitoring. https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/index.html Accessed October 12, 2020.
22 Li X, Xu W, Dozier M, et al. The role of children in transmission of SARS-CoV-2: A rapid review. J Glob Health. 2020;10(1):011101. doi:10.7189/jogh.10.011101.
23 Park Y, Choe Y, Park O, et al. Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020. Emerging Infectious Diseases. 2020;26(10):2465-2468. doi:10.3201/eid2610.201315.
24 BioNTech SE. Study to Describe the Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Individuals. (Clinical Trials.gov Identifier: NCT04368728). ClinicalTrials.gov/NCT04368728. Accessed October 13 2020.
25 Centers for Disease Control and Prevention. Multisystem Inflammatory Syndrome (MIS-C). https://www.cdc.gov/mis-c/ Accessed October 13, 2020.
26 Dufort, EM, Koumans, EH, Chow, EJ, Rosenthal, EM, Muse, A, Rowlands, J, Barranco, MA, Maxted, AM, Rosenberg, ES, Easton, D, Udo, T, Kumar, J, et al. Multisystem Inflammatory Syndrome in Children in New York State. New England Journal of Medicine. 2020; 383:347-358 DOI: 10.1056/NEJMoa2021756.

27 Krubiner, CB, Faden, RR, Karron, RA, et al. Pregnant women and vaccines against emerging epidemic threats: ethics guidance for preparedness, research, and response. Vaccine. 2019. https://doi.org.10.1016/j.vaccine.
28 US Department of Health and Human Services. Fact Sheet: Explaining Operation Warp Speed. https://www.hhs.gov/coronavirus/explaining-operation-warp-speed/index.html. Accessed October 15, 2020.
29 National Institutes of Health. NIH launches clinical trials network to test COVID-19 vaccines and other prevention tools. https://www.nih.gov/news-events/news-releases/nih-launches-clinical-trials-network-test-covid-19-vaccines-other-prevention-tools. Accessed October 15, 2020.
30 National Institutes of Health. Infectious Diseases Clinical Research Consortium. https://www.niaid.nih.gov/research/idcrc. Accessed October 15, 2020.
31 National Institutes of Health. Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV). https://www.nih.gov/research-training/medical-research-initiatives/activ. Accessed October 15, 2020.
32 National Institutes of Health. COVID-19 Prevention Network. About the COVID-19 Prevention Network (CoVPN). https://www.coronaviruspreventionnetwork.org/about-covpn/. Accessed October 15, 2020.
33 Gavi, the Vaccine Alliance. COVAX. https://www.gavi.org/covax-facility. Accessed October 15, 2020.
34 World Health Organization. “Solidarity” clinical trial for COVID-19 treatments. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments. Accessed October 15, 2020.
35 CEPI. Why and how do we harmonise assessment of COVID-19 vaccine trials? https://cepi.net/news_cepi/why-and-how-do-we-harmonise-assessment-of-covid-19-vaccine-trials/.