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| **Brighton Collaboration Viral Vector Vaccines Safety Working Group (V3SWG)**  **Standardized Template V2.1 for Collection of Key Information for Risk Assessment of Viral Vaccine Vector Candidates** | | | |
| **5. Target Pathogen and Population** | **Information** | **Comments/Concerns** | **Reference(s)** |
| **5.1** What is the target pathogen? | SARS-CoV-2 | SARS-CoV-2 belongs to the family Coronaviridae, genus Betacoronavirus, and subgenus Sarbecovirus. The virus is similar to betacoronavirus detected in bats, sharing 96.3% sequence identity to the BetaCoV/bat/Yunnan/RaTG13/2013 genome, a coronavirus isolated from an intermediate horseshoe bat (Rhinolophus affinis) in China. | Zhou P. Nature 2020;579:270, doi: 10.1038/s41586-020-2012-7 |
| **5.2** What are the disease manifestations caused by the target pathogen in humans, for the following categories: |  |  |  |
| * In healthy people | The spectrum of symptomatic infection ranges from mild (81%), severe (with dyspnea/hypoxia, 14%), and critical/death (5%); asymptomatic infections 30%–40%. Pneumonia is the most frequent serious manifestation, characterized by fever, cough, dyspnea, and abnormal chest imagings. Upper respiratory tract symptoms, myalgias, diarrhea, and smell or taste disorders, are also common. Complications of COVID-19 include respiratory failure; cardiac and cardiovascular; thromboembolic; and other inflammatory/autoimmune complications (e.g., Guillain-Barre syndrome, Multisystem Inflammatory Syndrome in Children [MIS-C]); and secondary infections. Prolonged symptoms and long-term sequelae of COVID-19, including post-intensive care syndrome (persistent impairments in cognition, mental health, and/or physical function following survival of critical illness) are being reported with emerging data. |  | McIntosh K. UpToDate. Available at: <https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-clinical-features> |
| * In immunocompromised people | Immunocompromised people are at increased risk of severe illness from COVID-19. |  | CDC. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html> |
| * In neonates, infants, children | Fewer children have been ill with COVID-19 compared to adults. Most children with COVID-19 have mild symptoms or are asymptomatic. However, infants under 1 year old and children with certain medical conditions might be at increased risk of severe illness: asthma or chronic lung disease; diabetes; genetic, neurologic, or metabolic conditions; congenital heart disease; immunosuppression; multiple complexity; and obesity. MIS-C, a Kawasaki-like inflammatory condition involving the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs, has been observed in healthy children with COVID-19. |  | CDC. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/children/symptoms.html>  CDC. Available at: <https://www.cdc.gov/mis-c/index.html> |
| * During pregnancy and in the fetus | Limited data to date indicates that pregnant women might be at increased risk for severe illness from SARS-CoV-2 infection. Pregnant women have disproportionately higher rates of COVID-19-associated hospitalizations compared to nonpregnant women. About 50% of hospitalized pregnant women are asymptomatic at admission. Severe illness (intensive care 15%, mechanical ventilation 8%, and death 1%) and pregnancy losses occur for 2% of hospitalized women; the later are experienced by both symptomatic and asymptomatic women. | In a Swedish study, SARS-CoV-2 test positivity in individuals in labor was associated with a higher prevalence of preeclampsia (prevalence ratio 1.84, 95% CI 1.004–3.36) and lower prevalence of induction of labor (prevalence ratio 0.64, 95% CI, 0.45–0.90). Mode of delivery, postpartum hemorrhage, preterm birth, 5-minute Apgar score, and birth weight for gestational age did not significantly differ between test positive and negative groups. | Delahoy MJ et al. MMWR Morb Mortal Wkly Rep 2020;69:1347, doi: 10.15585/mmwr.mm6938e1  Ahlberg M et al. JAMA 2020, doi:10.1001/jama.2020.19124 |
| * In elderly | The risk for severe illness from COVID-19 increases with age, with older adults at highest risk; 80% of COVID-19 deaths reported in the U.S. have been in adults 65 years and older (16% of COVID-19 cases). |  | CDC. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html> |
| * In any other special populations | People with the following conditions are at increased risk of severe illness from COVID-19: cancer, chronic kidney disease, chronic obstructive pulmonary disease, immunocompromised state from solid organ transplant, obesity (BMI of 30 or higher), serious heart conditions, sickle cell disease, and type 2 diabetes mellitus. Certain conditions might increase risk for severe illness including asthma (moderate to severe), cerebrovascular disease, hypertension, immunocompromised state from blood or bone marrow transplant, immune deficiencies, HIV, steroid use or other immunomodulators, neurologic conditions, liver disease, pulmonary fibrosis, smoking, thalassemia, and type 1 diabetes mellitus. |  | CDC ACIP. Available at: <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2020-08/COVID-05-McLung.pdf> |
| **5.3** Briefly, what are the key epidemiologic characteristics of the disease caused by the target pathogen (e.g. incubation period, communicable period*,* route/s of transmission,case fatality rate, transmissibility characteristics such as basic reproductive ratio *(*R0*)* etc.)? | The incubation period is on average 5 days, but can be as long as 14 days. Available data indicate that persons are infectious 1–3 days before their symptom onset. Persons with mild to moderate COVID-19 remain infectious no longer than 10 days after symptom onset, whilst those with more severe to critical illness or severe immunocompromise likely remain infectious no longer than 20 days after symptom onset. Asymptomatic individuals might transmit the infection. Routes of transmission include contact and droplet (primary); airborne; fomite; mother-to-child, and other possible modes. A basic reproductive number (R0) for COVID-19 is estimated to be between 2 and 4. The crude global case fatality ratio is roughly 3% and varies widely between countries, from less than 0.1% to over 25%. |  | Yu P et al. J Infect Dis 2020;221:1757, doi: 10.1093/infdis/jiaa077  Lauer SA et al. Ann Int Med 2020;172:577, doi: 10.7326/M20-0504  Cheng HW et al. JAMA Intern Med 2020, doi: 10.1001/jamainternmed.2020.2020  van Kampen J et al. Available at: [https://www.medrxiv.org/content/10.1101/2020.06.08.20125310v1external icon](https://www.medrxiv.org/content/10.1101/2020.06.08.20125310v1), doi: 10.1101/2020.06.08.20125310  CDC. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html>  WHO. Available at: <https://www.who.int/news-room/commentaries/detail/estimating-mortality-from-covid-19> |
| **5.4** What sections of the population are most affected by the target pathogen (e.g. pediatric, pregnant, lactating women (breast feeding), adult, elderly) | Data indicating that infants, older adults, pregnant women, and persons with certain medical conditions or with multi-morbidities (see 5.2) are at increased risk for severe illness from COVID-19. Men with COVID-19 have higher risk of all-cause death, severe infection, or ICU admission than women; the excess risk is not explained by age and comorbidities.  Race and ethnicity are also risk factors for severe illness. American Indian, Alaska Natives, Asian, Black or African American, and Hispanic or Latino are at higher risk for illness, hospitalization, and death compared with White, Non-Hispanic Persons. |  | Griffith DM et al. Prev Chronic Dis 2020;17:200247, doi: 10.5888/pcd17.200247.  CDC. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html> |
| **5.5** What is known about the correlates of protective immunity to the target pathogen or to the disease? | Challenge studies with other human coronavirus indicate multiple candidates (serum IgG, IgA, neutralizing titer, and mucosal IgA) that may serve as correlates of protection. In animal models, elicitation of high titers of neutralizing antibodies targeting the receptor binding domain (RBD) of the spike (S) protein are protective against re-challenge with SARS-CoV-2. Correlates of protection and their durability, however, have not been established in humans. | In an outbreak of SARS-CoV-2 on a fishing vessel with high (>85%) attach rate, neutralizing antibodies correlate with protection from SARS-CoV-2. | Huang AT, et al. Nat Commun 2020;11:4704, doi: 10.1038/s41467-020-18450-4  Rogers TF et al. Science 2020;369:956, doi: 10.1126/science.abs7520  Addetia A et al. medRixiv 2020. Available at: <https://www.medrxiv.org/content/10.1101/2020.08.13.20173161v1> |
| **5.6** Please describe any other key information about the target pathogen or population that may inform benefit risk | NA |  |  |
| **References** | **Information** | | |
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