Answering Key Questions About COVID-19 Vaccines

**The US government** is investing in rapid development of vaccines against coronavirus disease 2019 (COVID-19), several relying on new technologies. In the US, 4 vaccine candidates are in phase 3 studies with initial results expected soon. If studies succeed, 1 or more vaccines may become available within a few months. Clinicians are likely among the first to be offered COVID-19 vaccines and have a key role in helping patients make decisions about vaccination. Providing evidence-based information will be particularly important in an environment of polarization and mistrust. This Viewpoint focuses on common questions patients are likely to ask about COVID-19 vaccines.

**How Much Does a Vaccine Reduce the Risk of COVID-19 and Its Complications?** The US Food and Drug Administration (FDA) guidance set as an expectation for licensure that a COVID-19 vaccine would prevent disease or decrease its severity in at least 50% of people who are vaccinated. In reviewing the results of a study it is important to know there is a margin of error in estimating the percentage of cases or complications prevented. For example, a study might report a reduction in disease from 100 cases in the placebo group to 50 in those vaccinated. This difference would meet the standard of 50%, but it will be important to explain to patients the uncertainty surrounding that value. While the study showed a 50% reduction in illness, the confidence interval for the efficacy estimate might be 30% to 80%, meaning efficacy may be as low as 30% or as high as 80%. It will also be important to understand whether a vaccine reduces not only mild but also more severe disease, as well as hospitalizations and deaths. However, studies may have insufficient numbers of patients with severe outcomes to definitively evaluate those end points.

**How Safe Is a Vaccine Candidate?** Clinicians will want to know how safety was evaluated, including whether studies have been completed, as planned, with 15,000 or more people vaccinated and followed up for time periods sufficient to detect most safety issues (eg, 2 months). It is also important for vaccine developers to present all safety data, including from outside the US.

It is likely that vaccination will be associated with mild adverse events like soreness at the injection site, fever, fatigue, and myalgias. While such symptoms may be unpleasant, so long as they are not severe and resolve quickly, and patients anticipate them, these symptoms are not usually worrisome, unless they lead to additional health care encounters.

More serious reactions, such as otherwise unexplained neurologic or inflammatory processes, would raise concerns. While patients need to understand that serious adverse events may occur coincidentally following receipt of a vaccine, these adverse events could be signals of a safety problem. Comparing rates of adverse events between vaccine and placebo recipients can help determine whether a signal is vaccine-related, but for small numbers of rare events it may be inconclusive.

Patients should understand that rare adverse events may only be detected as a vaccine is widely used. Patients will want assurance that the US has mobilized enhanced safety systems to monitor, evaluate, and communicate about the safety of COVID-19 vaccines after they are released.

**Will the Vaccine Be Effective for All Patients?** COVID-19 is more common and severe among individuals often underrepresented in clinical trials, including older individuals, people with chronic illnesses, and persons in racial/ethnic minority populations. Different groups may not have the same responses to vaccination. When results become available, it will be important to evaluate the characteristics of people included in the trial and determine whether they are similar to patients seen in the practice setting. A given vaccine may be more appropriate for some patients than others, and knowing those differences will be important.

Trials involving children and pregnant women will start once vaccine safety is demonstrated in others, making it unlikely vaccines will initially have FDA indications for these groups. In considering use of a vaccine in patients not within FDA indications, available evidence and recommendations from the CDC’s Advisory Committee on Immunization Practices (ACIP) should be consulted.

**Was Important Information Made Public and Reviewed by Independent Experts?** It is important to know whether all relevant information that might support or contradict the findings of a vaccine trial has been made public. For example, preliminary reports might not include all patients studied or might include only selected results. It must be clear if any information is missing and the reasons for that missing information should be provided.

In addition, it is important that the study has been reviewed by experts without personal or financial interests in the research, as done by major medical journals. Such review helps reduce the risk of errors or bias.

**Is a Vaccine Licensed or Provided Under an Emergency Use Authorization?** FDA has a long track record of licensing vaccines that have protected individuals against diseases like measles, polio, and pneumonia. However, it has stated it will apply its usual high standards to COVID-19 vaccines. These standards mean clinicians can have confidence in what is known about the safety and efficacy of a licensed vaccine.

However, FDA could make an as-yet unapproved vaccine available through an Emergency Use Authorization (EUA). Rather than proven safety and effectiveness, EUAs...