Q&A on safety development COVID19 Vaccine

These question were asked during an online meeting with the EMA on COVID19, November 2020

Q: Are the evaluation requirements for this COVI19 different than the regular evaluation?

A: The evaluation requirements are the same for all medicines, including vaccines, as set out by legislation and complementary regulatory and scientific guidance (you can find more information on the required studies for approval here). So, for mRNA vaccines that include RNA of a coronavirus (SARS-CoV-2) antigen (such as the ones from Pfizer-BioNTech and from Moderna), as for any other vaccines, the same quality, safety and efficacy requirements apply. However, each request for authorisation is assessed individually and contextualised based on the evidence available at the time of evaluation throughout which there is a continued exchange with the applicant to clarify any outstanding issues. Only if the scientific evidence supports that the benefits outweigh the risks, will there be a positive opinion and subsequent approval of the vaccine.

Q: There is a concern that the Vaccine is going to change the DNA, can you explain?

A: In relation to your question about DNA sensitivity, please note that the RNA used in these vaccines cannot insert itself into the DNA of the person receiving the vaccine. It does not enter the host cell nucleus where the DNA is but uses the cell machinery present in the cytoplasm to make proteins, like any other human mRNA. And like all mRNA it is quickly broken down by mechanisms in the cell, and so remains only temporarily in the body.

In relation to vaccines based on modified adenovirus-based vectors that include DNA of a coronavirus (SARS-CoV-2) antigen, the adenovirus has been modified in two important ways: it cannot replicate, and its genome incorporates the genetic instructions for producing the spike protein that SARS-CoV-2 uses to infect human cells. This adenovirus does not cause disease in humans. The piece of DNA in the adenovirus that encodes for the spike protein is expected to enter nucleus of host cells where it is transcribed into mRNA, which then leaves the nucleus and is subsequently translated into spike proteins in the cell cytoplasm. The gene encoding the spike protein is not expected to integrate into the host genome but will remain free in the nucleus (episomal), which means it will be expressed only for a limited period. Therefore, the DNA from the vaccine does not persist in human cells; it is broken down. Moreover, because the adenovirus vector in the vaccine cannot replicate, no more copies of the genetic material are produced.

Q: As we see, the just developed vaccines have not a track record yet of monitored side effects. How will this handled?

A: As for all vaccines, long-term monitoring is needed to identify any potential new or changing side effects. This means marketing authorisation holders will have to:
- Monitor the safety of vaccines, report suspected adverse reactions to EMA, keep product information up to date.
- Conduct safety and effectiveness studies looking at performance of their products on the market
- Submit regular safety and benefit risk reports to EMA which will be assessed by the Pharmacovigilance Risk Assessment Committee (PRAC)

In addition, companies will need to:
- Follow people enrolled in the clinical trial for up to two years post vaccination
- Submit monthly safety reporting summaries in addition to the regular six months updates required in the legislation

Furthermore, the long-term monitoring includes:
- Intensive analysis of reports of suspected side effects from patients and healthcare professionals
- Additional independent studies performed in Europe on the safety of vaccines when used in real life
- International collaboration on COVID-19 vaccine monitoring

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