Investigating concerns over informed consent for pregnant women in RSV vaccine trial

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A debate has broken out over whether Pfizer should have told pregnant women taking part in its maternal respiratory syncytial virus (RSV) vaccine trial that a trial of a similar GSK vaccine was stopped over a safety signal around preterm birth, an investigation by *The BMJ* reveals.

Pfizer's vaccine, called Abrysvo, was recently approved for use in the US and the European Union, but is not yet authorized in the UK.

Some experts have criticized Pfizer for not informing participants, while others believe notification would have been premature and caused unnecessary anxiety, reports freelance investigative journalist Hristio Boytchev.

RSV is a common respiratory virus that usually causes mild, cold-like symptoms, but it can be severe, especially in young children, and is a significant cause of infant death globally.

Both GSK and Pfizer were developing recombinant RSV F protein vaccines to inoculate pregnant women and protect their babies.

In February 2022, GSK halted its phase 3 trial after a possible increased risk of preterm births emerged. GSK is still investigating the cause, which experts think may be unrelated to the vaccine, but it is no longer developing its vaccine.

Pfizer was also studying preterm births as an adverse event of special interest in its own phase 3 trial and a numerical (not statistically significant) imbalance in preterm births has recently emerged, though there is not enough data to understand if there is truly an increased risk or what the cause is.

After GSK's trial was halted, there was a split opinion between clinical trial ethicists and some vaccine researchers over whether Pfizer should have informed all participating women in its trial about the potential risk or updated its consent forms.

Charles Weijer, bioethics professor at Western University in London, Canada told *The BMJ* that informing pregnant women in Pfizer's trial

about GSK's results would have allowed women who had not yet received the jab to consider whether they still wished to get it, and the ones who had already received it to seek additional medical advice and follow-up.

"Any failure to provide new and potentially important safety information data to trial participants is ethically problematic," Weijer said.

Pfizer has also been criticized for a passage in some of its trial consent forms, seen by *The BMJ*, which said that its vaccine candidate was risk-free for the baby, assurances a research ethics expert described as "misleading" and "irresponsible."

Pfizer did not respond to *The BMJ*'s questions on the issue of informed consent.

Regulators have taken different approaches when approving Abrysvo, notes Boytchev. For example, the US Food and Drug Administration (FDA) approved it with conditions, including only administering to women who are 32-36 weeks pregnant and a warning in the prescribing information of a numerical imbalance in preterm births. The FDA is requiring Pfizer to conduct postmarketing studies to "assess the signal of serious risk of preterm birth."

Yet others such as the European Medicines Agency (EMA) and the UK's Joint Committee on Vaccination and Immunization (JCVI), did not consider a warning around the possible risk of preterm birth or restricting the use of the vaccine to the later weeks of pregnancy necessary.

As Pfizer didn't respond to the questions about whether it had informed expectant mothers in its trial about GSK's results, *The BMJ* contacted governmental health authorities in all 18 countries where Pfizer had trial

sites, as well as more than 80 trial investigators, and none answered saying that it had.

Some confirmed that Pfizer continued to enroll and vaccinate women for months after the news of the potential risk of preterm birth in GSK's vaccine trial was made public.

One trial investigator, speaking anonymously because they had signed a confidentiality agreement with the company, said they questioned Pfizer early in 2022 about the potential risk of preterm birth given the similarity between Pfizer and GSK's products, but was told their data hadn't shown any increase in risk.

Other trial investigators disagreed with the notion that participants should have been informed. Beate Kampmann, director of the Centre for Global Health at Charite University Hospital Berlin, one of the lead authors of Pfizer's phase 3 trial paper, and who was responsible for a trial site in the Gambia, said that GSK's results weren't relevant to her trial participants "as most participants were already in follow-up."

Some Pfizer trial consent forms seen by *The BMJ* contain contradictory statements, both warning of possible "life-threatening" effects of the vaccine on the baby while simultaneously carrying a passage that said only the expectant mother is at risk from adverse effects.

"Knowing what we know now, the statement in question is irresponsible, and given the benefit of hindsight, is actually factually incorrect," said Rose Bernabe, professor of research ethics and research integrity at the University of Oslo. "Considering the gravity of the risk that this irresponsible statement veils, this misleading statement should be a ground for questioning the validity of the consent process."

More information: Concerns over informed consent for pregnant

women in Pfizer's RSV vaccine trial, *The BMJ* (2023). DOI: 10.1136/bmj.p2620