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Food and Drug Administration Bone, Reproductive and Urologic Drug Advisory Committee Regarding Makena:
A Lack of Substantial Evidence of Effectiveness
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I am Meena Aladdin, health researcher at Public Citizen's Health Research Group, and I have no financial conflicts of interest.

Public Citizen strongly urges the committee to recommend that the FDA withdraw approval of Makena from the market, as there is a lack of substantial evidence that the drug is effective. Public Citizen has petitioned the agency to take such action.

During the initial review of the new drug application for Makena, the lead FDA statistician strongly recommended against the drug's approval, noting the following regarding the single, seriously flawed premarket phase 3 clinical trial:

> From a statistical perspective, the level of evidence from Study 17P-CT002 is not sufficient to support the effectiveness of 17P. The primary reason is the absence of a second, confirmatory study. …. Study 17P-CT002 was not designed for drug approval.
>
> The results of the analyses of the 32 and 35 week endpoints suggest their false positive rates could be as great as 1/40.

The PROLONG trial (Trial 003) was a well-designed, well-conducted, appropriately powered, clinical trial, the design of which was mutually agreed upon by the sponsor and FDA. It did not suffer from the multiple flaws seen in the premarket trial (Trial 002).

Most importantly, the PROLONG trial failed to show a statistically significant treatment effect for Makena on any primary or secondary endpoint. The FDA concluded:

> In summary, Trial 003 did not demonstrate a treatment benefit of Makena on reducing the neonatal composite index or the rate of spontaneous preterm birth prior to 35 weeks

> gestation, nor was there evidence of a treatment benefit on the rate of spontaneous preterm birth prior to 37 weeks or 32 weeks gestation.

Furthermore, the FDA concluded that the unplanned exploratory subgroup analyses conducted by the Sponsor (stratified by geographic region and race) "do not provide convincing evidence of efficacy over placebo in any subpopulation and there is no statistically significant interaction between Makena and any of these risk factors."

Maintaining approval of Makena in the absence of any clinical benefits being demonstrated by Trial 002 or Trial 003 would make a mockery of the more than 50-year FDA legal standard requiring substantial evidence of a drug's effectiveness. Therefore, Public Citizen strongly urges the committee to recommend that the FDA withdraw approval of Makena from the market, as it fails to provide any clinical benefit.