Doshi public comments at FDA VRBPAC meeting, Feb 26, 2021
3 minutes.

Hello and thank you. I'm Peter Doshi. I am on the faculty at the University of Maryland and a medical journal editor at The BMJ. I have no relevant conflicts of interest, no one has paid for my attendance, and these comments are my own.

First point - I'm nervous about the prospect of there never being a covid vaccine that meets the FDA's approval standard. The agency has already authorized two covid vaccines as meeting the EUA standard of "may be effective." Granting another EUA to Janssen would begin to create a kind of marketplace of vaccines good enough to be authorized, but never approved.

The briefing documents say Janssen is seeking an EUA, but they don't say why. My question is, if Janssen is fully confident in the data, why not seek a full approval – a BLA?

Looking forward, I worry about FDA lowering its approval standards. Last June, FDA outlined its expectations for an approvable vaccine, saying participant follow-up should continue for "at least one to two years." We know Moderna and Pfizer can't meet this standard, as placebo recipients are already being vaccinated. And in its briefing document, Janssen says if an EUA is granted, they will unblind their trial. It is quickly seeming the only way a vaccine will ever be approved is if FDA lowers its standards to the "may be effective" standard of the EUA. Is this what we want? And if the FDA now believes that a few months of follow-up is sufficient to be certain benefit outweighs risk, the agency needs to tell us why it changed its mind.

We thankfully have a waning epidemic in the US right now, and manufacturing capacity of already EUA'd vaccines continues to grow. The argument that we don't have the luxury of time to demand better evidence doesn't hold as much water as it might have two months ago.

Second, I worry about process. The way it's supposed to work is the FDA asks the advisory committee for its honest, independent view. But the media reporting on this suggests an EUA is a foregone conclusion. I want to know if FDA is doing anything to ensure advisory committee members can truly vote their mind, and not bow to the pressure that there is only one right decision?

Third, it is unreasonable to accept Janssen's labeling of its primary endpoint as "moderate to severe/critical Covid-19," because included what most would call mild disease. A lab-positive test plus 2 symptoms (like cough and headache) would be sufficient. Everyone knows that the majority of covid cases are mild; yet in Janssen's trial, there were only 4 cases of mild covid compared with 390 so-called "moderate" cases (see p.17) . Clearly Janssen's "moderate" is what everybody else would call "mild." The case definition of "severe" covid also needs scrutiny as PCR-positive cases with no other symptoms other than a blood oxygen saturation of 93% or less would qualify.

There's a real urgency to stand back and look at the forest here as well as the trees and I urge the committee to consider the effect FDA's decisions may have on the entire regulatory approval process. **Thank you.**