The Center for Biologics Evaluation and Research's (CBER), Vaccines and Related Biological Products Advisory Committee (*VRBPAC*) October 22,2020

A Physician's notes on the VRBPAC meeting for BioNTech's vaccine.

At the end of the day I am struck with the fact that FDA and Pfizer refused to comment on their results occurring since November 14, despite being asked twice. And FDA essentially refusing to inspect the plant, and waffling about about it in the meeting, about how they have reviewed all the manufacturing documents.

Very early Dorin Fink said that even if one vaccine got licensed so it would become an existing alternative, that still would not prevent an EUA being issued for other Covid vaccines, since the supply would be limited.

There was some mention of the fact that an EUA product cannot be sold commercially…while a lot of money is changing hands to obtain them

Mention that the path to a full license application would require 6 months of data.

CDC's Eric Will (?) estimated there have already been 53.9 million infections in the US. Using a similar "multiplier" as they use to estimate flu cases.

Someone calling in named Julie Omohundro said she reviewed all the relevant rules on experiments/informed consent and that the patient fact sheet was not sufficiently understandable for subjects, some clarity missing re research vs treatment, informed consent for EUAs a gray area. She begged FDA to run their consent forms/patient fact sheet through an IRB. Sounded like there could be a legal issue to exploit here.

Many people spoke about the need to gain the public's trust

Pfizer presentation:

The vaccine can stay at fridge temp for 5 days (2-8 degrees centigrade)

The vaccine contains "a mutated full spike protein"

Animal studies were performed in March-April, then human studies (Phase 2/3) began in late July

Pfizer alleged they understand the need to consistently manufacture "at the highest quality standards" and FDA has "reviewed" the cGMP data.

Teratogenicicty and prpegnancy data will be available late December

They have seen no evidence of disease enhancement.

Obesity was the most striking risk factor for developing Covid. I was not clear if the obese population, which was 35% of subjects, was evenly divided by number and BMI between the vaccine and placebo groups.

There is no definite correlate of protection (antibody or other serum marker that definitely connotes protection). Someone argued that there was no evidence that the N protein being measured (to define an infection?) was appropriate.

Someone alleged that MRNA stimulated toll like receptors 7 and 8. Dr. Sahli, the inventor, said NO

Pfizer claimed there had been no allergic signal seen. (However FDA had data showing minor allergic reactions 15-20% more after with vaccine)

Pfizer was asked about the stimulation of chemokines and cytokines by the vaccine, and they said "We did not look at chemokines and cytokines in our phase 1-2-3 trials". Which suggested to me they had looked at them in animal or perhaps other human studies or invitro. How would they NOT??

Dr. Moore asked (the first of 2 people asking about this issue) whether mRNA can be recycled into a different RNA or into a DNA via reverse transcriptase? no specific answer. Meissner also asked about this later, specifically asking whether a fetus might be at risk of having its DNA changed via reverse transcriptase if mother was vaccinated.

Pfizer did say "We have not analyzed the 8 vaccine failures yet"

Questions were asked about the very low infection rates in the control group. Pfizer had no answer, claimed these were typical disease rates. Along this same vein, Pfizer was asked if perhaps higher risk subject were enrolled later, explaining low infection rates. Pfizer would not really deal with this issue eihter.

One sharp epidemiologist noticed that the protection curve after the first dose and second dose were identical, superimposable. There was no evidence from infection rates that the second dose provided any additional protection. The response was more handwaving by Pfizer's chief spokesperson, Dr. Katherin Jansen.

(The impression I got from Dr. Jansen and Dr. Marion Gruber at FDA, both it seems originally from Germany, and each I think in charge of their part of the dog and pony show, was that this is a done deal, just shut up, let's get to the vote.)

The two age cohorts used were 18-55 and 65-85. Guess they did not enroll anyone between 56 and 64

The primary endpoint was a case occurring at least 7 days after the 2nd dose. The secondary endpoints were a bit confusing.

There is one month follwup for unsolicited AEs and SAEs.

I think there is active surveillance for only a week after each dose. But it was claimed there would be followup for 3 years for serious AEs or deaths

I did not understand how the total numbers of subjects were ascertained:

There were 43,448 enrolled.
40,277 were in the efficacy assessment—some had dropped out or were ineligible I guess
But only 37,586 were being assessed for safety. It seemed you could hide a lot in the nearly 6 thousand lost since enrollment. Why are fewer being assessed for safety than for efficacy? 1500 in each group did not receive the second dose. We were not told the reasons why. So are these the ones who are not being followed for safety, even though probably many dropped out because of safety issues?

Roughly 81% of the vaccine group had a signif or notable reaction, enough to unblind them, while just 11% of the placebo group did

In the future Pfizer plans three safety studies:

1. healthcare workers, using the HEROES registry
2. DOD-using the EMR
3. VA- Using the EMR

of the AEs seen in the trials, FDA attributed a shoulder injury and lymphadenopathy to the vaccine. They did not attribute Bell's palsy to the vaccine. I think (not certain) there were no anaphylaxis cases in the US trial.

Sheldon Taubman, the consumer rep, said we really need those last 26 days of data—the ones FDA claimed it could not provide cause it takes so long to get the meeting package ready. Pfizer was dead silent, never said oh well, it is just the same as what we are presenting. Taubman also wanted to see the severe adverse event details. They ignored him.

Pfizer claimed "WE don't have it. Our early data are compelling"

Kurilla said, "YOu dont think Bell's Palsy could be a VAE? Then he went into more details and became muted, I think deliberately. He went into the problem of so many cases being mild disease. Chair Monto told him the committee would ignore his question about innate immunity. Monto also let slip that there was a delay, so when people didnt mute themselves there would be an echo delayed by a couple of seconds.

After this there was a lot of muting and loss of signal intermittently, and the Pfizer lead had to dial back in once. Some of these occurred at crucial times, others not.

Paul Offit was concerned about the label warning about allergies, and the millions of people of carry epipens who will not be able to get the vaccine. He did point out that the label says to avoid the shot if you have previously had a reaction to these ingredients. But someone pointed out that no one has gotten these ingredients before! So the warning is disingenuous.

No data were presented on viral carriage post vaccinatin or spread. Arnold Monto chimed in that CDC would be conducting observational studies to sort this out.

Eric Will of CDC said, "We believe there is still underreporting of Covid deaths"

Lisa Messonnier spit out a laundry list of all the programs that would collect some types of AE data, which included: V-safe (text messaging reminders to recipients to fill in a form re side effects), VAERS, DOD's DMSS (which has refused to make its data public since 2001) , VA, NHSN, CISA, VSD,FDA "best" and "Prism", "Genesis" 250 longterm care facilities watched with NIAID and Brown University, CMS claims data and VaST.

Asked whether the US is coordinating with data from other nations, Messonnier waffled that CDC was looking at coordinating such a group

Someone asked where the future safety data would be going. to FDA? CDC? Messonnier waffled while her answer kept breaking up. She did not like that question. Finally she said CDC is discussing a contract with NAS' NAM to look at safety.

Katrin Jansen from Pfizer finally said that in primates, the vaccine prevents lung infection and viral carriage is MORE TRANSIENT in the vaccinated. IE it reduced but did not prevent spread in monkeys. Pfizer is looking into doing such study in humans.

Pfizer was asked whether AEs were greater in those who demonstrated prior infection. 500 people (claimed 2-3% os subjects, but that must only be in the group that got the real vaccine) were seropos at recruitment and Pfizer said they did not fare worse.

Pfizer excluded those who were PCR positive at the time of a visit.

Meissner said there were not enough data on 16 and 17 year olds. He did not htink they should be approved for vaccine.

It seemed this was a critical issue for FDA (and Pfizer) as they had come up with a plan (identical to the plan Christine Grady had come up with for anthrax vaccine tests in children) that you give the vaccine to the 16-17s, then to those slightly younger, and travel down the age groups till all ages are included. So FDA and Monto were very antsy about cttee members who wanted to up the age range and who asked for a vote on that question. Basically the excuse was we have to hurry up and they were not given that option, which led to at least 2 of the members voting NO or abstained (Chatterjee and Meissner). The other 3 no votes were the consumer rep Fuller and Drs. Kim and Kurilla.

Hope it helps. I have a little more detail in my handwritten notes, but these notes are what seemed relevant.