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Memorandum

To: Trialists

Fr: Curtis Meinert

Re: More on COVID-19 vaccine trials

IV: Broadly, drug trials are classified by stage of activity; phase 1, 2, 3 and 4; aka phase I, II, III, and

Phase 1: The first stage in testing a new drug in human beings. Performed as part of an approved Investigational New Drug Application under Food and Drug Administration guidelines; done to provide information on metabolism, pharmacologic action, and safety as in dose escalation designs; usually without benefit of concurrently enrolled comparison groups.

Phase 2: Usually the second stage in testing; performed as part of an approved Investigational New Drug Application under Food and Drug Administration guidelines. Generally carried out on persons having the disease or condition of interest; purpose to provide preliminary information on efficacy of the drug and to provide additional information on safety and associated side effects; may be designed to include a control treatment and random assignment of patients to treatment.

Phase 3: Usually the third and final stage in testing a new drug in human beings. Performed as part of an approved Investigational New Drug Application under Food and Drug Administration guidelines. Concerned with assessment of dosage effects, efficacy, and safety and aimed at providing information for labeling in relation to use in clinical settings. Usually designed to include a control treatment and random assignment to treatment.

Phase 4: When done, usually after FDA approval of the drug; typically done to determine if the treatment used long-term is safe and effective; typically done under circumstances approximating real-world conditions, with a clinical event as the primary outcome measure and randomized and placebo-controlled. Not to be confused with post-marketing surveillance; usually observational devoid of designed concurrent comparison groups and randomization.

There are no hard and fast lines of demarcation separating phases. Hence, a trial registered as a phase 1 by one set of investigators may be registered as a phase 2 by another set of investigators. Further, phases can be combined so a trial may be registered as a phase 1 trial by one set of investigators, a phase 2 by another set of investigators, and as a phase 1/2 trial by a 3rd set of investigators.

My posting about the Moderna vaccine trial (dated 9 September 2020) prompted calls for a more complete picture of where we stand in the hunt for vaccines. Finding them is not easy. There are dozens of registries (we need a single universal registry) with varying formats and terminology.

For the table below I relied on the NY Times interactive website (<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>). Clicking on "Phase 3" produces a list of ten trials; classified as "phase 3" on the site but as seen from Col C in the table below, range from phase 1 to phase 4.

Registration numbers (Col B) were found by Googling. The information in Col C thru Col G was extracted from registrations. The accuracy of the information depends on when registrations were last updated; sometimes months back.

COVID vaccine trials (identified on NY Times interactive website by clicking on "phase 3")

Col A Trial	Col B Reg. no.	Col C Status	Col D Design	Col E Primary outcome	Col F Sample size	Col G Completion date
Moderna (US)	NCT04470427	Phase 3; enrolling	Rz, DM, PC	COVID-19	30,000	Oct 2022
BioNTech (Germany) Pfizer (US), Fosun Pharma (China)	NCT04368728	Phase 2/3; enrolling	Rz, DM, PC	COVID-19	29,481	Nov 2022
CanSino Biologics (China)	NCT04341389	Phase 2; active but no longer enrolling	Rz, DM, Xover	Adverse reactions	508	Jan 2021
CanSino Biologics (China)	NCT04526990	Phase 3; not yet enrolling	Rz, DM, PC	COVID-19	40,000	Dec 2021
Gamaleya Research Institute (Russia),	NCT04436471	Approved for early use; completed	Obs; notRz	Change antibody levels against SARS-CoV	38	Aug 2020
AstraZeneca; (UK; Sweden) University of Oxford	NCT04516746	Phase 2/3; not yet enrolling	Rz, DM, PC	COVID-19	30,000	Oct 2022
Sinovac Biotech (China)	NCT04352608	Active but no longer enrolling; approved for early use	Rz, DM, PC	Adverse reactions	744	Jul 2020
Wuhan Institute of Biological Products (China)	NCT04053010	Phase 4; completed	Rz, SM	Seroconversion rate	702	Dec 2019
Beijing Institute of Biological Products (China)	NCT04313127	Phase 1; active but no longer enrolling	Obs	Adverse reaction post vaccination	108	Dec 2022
Murdoch Children's Research Institute (Australia)	NCT04327206	Phase 3; enrolling	Rz, DM, PC	COVID-19	10,078	Mar 2022

Rz: randomized; notRZ: not randomized; DM: double-masked; SM: single-masked; PC: placebo-controlled; Xover: crossover; Obs: Observational