Obligations to COVID Vaccine Research Subjects

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Disclaimer

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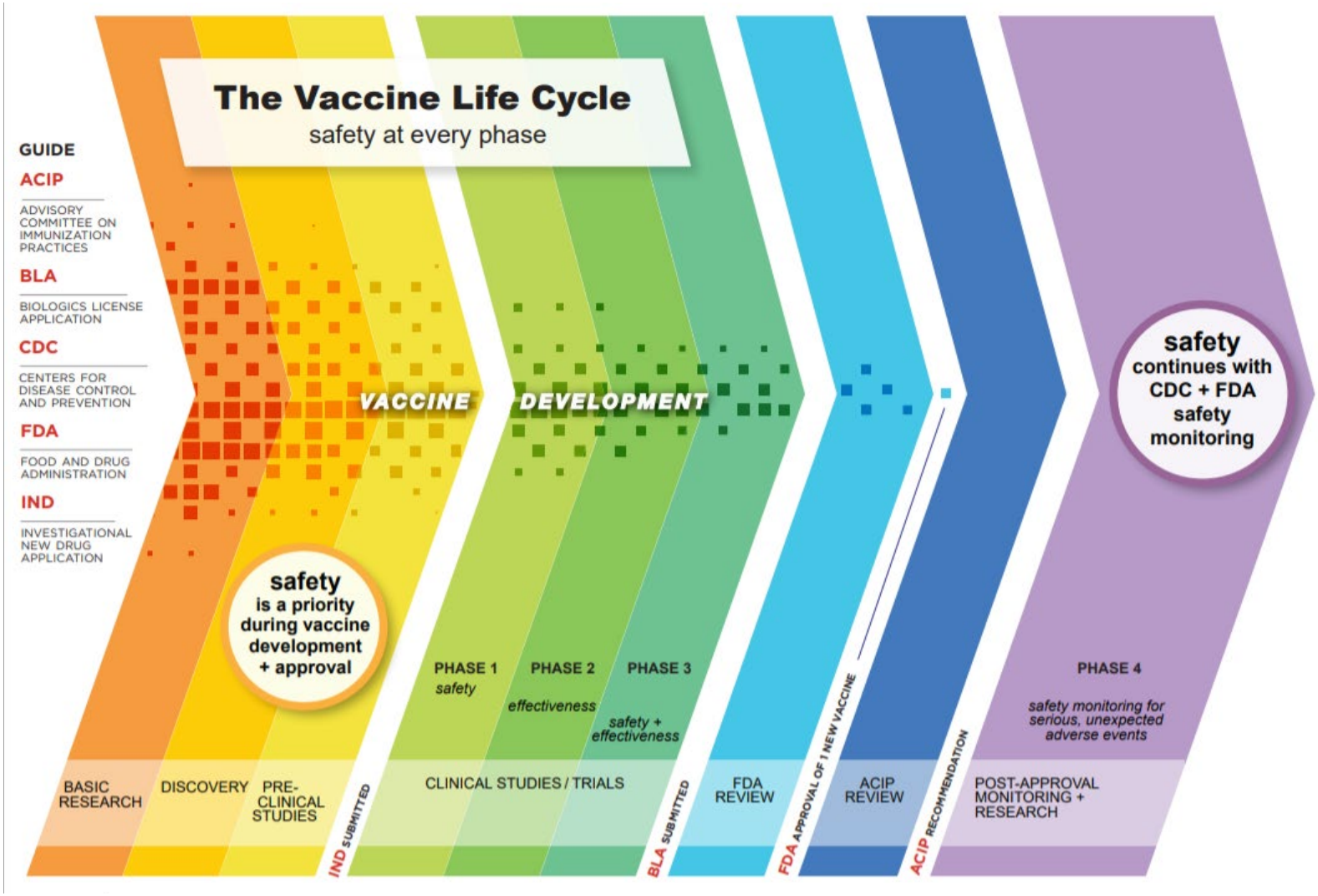
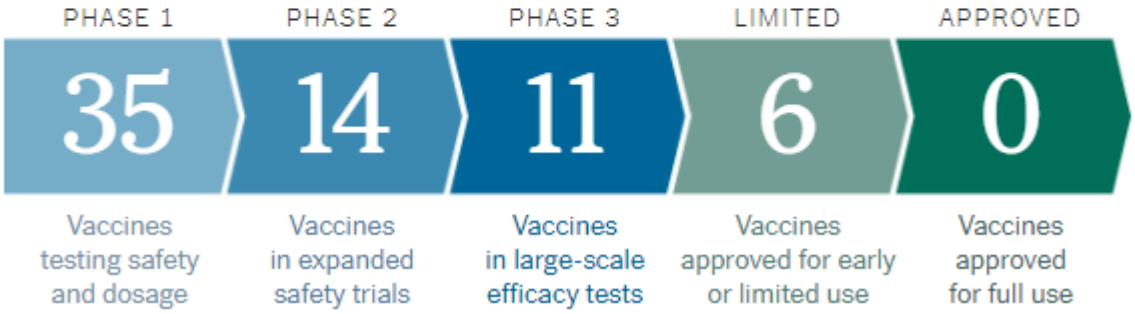

The Vaccine Life Cycle
safety at every phase
GUIDE
ACIP
ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES
BLA
BIOLOGICS LICENSE APPLICATION
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION
FDA
FOOD AND DRUG ADMINISTRATION
IND
INVESTIGATIONAL NEW DRUG APPLICATION
VACCINE DEVELOPMENT
safety is a priority during vaccine development + approval
PHASE 1
safety
PHASE 2
effectiveness
PHASE 3
safety + effectiveness
PHASE 4
safety monitoring for serious, unexpected adverse events
safety continues with CDC + FDA safety monitoring
BASIC RESEARCH
DISCOVERY
PRE-CLINICAL STUDIES
IND SUBMITTED
CLINICAL STUDIES / TRIALS
BLA SUBMITTED
FDA REVIEW
FDA APPROVAL OF 1 NEW VACCINE
ACIP REVIEW
ACIP RECOMMENDATION
POST-APPROVAL MONITORING + RESEARCH

COVID Vaccines under Study

The New York Times

Coronavirus Vaccine Tracker

By Jonathan Corum, Sui-Lee Wee and Carl Zimmer Updated October 29, 2020



Obligations to Research Subjects

- During the study
  - Provide clinically actionable information
  - Provide information relevant to decision to remain enrolled (i.e. something that shifts the risk, benefit balance)
- After the study
  - Disseminate findings
    - Publication

Obligations to Research Subjects

- Phase III Randomized Controlled Trial
  - Randomized to receive novel intervention v. placebo
  - At the end of the study (or during interim analysis) novel intervention determined to be better than placebo

Does the investigator have a responsibility to make sure those who received placebo have access to the novel intervention?

Obligations to Research Subjects

- Post Trial Access
  - Obligation to subjects
  - Obligate to community from which subjects were drawn
  - Obligation to region
  - Obligation to country….

Obligations to Research Subjects

- Post Trial Access
  - **Obligation to subjects**
  - Obligate to community from which subjects were drawn
  - Obligation to region, country etc….

Obligations to Research Subjects

- Who has the obligation?
  - Investigator
  - Sponsor
  - Health system
  - Government
- For how long?
  - Treatment for HIV
  - Vaccine?

First large-scale US Covid-19 vaccine trial reaches target enrollment of 30,000 participants

By **Elizabeth Cohen**, CNN Senior Medical Correspondent

Updated 10:16 AM ET, Thu October 22, 2020

News | Coronavirus pandemic

ALJAZEERA

Pfizer may seek US green light to use COVID vaccine in late Nov

THE WALL STREET JOURNAL.

BUSINESS | HEALTH CARE | HEALTH

Pfizer Could Apply for Emergency Use of Covid-19 Vaccine by Late November

Application with FDA would come if trial data, due this month, is positive

FDA Guidance – June 2020

- "Efficacy trials should include contingency plans for continued follow up and analysis of safety and effectiveness outcomes in the event that a safe and effective vaccine becomes available (e.g., as demonstrated in a planned interim analysis or as demonstrated in another clinical trial). *In that case, discussion with the agency may be necessary to address ethical arguments to break the blind and offer vaccine to placebo recipients*."

https://www.fda.gov/media/139638/download

FDA Guidance – October 2020

- "FDA does not consider availability of a COVID-19 vaccine under EUA, in and of itself, as grounds for stopping blinded follow-up in an ongoing clinical trial. An EUA request should include strategies that will be implemented to ensure that ongoing clinical trials of the vaccine are able to assess long term safety and efficacy … in sufficient numbers of subjects to support vaccine licensure. These strategies should address how ongoing trial(s) will handle loss of follow-up information for study participants who choose to withdraw from the study in order to receive the vaccine under an EUA."

https://www.fda.gov/media/142749/download

Obligation to Current Subjects

- **Let's assume:** Moderna candidate found to be "safe and efficacious" (50% fewer subjects on vaccine developed symptomatic disease when compared to placebo)
  - Should we continue the trial?
  - Should we unblind those on the trial?
  - Should we offer the vaccine candidate to those on the placebo arm?

Obligation to Current Subjects

- Moderna trial is designed to collect 2 years work of follow-up data on subjects.
  - Delayed side effects
  - Point estimate of efficacy
  - Duration of immunity
  - More of less efficacious in subgroups

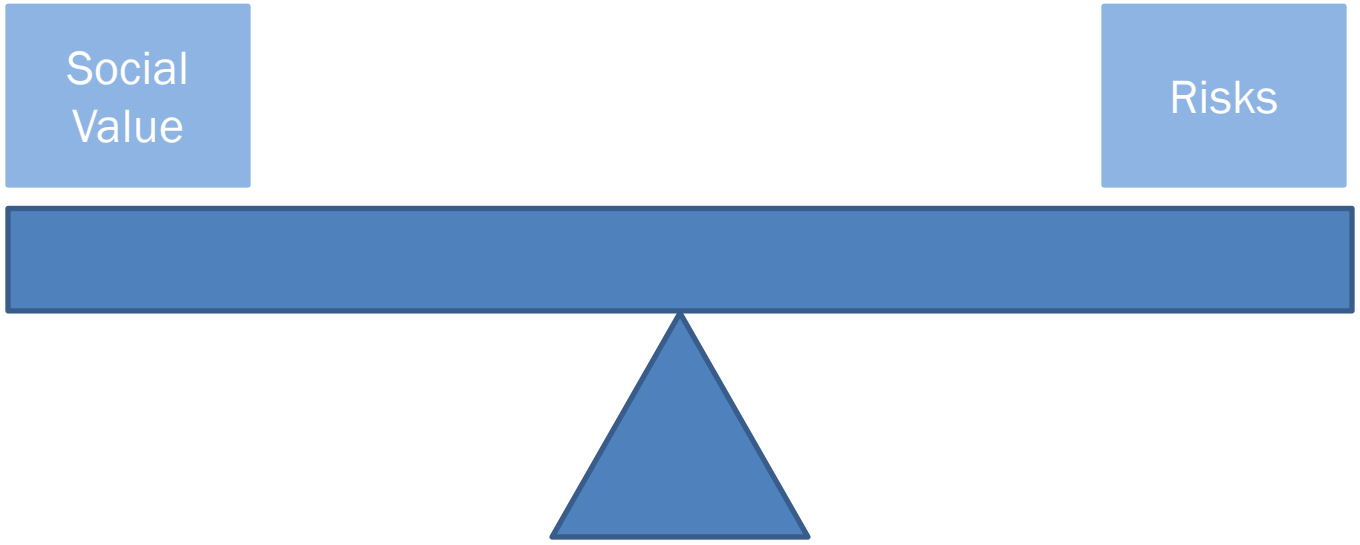
Continuing trial may result in collection of socially valuable data.

Obligation to Current Subjects

- Once vaccine found to be “safe and efficacious” those on placebo arm at higher risk of developing symptomatic disease than those on the placebo arm
  - What level of risk?
    - May vary by personal characteristics: age, co-morbidities
  - Alternative modes of prevention?

Obligation to Current Subjects

- Are the risks low enough to justify asking some or all of the subjects to continue?



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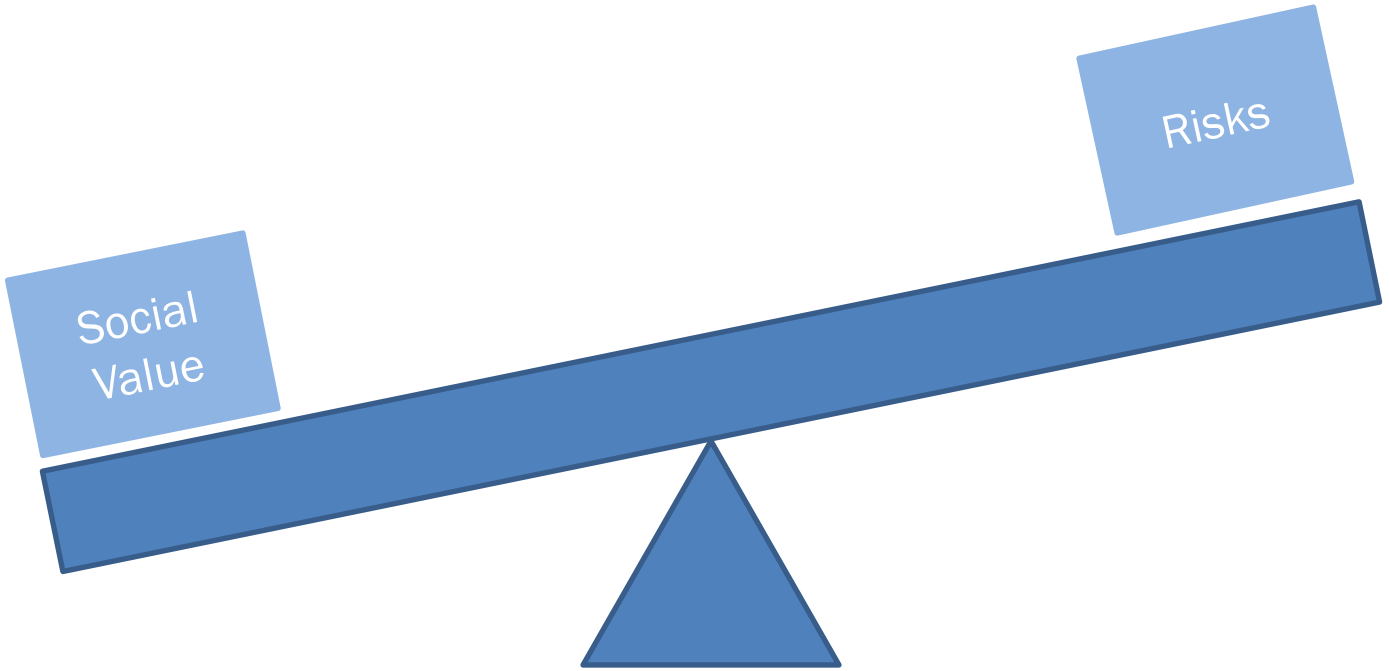

Obligation to Current Subjects

- Unblind subjects, offer access to vaccine candidate
- Who has the obligation to provide the vaccine candidate to those on the placebo group?
  - Investigator
  - Sponsor

Obligation to Current Subjects

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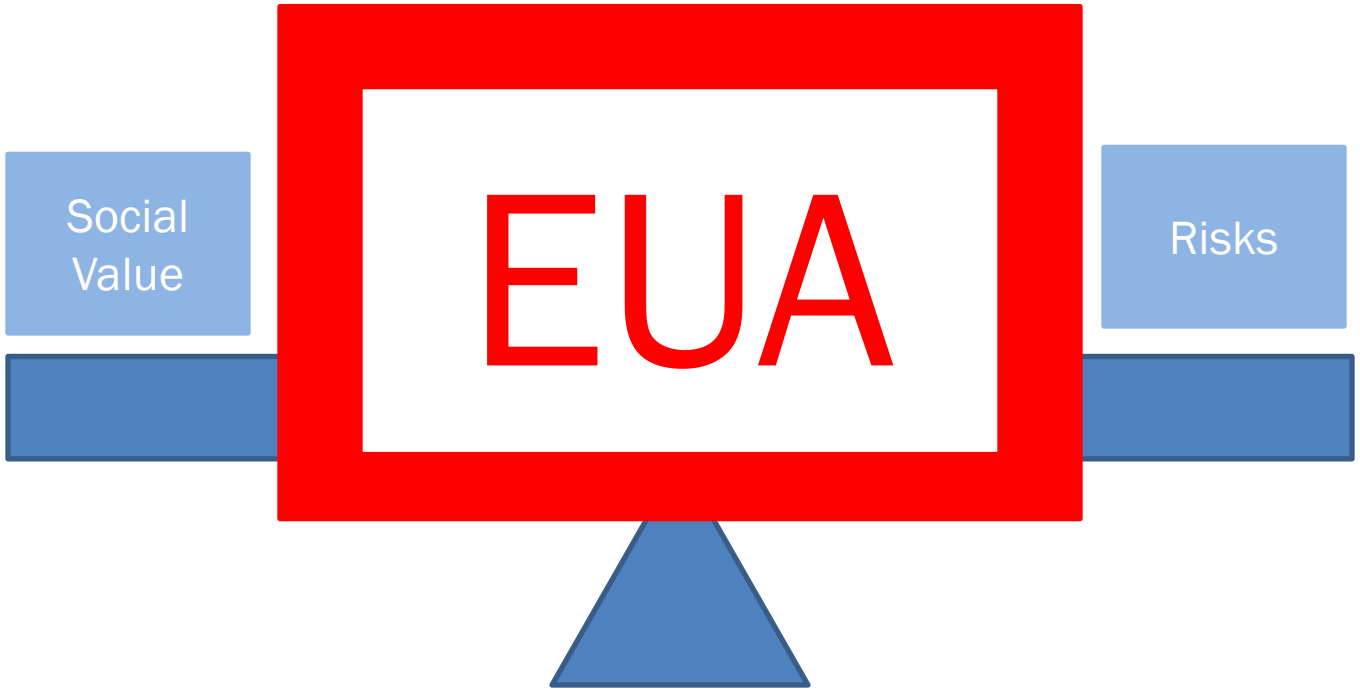

Obligation to Current Subjects

- How does this change the balance?
  - Is there enough to go around?
  - Should those who received placebo be prioritized over others?
- What happens with all the other ongoing trials?
  - Does Moderna vaccine candidate need to be considered as comparator?

Obligation to Current Subjects

- Ethics analysis needs to keep pace with advancement of knowledge, science