Ethical and Regulatory Issues in the Vaccines Race

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Caveat

- The presenter / author is a member of the Access to COVID-19 Tools (ACT) Accelerator Ethics Working Group of the World Health Organization.
- All views expressed are personal to the presenter / author.
Considerations

- Immediate: Should (and can) clinical trials continue?
  - Yes, because the long term safety and effectiveness of vaccines need to be established. (Note new mRNA technology.)
  - Yes, because one or two vaccines will not be able to meet global needs.
    - But should high-priority individuals (e.g. front-line workers) be denied of access (e.g. if they are enrolled in double-blind placebo controlled trials)?
    - And can trial participants be prevented from withdrawing from trial participation?
- Longer term:
  - Support for LMICs (particularly if inadequate supply of vaccines)
    - Coping with COVID-19
    - Scientific and regulatory capacities
  - Global health research policy:
    - Ensure long term benefits not displaced by short-term needs
    - More effective coordination (in contrast to competition / nationalism)
      - Scientific
      - Regulatory
Multiple vaccine candidates; Multiple technologies

Source: Alice Park, When will we get a vaccine, Time Magazine, 21-28 Sept 2020
Stages of Clinical Research

Vaccine Development in China

Vaccine Development by Technology

Source: China Newsweek, 14 September 2020
Philippines First Country to Test Russia's 'Sputnik V' Coronavirus Vaccine Amid Concerns

The Philippines' health regulators would conduct Phase II and III trials to test its effectiveness from October.

By Krishnendu Banerjee
August 14, 2020 16:27 +08

Russia's rushed development of Sputnik V, the world's first Coronavirus vaccine, has met with skepticism from healthcare experts. However, the Philippines has agreed to take the vaccine, albeit after conducting a large-scale clinical trial.

The vaccine, developed jointly by the Gamaleya research institute and the Russian defense ministry, was supposed to be the country's 'Sputnik moment' (first man-made satellite to put in orbit by Russia in 1957). But the clinical trial data and limited test volunteers have every expert questioning the vaccine's effectiveness. But Russia went ahead anyway with regulatory approval after just two months of testing and hailed the country's scientific prowess.

In its combined Phase II and III clinical (human) trial phase, the institute tested the vaccine only on 38 volunteers. And that's not sufficient when it comes to mass production. Compare that to the vaccine currently being developed by Oxford University and AstraZeneca, which has already been tested on thousands of volunteers. Even vaccines that are being developed by China are being tested in the United Arab Emirates, Pakistan and Brazil besides Canada on thousands of people as has been the norm.

Hence, when Russian officials reached out to Operation Warp Speed, a multi-level U.S. agency to accelerate treatment and vaccine for COVID-19, the latter refused. The agency officials told CNN that the Russian vaccine was not reliable as it didn't go through rigorous testing.

China's Sinopharm launches Phase III trial of Covid-19 vaccine in UAE

17th July 2020 (Last Updated July 17th, 2020 07:29)

China-based pharmaceutical company Sinopharm has initiated a Phase III clinical trial to assess its Covid-19 vaccine candidate in Abu Dhabi, UAE.
First Vaccinations Begin in Africa for COVID-19 Trial

Africa’s first participation in a COVID-19 vaccine trial has begun as volunteers received injections, while officials say the continent of 1.3 billion people cannot be left behind.

By Associated Press, Wire Service Content June 24, 2020

A vaccine volunteer gets an injection at the Chris Hani Baragwanath hospital in Soweto, Johannesburg Wednesday, June 24, 2020. Africa’s first participation in a COVID-19 vaccine trial has begun as volunteers received injections developed at the University of Oxford in Britain. The large-scale trial is being conducted in South Africa, Britain and Brazil. (AP Photo/Siphiwe Sibeko) THE ASSOCIATED PRESS

J&J adds Chile, Argentina and Peru to Latin America COVID-19 vaccine trials

By Fabian Cambero, Marco Aquino

SANTIAGO AND LIMA (Reuters) - U.S. pharmaceutical company Johnson & Johnson has added Chile, Argentina and Peru to the Latin nations where it plans to conduct Phase III trials for its vaccine against COVID-19, the company confirmed on Wednesday. The study will involve 60,000 volunteers from Brazil, Chile, Colombia, Peru, Argentina and Mexico and will be coordinated by J&J’s pharmaceutical unit Janssen and local academic centers.

The company told Reuters it was waiting for regulatory approval in Chile, Argentina and Mexico.

“This multilateral collaboration...demonstrates the progress and commitment of collective efforts to find solutions for the COVID-19 pandemic,” it said in a statement.

Miguel O’Ryan of the University of Chile’s School of Medicine, which will host the J&J trial, said the parameters were still being worked out but his team was prepared to recruit up to 1,000 volunteers for trials funded by the vaccine developers.
Mass Access in rapid succession
Many Trial Volunteers Got Placebo Vaccines. Do They Now Deserve the Real Ones?

Some vaccine experts worry that "unblinding" the trials and giving all of the volunteers vaccines would tarnish the long-term results.

Ethical Obligation to Trial Participants?
Should Clinical Trials Continue?

Placebo-Controlled Trials of Covid-19 Vaccines — Why We Still Need Them

Recent announcements that some Covid-19 vaccines are estimated to have high short-term efficacy provide new hope that vaccination will soon contribute to controlling the pandemic.

The initial roll-out of limited quantities of vaccines that are still investigational will provide the opportunity to ethically obtain pivotal data to improve regulatory and public health decision making, thereby increasing public and professional confidence in those and other vaccines.

After relatively short follow-up in phase 1 trials, even when vaccine efficacy appears to be high, reliable information will still be needed on longer-term safety and duration of protection. Other information gaps will include more comprehensive assessments of short-term safety, knowledge of whether waning of vaccine-induced protection may lead to vaccine-enhanced disease if a vaccine becomes infected on exposure to SARS-CoV-2, information on protection against clinically severe forms of Covid-19 and knowledge of any associations between the degree of protection and the recipient’s age or underlying conditions. Even after the first vaccines become available, it will still be important to evaluate additional vaccines to meet worldwide needs.

On November 6, 2020, we, as participants in a World Health Organization (WHO) ad hoc consultation on the next steps for Covid-19 vaccine evaluation, discussed what critical additional data should be sought to inform regulatory and policy recommendations for the first successful vaccines and subsequent optimisation. Consensus emerged that while it is still feasible and ethical, ongoing studies and others that are about to start should continue to collect high-quality information using directly randomized comparisons against placebo to address as many of the data requirements as possible. While vaccine supplies are limited, available vaccines are still investigational, and public health recommendations to use those vaccines have not been made, we believe it is ethically appropriate to continue blinded follow-up of placebo recipients in existing trials and to randomly assign new participants to vaccine or placebo. Moreover, under these conditions, we believe that trial sponsors are not ethically obligated to provide treatment assignments for participants who desire to obtain a different investigational vaccine. People who enroll in clinical trials for altruistic reasons would probably understand the value of gathering data that will further elucidate the safety

International Coalition of Medicines Regulatory Authorities

Participating Regulatory Authorities

ICMRA provides a global architecture to support enhanced communication, information sharing, crisis response and evidence translation.

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Statement on continuation of vaccine trials

We, (ICMRA members; a global coalition of medicine regulators) have an important role in supporting the worldwide effort to ensure the quality, safety and efficacy of licensed vaccines and to make them available to the public. We have stepped up our global collaboration to facilitate and expedite the development and evaluation of vaccines against SARS-CoV2 (causing COVID-19-disease).

This statement in support of continuing COVID-19 vaccine trials to collect critical data to support regulatory actions and deployment, for as long as is feasible, is intended for all stakeholders, vaccinees, researchers and investigators, academia, regulators and the pharmaceutical industry.
Considerations

- Ethical obligation towards vulnerable groups currently enrolled in placebo-controlled RCTs?
  - Frontline workers
  - Elderly with chronic disease

- How do we think about the concept of equipoise?
  - Benjamin Freedman (1987): There is genuine uncertainty in the expert medical community over whether a treatment will be beneficial.
  - Implications of regulatory approval for emergency use?
  - “Sufficiently compelling evidence” of safety and efficacy
  - WHO's Emergency Use Listing procedure for public health emergency (time limited and prior to pre-qualification application)

- Right of research participants:
  - To unblind (if placebo controlled)?
  - To withdraw?

- Impact on existing clinical trials and vaccines still under development?
  - Early stoppage?

- Long term data?
Can International Law help to sustain longer term interests?

- Global Justice and Solidarity
  - Support for LMICs (limited supply of vaccines)
  - Coping with COVID-19
  - Scientific and regulatory capacities
    - Technology and surveillance
- Global health research policy:
  - Ensure long term benefits not displaced by short-term needs
  - More effective coordination (in contrast to competition / nationalism)
    - Scientific and Regulatory Collaboration and Partnership
    - Data and Sample Sharing
    - Technology transfer
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**ZOOM Workshop 2**
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8 December 2020, Tuesday
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