Key Criteria for the ethical acceptability of Covid-19 human challenge studies

Principales criterios para la aceptabilidad ética de los estudios de exposición con seres humanos en el contexto de la COVID-19

On behalf of:


WHO Global Health Ethics Unit
A type of research involving:

1. Intentional infection of research participants

2. With aim to
   a) Test vaccines / drugs
   b) Study infection / immunity
   c) Develop models of infection

3. In a highly controlled setting
>100 Covid-19 vaccine candidates

Complexities of vaccine field trials
- Involve >10,000 participants
- Require months-years (depend on local transmission levels)

Uncertainties of public health measures
- Based on incomplete knowledge re: infection & immunity

Infection in young adults >1000 times less risky than older people
Vaccine field trials: when and where?

- Elimination (or pre-introduction)
  - New Zealand etc.

- Suppression (or low-level endemicity)
  - Lockdown

- Epidemic
  - Most of the world

Trials commencing prior to the epidemic peak rapidly accrue events. Post-trial vaccination can benefit the host population.

Vaccine efficacy trials are not possible.

Low average daily incidence prolongs vaccine efficacy trials.
Size of epidemics for field trials

- WHO minimum standard for COVID-19 vaccines (50% VE)
- Monovalent H1N1pdm09 vaccine (69% VE)
- Live attenuated influenza vaccine (83% VE)
- 2-dose measles-containing vaccine (93% VE)

Minimum number of population infections required for trial (mixed population of 5 million people)

Minimum incidence of infection in placebo group

Group size in trial (total participants is the group size by the number of groups)

alpha 5%, beta 90%, minimum VE 30%

Heriot & Jamrozik, Medical Journal of Australia, 2020
Daily confirmed cases: UK

The graph shows the daily change of confirmed cases in the UK from April 23 to October 18. The cases peaked on October 26 with 20,890 new cases reported.
SARS-CoV-2 challenge studies must have strong scientific justification

Los estudios de exposición al SARS-CoV-2 deben tener una justificación científica poderosa.

- Aim for important results, e.g.,
  - Selecting vaccines
  - Informing public health measures (e.g. with data regarding infection & immunity)

- Specify role in development pathways

- Aim to obtain maximum scientific knowledge per individual challenged
2 Risk-benefit assessment / Evaluación de riesgos y posibles beneficios

It must be reasonable to expect that the potential benefits outweigh risks

Debe ser razonable prever que los posibles beneficios de los estudios de exposición al SARS-CoV-2 superen los riesgos.

- Especially systematic assessment

- Where possible, benefits and risks should be:
  - Inclusive of benefits & risks to participants, third parties, and society in general
  - Quantified
  - Compared with alternative study designs

- Risks should be minimized, expected benefits should be maximized
The research should be informed by engagement with the public, relevant experts, and policy-makers.

Los programas deben basarse en consultas e involucramiento del público, así como de los expertos y los responsables de formular políticas pertinentes.

- **Consultation**
  - Ensure ethical criteria met
  - Ensure research designs optimised in light of expert consensus and public engagement

- **Public engagement**
  - Assess local acceptability & respond to concerns
  - Maximize transparency
  - Understand the potential impact of the research
4 Co-ordination / Coordinación

Co-ordination should involve researchers, funders, policy-makers, and regulators

Debe haber una estrecha coordinación entre investigadores, financiadores, responsables de formular políticas y reguladores.

- Situate studies within coherent international programmes of research
- Aim to maximize public health benefits, safety, efficiency
- Must be pre-registered, ideally standardized (insofar as possible)
- Appropriate co-ordination with local public health response
5 Site selection / Selección de los centros

*Site selection should ensure the highest scientific, clinical and ethical standards*

*Deben realizarse en lugares donde la investigación pueda llevarse a cabo de acuerdo con los estándares científicos, clínicos y éticos más rigurosos.*

- Initial SARS-CoV-2 challenge studies only in experienced centres
- Ideally centres with community engagement capacity
- Consideration of local conditions
  - Background risk
  - Disruption of public health response (e.g., clinicians & PPE diverted to challenge study research)
Participant selection criteria should limit and minimize risk

Deben asegurarse de que los criterios para la selección de participantes en estudios de exposición al SARS-CoV-2 limiten y minimicen el riesgo.

- Selection should aim to make participation as safe as possible
- Initial studies limited to young healthy adults 18-30 years
- Other considerations
  - Exclusion of vulnerable individuals
  - Background risk
  - Generalisability of results
Review by a specialized independent committee

deben ser revisados por un comité independiente especializado.

- In addition to or in conjunction with standard local ethics review

- Review procedures:
  - High levels of expertise
  - Rapid, without compromising stringency
  - Ideally at the national or international level

- Ongoing consultation between investigators and ethics committee(s)
Rigorous informed consent

deben siempre contar con un proceso riguroso de consentimiento informado.

- Designed to ensure information understood
- Incorporate tests of understanding
- Include best available data on risks and uncertainties
- There should be “virtually no doubt that participants comprehensively understand the potential risks of participation and that consent is voluntary”
Conclusion 1: Impact of Key Criteria

- Set timely standards for challenge studies (May 2020)
- Influenced development of WHO technical report*
- All 8 requirements incorporated in challenge study designs
- Co-ordination requirement aligned with other pandemic research norms (e.g. SOLIDARITY)
- Widely cited in ethical and scientific debates

*See Levine et al., CID 2020, DOI: 10.1093/cid/ciaa1290
## Conclusion 2: Progress in meeting Criteria

1. Scientific justification - Plausibly strong
2. Risk-benefit assessment - Plausibly favourable
3. Consultation & engagement - Commenced
4. Coordination - Commenced
5. Site selection - Commenced
6. Participant selection - As per Key Criteria
7. Expert review - Commenced
8. Informed consent - As per Key Criteria
Thank you!

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