Third Human Challenge Trial Meeting

February 6-7, 2020

Pembroke College, Oxford, United Kingdom

Summary of the meeting:
The third Human Challenge Trial Meeting brought together a broad range of international stakeholders, including academia, regulators, funders and industry, with a considerable delegation from Low- and Middle-Income Countries (LMIC).
Controlled human infection models (CHIMs) can be helpful to study pathogenesis and for the development of vaccines (or anti-infective drugs). In CHIMs, challenge agents are used to infect healthy volunteers. Therefore, ethical considerations include that the challenge studies need to be safe and results should be meaningful, e.g. contribute to better cure, or at least better understanding of the disease.
While everyone agreed on ethics for CHIMs in the adult population, no consensus was reached on the performance of CHIMs in children. If alternatives are available, CHIMs on children should not be done. However, some participants felt that situations were conceivable under which CHIMs on children would be deemed acceptable, for example through the use of attenuated vaccine strains.
The meeting provided the state-of-the-art on a wide range of CHIMs, including viral, bacterial and parasitic challenge agents.

Recommendations:

- There is a great and widely felt need for globally aligned guidance documents for CHIM studies, preferably endorsed by regional/global organizations, such as AVAREF and/or WHO. The development of these guidance documents should be a priority.
- There was a strongly presented view that challenge studies should not be classed as different from other clinical development studies, indeed the risks are more likely to be foreseeable than in the case of phase I studies of novel drugs. Thus, it seems appropriate to use existing ethical and regulatory guidance with emphasis adapted for challenge agents.
- Further discussion is needed to specify the definition of a CHIM, based on the challenge agent used: a wild-type organism; a genetically modified organism (e.g. dengue); or an attenuated live vaccine (e.g. rotavirus oral vaccine)
- Standardization of methodology and study endpoints will make it easier to compare study outcomes and perhaps perform meta-analyses.
- CHIM studies performed in naïve participants from High-Income Countries may be less relevant as a model for non-naïve/pre-immune participants in endemic LMIC, but for many diseases, non-immune adults may be present in the LMIC communities (e.g. in malaria free cities), who may be more representative of the target age group. However, CHIM for immune/semi-immune individuals will have to be performed in LMIC adults. Hence, there is a need for capacity building in these countries, in performance as well as regulation of the studies.
- As compensation for participation in CHIM studies may be perceived as undue inducement (reducing appropriate judgement of risks), compensation needs to be considered carefully. It should be related to local wages (i.e. accepted values for the

minimum wage). There was a robust discussion of the need to consider appropriateness of additional compensation for actual harm.

- To be able to perform CHIM studies, prepare well in advance. Strong engagement is needed, and trust takes time to build.