



CHIM trials

Regulatory gaps to be filled,

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CHIM

Definition:

Controlled human infection models: A CHIM could accelerate the development of vaccines and therapies by these models (CHIMs), enabling faster, more accurate insights into their safety and effectiveness.

By executing controlled human infection models, a cutting-edge research approach that enables the evaluation of new vaccines, antiviral treatments, and monoclonal antibodies in a controlled environment. In a controlled human infections study, healthy volunteers are carefully inoculated with a challenge strain which has been produced according to Good Manufacturing Practice (GMP) standards. This controlled exposure allows for the study of immune responses and the efficacy of therapeutic interventions in real-time.

CHIM

Type's:

Controlled human infection models 1:

- CTR* for testing a CHIModel, without testing a new chemical entity, there is no IND** application and an EC***-approval is required, but no official NRA approval is needed.

Controlled human infection models 2:

- CTR to test an IND in a “Proof of Concept” (PoC) situation
- A lot of requirements:
 - GMP/GLP/GCP
 - Can the challenge strain be produced GMP-wise?
 - ✓ Yes, if we talk about a COVID virus, no if we talk about a schistosomiasis parasite (as they are cultured in snakes)

CHIM

The issue of the CMC of the challenge strain has been discussed @ a IABS/PEI/Wellcome Trust (WT) meeting and resulted in a few documents:

- **Meeting report:** <https://doi.org/10.1016/j.biologicals.2020.04.005>
- **WT invested in a writing of a white paper on challenge strain quality:**
 - On WT the document is not consultable
 - It is on: <https://repository.sciensano.be/bitstreams/a88e332e-4c81-4f62-8983-3299f952aad3/download>
- **However, an official EU document is not available on this matter**

CHIM

Several articles contest the lack of regulatory harmony on this matter. However, at a regulatory IABS meeting in Kenya (Mombasa)* on this matter there was consensus that a large guidance document for all different CHIM trials (flu, COVID, malaria, dengue, schistosomiasis, hookworm, salmonella, pertussis, ROTA...) is not feasible... A CMC file for COVID can not be compared with a schistosomiasis parasite file

The advice at that meeting was rather straight forward:

- Seek advice at the NRA before submitting the CTA
- Discuss with the NRA the GMP issues
- Decisions will be taken on a case-by-case basis

* Report of this meeting: <https://doi.org/10.1016/j.biologicals.2024.101745>

CHIM

- **Decisions will be taken on a case-by-case basis**

Elements for this discussion:

- **GMP production of challenge strain**
 - Possible or not
 - GMP documentation
 - Facility inspection
- **CHIModel itself**
 - Complexity of the model
 - Outcome discussion viral versus clinical parameters
 - B/R equation on how big can the placebo group be?

CHIM

- CHIM trials are not part of the current EU revision of the pharmaceutical directive, that will become a pharmaceutical legislation (PL):
 - CTR is not included in the revision
 - CHIM is not part of CTR legislation and neither of (PL)
 - Thus, CHIM stays in a grey zone: the case-by-case principle

Conclusion:

- Case-by-case approach disputable?
- General CMC guidance might be possible on central EU level
reference is made to WT white paper.

**Thank for your attention,
Questions?**