Ministry of Health, Environment & Sustainability
Cayman Islands Government

APPRAISAL OF CLINICAL TRIAL APPLICATIONS IN THE CAYMAN ISLANDS.

Background

1. Currently, clinical practitioners in the Cayman Islands may undertake research only with the explicit permission of the Health Practice Commission (HPC)[1].

2. The granting of such permission is not trivial given that, by definition, the effectiveness and safety of a medicine or procedure that is the subject of such a trial does not have well-established safety and, or, outcome data (otherwise a trial would be unnecessary).

3. The following advisory note is based around UK clinical trials practice adapted from the resources developed by the National Institute for Health and Care Research at: https://www.ct-toolkit.ac.uk/routemap

Best practice

4. Ideally, in a constituency that has access to a well-resourced research infrastructure, the best practice for granting of permission to conduct a clinical trial ordinarily requires several steps to be undertaken by the regulator including, but not restricted to:

    i. Peer review of the trial protocol, usually by a group of independent experts, preferably including appropriate clinicians, scientists, and statisticians;

    ii. Ethical review, usually undertaken by a standing research ethics committee. This is separate to the peer review process, which must be independent from the research team proposing the clinical trial. The ethical elements examined usually include analysis of the importance of the research, how the recruitment of trial subjects is conducted (including standards of information given to patients and the process for obtaining informed consent), and the qualification and experience of the trial team. Ethical review should also consider potential risks or benefits to the subjects, as well as data governance and protection;

    Ethical review will not usually be undertaken until the proposed trial protocol has passed peer review process.

    iii. Special technique reviews are sometimes also required where other controlled processes are involved in providing the clinical care, or more particularly evaluating endpoints in any way that would not ordinarily be required in that patient's care; for example an increased exposure to ionising radiation.

[1] S9(1) of the Health Practice Law (2021)

5. The regulator also needs to ensure that there is appropriate indemnity/insurance in place to protect the interests of the trial subjects.

6. However, the duties of the regulator are not discharged at this point, and there is an ongoing requirement that they maintain supervision of the trial to ensure that the welfare of the trial subjects is protected.

7. The regulator should, therefore, also set out any special conditions for the trial which should always include the requirement for the trial organisers to immediately report any serious unexpected side effects or complications.

8. The permission to conduct a clinical trial must contain an explicit direction that the agreement is conditional on the ongoing safety and good conduct of the trial and that the permission to conduct the trial may be withdrawn at any time should the regulator have concerns.

9. Permission to undertake a trial should contain a conditional clause to allow regulators to review studies once they are underway. Such reviews may include an examination of trial documentation to ensure agreed protocols are being followed, records are appropriately maintained and stored, and adverse effects are being reported.

10. At the end of the trial the regulator must receive a copy of the trial findings and results in order to satisfy itself that the trial was conducted appropriately, and safely.

11. It is expected that all trials will result in the submission of an academic publication to an appropriate peer-reviewed journal regardless of whether the outcomes are positive or negative.

12. Failure to observe trial protocols, support the oversight of the regulator, or submit results for publication will be a significant issue in evaluating any subsequent application to conduct any other clinical trial.

Granting and oversight of research in the Cayman Islands

13. In practice, the Cayman Islands does not have an established clinical research oversight infrastructure. Nor does it have a well-resourced academic community that could offer a base from which to develop such expertise. Nevertheless, the law permits registered healthcare providers to seek permission to undertake clinical trials, which must be given due consideration, within the available local resources. We are not permitted to refuse applications simply on the grounds of lack of resource or competency.

14. The granting of a licence to undertake clinical research places a significant responsibility on the granting authority, whose remit is to ensure the protection of the trial subjects. The granting authority must diligently ensure that they have taken all reasonable steps to reassure themselves that the trial is necessary, safe, and well designed.

15. It should be borne in mind that a licence to undertake clinical research is an exception to the ordinary practice of medicine. The granting authority should, therefore, be fully convinced of the need for the research to take place, that it is safe, and that it can be undertaken appropriately within the ability of the local health care services to support any misadventure. Otherwise, the default position of the granting authority should be to refuse to grant a licence for that research.

16. Therefore, the review of applications must be subject to tests which can be applied in an objective manner, using local resources, and which cover all the principal areas of concern.

17. As the primary aim of these tests is protecting patients, the suggested minimum standard for each of these elements is based on a principle of providing a high level of protection for trial subjects.

18. It is important to note that this framework cannot replace a full ethics-based review system, but is a modified and systematised way of giving the best degree of protection that we can offer in absence of a suitable local academic and ethics support network.

Application of these standards

19. Where the granting authority seeks advice on applications to undertake clinical trials from the Chief Medical Officer (CMO) the CMO will use the following standards to guide their advice.

20. Where the granting authority seeks advice from any other body, or persons, the granting authority should make that body, or persons, aware of these standards and ask them to justify any divergence from them when giving advice to the granting authority.

21. These standards should not be seen as comprehensive, and where an application for research needs, on its own merits, to have additional consideration made, in order to justify that it is a necessary, safe, and well-designed trial proposal, then appropriate additional tests and requirements must be made of the researcher sponsors in addition to the core elements set out in this document.

Phase 1 trials

22. Phase 1 trials[2] of medicines or procedures not previously tested in humans, are designed to be the first test of the safety of a new treatment and are, therefore, by their very nature ones where the safety profile of that medicine, or treatment, is uncertain. Internationally such trials are often only undertaken within very specialised, dedicated, research health care settings that are expert in monitoring and managing unexpected events.

[2] Phase 1-4 trials definitions are contained in *Appendix: Notes on the classification of types of trial*

23. No such infrastructure exists in the Cayman Islands, therefore, it is not foreseeable that phase 1 trials can be safely undertaken in the Cayman Islands.

Phase 2/3/4 trials

24. Phase 2 trials hold some of the risk of phase 1 trials and ordinarily may not be permitted unless there is exceptional evidence of safety from well-constructed and convincing phase 1 trial evidence.

25. Phase 3/4 trials are more likely to be acceptable given the overall clinical resource of the Cayman Islands to support unexpected misadventure.

Is there evidence to support the therapeutic intervention as being potentially beneficial

26. It is not appropriate for any trial to be given permission to proceed unless there is a clear unbiased review of peer reviewed literature supporting the biological plausibility of the intervention, and prior early trial evidence of therapeutic effect (phase 1/2 trial data).

27. It is the responsibility of the researchers to develop and present such evidence, not the HPC or CIG officials.

Is there evidence that the therapeutic intervention is likely to provide a positive benefit, or be not inferior to, an established care modality

28. This should come from a prior phase 2/3 trial.

29. It is the responsibility of the researchers to develop and present such evidence, not the HPC or CIG officials.

Is there evidence that the likely side-effect profile is tolerable and that there is a therapeutic rescue option available.

30. This should come from a prior phase 2/3 trial.

31. It is the responsibility of the researchers to develop and present such evidence, not the HPC or CIG officials.

Clear endpoints

32. The trial design should be based upon *a priori* assessments of definable beneficial clinical success using established metrics, for example, pain scales, disability scales, and indications of normalisation of physiological markers.

33. The trial design must also include definitions of serious adverse event(s), how they are recognised and reported, and the mechanism by which trials are suspended, or terminated in a timely way.

34. It is the responsibility of the researchers, not the HPC or CIG officials, to present evidence that the proposed endpoints are robust, are recognised as being well validated, correlate to the proposed purposes of the trial, and are discriminatory such that they can give evidence of clinical utility.

Statistical design and oversight

35. All trials should include a power calculation based on the capability of demonstrating statistically significant and clinically important outcomes.

36. Trials should preferably include control groups, however, other comparators of outcome can be acceptable. Trials of proof of concept without comparator groups may be acceptable for adaptations of, or real-world introduction of new, but already evidenced interventions.

37. Statistician oversight, especially to determine need for early abandonment of a trial due to either clear benefit, or clear disbenefit, is essential.

Consent

38. All trial subjects must give informed written consent to being included in the trial.

39. Best practice is that written trial documentation is given to all potential trial participants that sets out in clear language the purpose of the trial, who is undertaking and funding the trial, the potential risks to trial participants, and how any untoward events will be handled, including the insurance cover that has been obtained to support them in the case of misadventure.

40. Trial documentation must make it clear that participants have the right to withdraw from the trial, without necessity of giving reason, and at no financial penalty to themselves.

41. Trials should clearly state the inclusion and exclusion criteria for the study participants.

42. Trials will not normally be permitted that include the following classes of people:

- People who lack the capacity to give informed consent of any age
- Children under 16-years of age
- Pregnant women
- Prisoners

Data protection and governance

43. The application must refer to the extant law and best practices for data protection and governance in the Cayman Islands and demonstrate how the eight principles of the Data Protection Law are being met by the researchers.

Skills of the researchers

44. The development of the research proposal and oversight of the study, ought only to be undertaken by people who can evidence, from their CVs, skills in initiating and supervising clinical research.

45. The staff delivering the care must demonstrate that they have the qualifications and skills to undertake the proposed interventions, including training in recognising and responding to foreseeable side-effects/complications.

46. The trial protocol ought to identify the individuals fulfilling, as a minimum, the roles of chief investigator and data controller.

47. The chief investigator and other key members of the research team ought to be able to demonstrate that they have been trained in Good Clinical Practice[3] (GCP) for clinical trials.

48. It is the responsibility of the researchers, not the HPC or CIG officials, to present evidence on these issues.

Support from other clinical providers

49. The researchers must document that they have made other clinical providers aware, who may be needed to support the response to any untoward outcomes/side-effects/complications of the research trial, and give evidence that these providers are content to provide such support if needed.

Declaration of interest

50. All parties to the research (host clinical providers, and allied clinicians, as well as all the principal researchers) must make a declaration of any potential conflicts of interest, including sponsorship from the pharmaceutical industry, device manufacturers, and research granting bodies.

Non-profit

51. Participants must not be charged, in any manner or under any pretext, for their participation in a clinical trial, irrespective of the trial's outcome.

[3] Good Clinical Practice (GCP) is a set of internationally recognised ethical and scientific quality requirements that must be followed when designing, conducting, recording and reporting clinical trials that involve people.

Guidance on good clinical practice has been produced by the international conference on harmonisation of technical requirements for registration of pharmaceuticals for human use (ICH). See: https://www.ich.org

Granting extension/renewal of research permissions

52. Ordinarily there should be no renewal of permission to extend a trial beyond the agreed recruitment numbers or the agreed duration[4]. If no benefit is discernible in a trial based on a power calculation, the study has *de facto* failed to achieve its ends.

53. Extending trials that have not been able to recruit to the calculated target numbers may be acceptable if there are good logistic reasons to explain[5].

Additional considerations

54. All trials must produce a report of the findings including:

    i. a detailed statistical analysis of the outcomes;

    ii. a thorough breakdown of all untoward events/side-effects/ complications irrespective of severity;

    iii. plan for promulgation of all of these findings, including publication of negative outcomes.

55. Failure to complete studies, or provide end-of-study reports of sufficient quality, will be significantly detrimental to any applications for future research permissions, unless there are clear and reasonable explanations for such failures.

56. All clinical research applications must also contain an undertaking that the Chief Investigator will notify the HPC and the CMO immediately of any breaches of Good Clinical Practice for Clinical Trials (GCP), or the trial protocol authorisation, or any significant event, complication, or unexpected side-effect of the treatment under trial. Immediately means within 24-hours. Failure to do so may be a matter of professional malpractice reportable to the appropriate health professional council.

[4] Any application for the renewal of permission to undertake clinical research must be treated as a new application. The grant of such an application must be exceptional, with, for example, a demonstration of need that takes into account any new scientific evidence available to justify further research. The application must be judged according to the standards agreed by the HPC at the time that the HPC makes consideration of that application.

[5] An extension to enable recruitment to the calculated target numbers, must be time limited to no more than 12-months, and not subject to further extension after the grant of such an extension. The extension must also be limited to the recruitment of the numbers of cases needed to reach the original study power calculation based recruitment numbers. The application must be judged according to the standards agreed by the HPC at the time that the HPC makes consideration of that application.

Inability to judge the benefit, utility, or safety of a trial

57. Where, despite best efforts to review an application to conduct clinical research, the reviewer cannot reassure themselves of the benefit, utility, safety, or any other reasonable matter, then they must, by default, refuse to issue a positive recommendation to the granting authority; and the granting authority must respect that and not grant permission for the clinical trial to be conducted.

58. A reasonable basis for refusing to issue a positive recommendation includes the reviewer assessing that they do not have the necessary knowledge and skills to make a reasoned judgement on an application.

59. A reasonable basis for the granting authority to refuse to grant permission to conduct a clinical trial is that they cannot obtain a review from an appropriately skilled person, or persons, resident in the Cayman Islands.

Summary

60. Granting of permission to undertake clinical research should be based upon the principle of affording patients a high level of protection.

61. A grant of permission to conduct a clinical trial is a privilege that should only exceptionally be allowed, and not a right that can be demanded.

62. The granting of permission to conduct clinical trials is not trivial and ordinarily relies upon the availability of a significant academic infrastructure to source the knowledge and expertise necessary to review such applications. As there is no ready access to such resources in the Cayman Islands it is foreseeable that the members of the granting authority (The Health Practice Commission) will need to routinely seek support to make these decisions. Any person providing such support should use the criteria set out paragraphs 22-58 above.

The Health Practice Commission of the Cayman Islands

9th January 2026

Appendix: Notes on the classification of types of trial

Clinical intervention trials are usually categorised as phase 1, 2, 3, or 4. The general meaning of these types of trials is as follows:

Phase I - trials aimed to test the safety of a new treatment

i. These trials look primarily at the potential side effects of a treatment. They usually involve only a small number of healthy volunteers. They are usually only applicable to trials of pharmacological agents.

ii. Such trials need to be undertaken in special units that can offer close clinical supervision and access to clinical care infrastructure that can treat unexpected side-effects.

iii. Phase I trials should not be undertaken in the Cayman Islands as no such specialist units exist and there is not a clinical care infrastructure capable of responding to managing complex side-effects.

Phase II - trials to test the new treatment in a clinical target group

i. These trials are usually undertaken in people who have the condition for which the treatment is designed. Their purpose is to determine that the treatment is safe and achieves some evidential effect on that condition. They may include variation of dosage to establish effective therapeutic ranges.

ii. It is unlikely that such trial would be proposed in the Cayman Islands as the science infrastructure to supervise such trials is limited.

Phase III - trials involve larger numbers of patients

i. Trials usually involve larger numbers of patients, usually randomised to receive the new treatment, or the best available current treatment, or placebo. They aim to properly define the benefits of new treatment works.

ii. It is only likely that such studies could take place in the Cayman Islands as one limb/site of a multi-centre trial.

Phase IV - trials post approval

i. Trials are conducted after a medicine or device has been approved by an appropriate regulatory authority. They are carried out to gather information on the performance of the medicine/intervention in general clinical use and have particular utility in uncovering side-effects associated with long-term use.

ii. It is only likely that such studies could take place in the Cayman Islands as one site/limb of a multi-centre trial, or as part of general pharmacovigilance.