Health and Disability Ethics Committees
Ministry of Health
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25 November 2020

Mr Christian Schwabe
ACS Auckland Clinical Studies
3 Ferncroft Street
Grafton 1010

Dear Mr Schwabe

Re:	**Ethics ref:**	**20/STH/190**
	Study title:	BP02-101: A randomized, double-blind, single-dose, 3-way, parallel-group, comparator-controlled study to evaluate the pharmacokinetics, safety, tolerability, and immunogenicity of BP02 (trastuzumab) compared to Herceptin (EU-approved and US-licensed) in healthy adult male volunteers.

I am pleased to advise that this application has been ***approved*** by the Southern Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Summary of Study

1. CuraTeQ has developed their own preparation of trastuzumab, called BP02. This study aims to show that BP02 has a high degree of similarity to Herceptin, in terms of levels of drug in the blood over time, safety and side effects, and the development of anti-drug antibodies.

Summary of resolved ethical issues

The main ethical issues considered by the Committee and addressed by the Researcher are as follows.

1. The Committee requested further clarification for what 'at-risk' for COVID-19 means in this context as the whole population is considered at risk, and that a chest-x-ray would be required if considered at risk. researcher clarified that the protocol regarding this has been provided from overseas sponsor, but local practice will be investigator discretion based on symptoms. A swab will be performed as part of usual clinical care.
2. The Committee queried if the echo is enough given the danger of administration on the heart. The researcher responded that this is the preferred tool to monitor for cardiac toxicity in this context, but the risk in healthy males in single dose is exceedingly small.

Summary of outstanding ethical issues

The Committee requested the following changes to the Participant Information Sheet and Consent Form:

3. In addition to hepatitis B etc, COVID-19 is also notifiable to the Medical Officer of Health.
4. Risks of BP02 section: some risks do not have % reported e.g. anaemia = very common (>10%), neutropaenia = very common (>10%), cardiomyopathy = common (1-10%) – please add, as this is known with Herceptin e.g. https://medsafe.govt.nz/profs/Datasheet/h/Herceptininf.pdf
5. Please clarify if there is additional reimbursement (to the $3700) for the 6, 9 and 12 month post-dose extra tests, or if reimbursement be only for travel.
6. Please include information about how many participants have had BP02.
7. Please include a lay-title.
8. Please highlight that this is a single dose only.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Southern Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at *any* locality in New Zealand, it must be registered in a clinical trials registry. This should be a WHO-approved registry (such as the Australia New Zealand Clinical Trials Registry, www.anzctr.org.au) or https://clinicaltrials.gov/.

3. Before the study commences at *each given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

Non-standard conditions:

- please update the Participant Information Sheet and Consent Form, taking into account the suggestions made by the Committee.

Non-standard conditions must be completed before commencing your study, however, they do not need to be submitted to or reviewed by HDEC.

If you would like an acknowledgement of completion of your non-standard conditions you may submit a post approval form amendment through Online Forms. Please clearly identify in the amendment form that the changes relate to non-standard conditions and ensure that supporting documents (if requested) are tracked/highlighted with changes.

For information on non-standard conditions please see section 128 and 129 of the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz)

After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your next progress report is due by 24 November 2021.

As your study is an intervention study involving a new medicine, all progress reports must be accompanied by an annual safety report. While there is no prescribed format for annual safety reports, they must be no longer than two pages in length, written in lay language, and include a brief description and analysis of:

- new and relevant findings that may have a significant impact on the safety of participants
- the safety profile of the new medicine and its implications for participants, taking into account all safety data as well as the results of any relevant non-clinical studies
- the implications of safety data to the risk-benefit ratio for the intervention study, and whether study documentation has been or will be updated
- any measures taken or proposed to minimise risks. (Where such a proposed measure would be a substantial amendment, it must be submitted for HDEC review in the normal way)

For the avoidance of doubt, Development Safety Update Reports (DSURs) may serve as annual safety reports to HDECs provided that they contain the information outlined above. These summaries should usually be accompanied by comment from the New Zealand CI of the study.

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* paragraphs 206 - 208 for further information.

Participant access to ACC

This clinical trial is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Section 32 of the Accident Compensation Act 2001 provides that participants injured as a result of treatment received as part of this trial will **not** be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Mrs Helen Walker
Chairperson
Southern Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted

Document	*Version*	*Date*
CV for CI: 1. Christian Schwabe Curriculum Vitae	NA	18 September 2018
Evidence of CI indemnity	NA	11 December 2019
Evidence of scientific review: 3. BP02-101 SCOTT Review Confirmation Letter	NA	20 October 2020
Evidence of sponsor insurance	NA	20 October 2020
Investigator's Brochure: 5. BP02 Investigator's Brochure	2	05 October 2020
6. BP02-101 Data and Tissue Management Guide	1.0	27 October 2020
8. Generic Participant Card ACS	3	16 May 2018
9. Generic SMS Reminder Exemplar ACS	1	08 May 2017
PIS/CF: 10. BP02-101 PISCF	1.0	27 October 2020
Protocol: 11. BP02-101 Protocol	Original	22 October 2020
7. BP02-101 Advertising Exemplars ACS	1	27 October 2020
Application		28 October 2020

Appendix B
Statement of compliance and list of members

Statement of compliance

The Southern Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008713) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*	*Present on 10/11/2020?*	*Declaration of interest?*
Mrs Helen Walker	Lay (consumer/community perspectives)	19/08/2020	19/08/2021	Yes	No
Dr Pauline Boyles	Lay (consumer/community perspectives)	05/07/2019	05/07/2022	Yes	No
Dr Paul Chin	Non-lay (intervention studies)	27/10/2018	27/10/2021	Yes	No
Mr Dominic Fitchett	Lay (the law)	05/07/2019	05/07/2022	Yes	No
Dr Sarah Gunningham	Lay (other)	05/07/2016	05/07/2022	Yes	No
Assc Prof Mira Harrison-Woolrych	Non-lay (intervention studies)	28/06/2019	28/06/2020	Yes	No
Professor Jean Hay-Smith	Non-lay (health/disability service provision)	31/10/2018	31/10/2021	No	No
Dr Devonie Waaka	Non-lay (intervention studies)	18/07/2016	18/07/2019	Yes	Yes

Unless members resign, vacate or are removed from their office, every member of HDEC shall continue in office until their successor comes into office (HDEC Terms of Reference)

http://www.ethics.health.govt.nz