EXTRACT from

MINUTES OF MEETING
Held at 4.00pm on 23 January 2006
in the Post Graduate Centre
Central Middlesex Hospital

06.06 Applications for Review: New.

06/Q0408/8 – A PHASE-I, SINGLE-CENTRE, DOUBLE-BLIND, RANDOMISED, PLACEBO-CONTROLLED, SINGLE ESCALATING-DOSE STUDY TO ASSESS THE SAFETY, PHARMACOKINETICS, PHARMACODYNAMICS AND IMMUNOGENICITY OF TGN1412 ADMINISTERED INTRAVENOUSLY TO HEALTHY VOLUNTEERS.

Investigator: [redacted]

Wing May Kong summarised the study for the committee.

The committee reviewed the following documents.

Document	*Version*	*Date*
Application		04 January 2006
Investigator CV		22 December 2005
Protocol TGN1412-HV	2.0	21 December 2005
Covering Letter		04 January 2006
Compensation Arrangements PAREXEL-Insurance policy		01 November 2005
GP/Consultant Information Sheets	03	08 February 2005
Participant Information Sheet	01	23 December 2005
Participant Consent Form	01	23 December 2005
Investigator's Brochure TGN1412	1.1	19 December 2005
Request Form for authorisation from MHRA		
Insurance cover for TeGenero AG		04 January 2006

The committee discussed the following matters.

1. The Committee commented that section A9 on the COREC Application Form was too technical and not in language comprehensible to a lay person.
2. The Committee requested clarification as to who will be doing the outpatient assessments as detailed in section A10 on the COREC Application for.
3. In section A12 of the COREC Application Form the average number of patients has not been completed.
4. The Committee requested clarification of the number of days that the study will take place.
5. The Committee requested an explanation on what the policy was for contacting the GP if PAREXEL found one of the participants suffering from a serious condition when they were screening the potential participants.
6. The Committee requested clarification as to whether the answer to question B3 was "de-identified" or "anonymous".
7. The Committee requested an explanation as to who the researchers would consult if they detected T-cell abnormalities.
8. The Committee requested clarification of any risks to participants from the study drug if they may be HIV or suffering from TB and what assurance could the investigators give for

potential participants who may be in the "window of conversion" for HIV or not suffering from TB but were carriers. Would the researchers screen for TB.

9. The Committee felt that the payment of £2K has high in comparison with other studies of a similar length of time, including stays at the unit and outpatient visits. The Committee wanted and explanation to assure it that the payment was not higher to induce recruitment. The Committee requested that the researchers submit a payment calculation.
10. The Following revisions were required on the PIS;
    - The information is too technical and needed to be simplified.
    - Please state clearly the PAREXEL is independent of Northwick Park Hospital and is not part of the hospital.
    - On page 5 of 11 the information "study drug to the unborn foetus is unknown" may make the male participants think that this only applies to the female participants. The Committee requested this to be written to clearly inform both men and women.

[redacted] and [redacted] were invited to join the meeting at 7.05 pm. The Chair explained that the researcher would be sent a letter, following the meeting, which would set out the Committee's concerns and any amendments required to the documentation. The following points were discussed at the meeting:

1. The Chair asked [redacted] for a summary of the research for the committee members. [redacted] replied that from animal experiments it was indicated that the safety of the drugs could now be assessed in humans. This is a new way of building antibodies for diseases such as leukaemia and rheumatoid arthritis by targeting T-lymphocytes in the body's immune system.
2. The Chair asked [redacted] what they would do if they found abnormal T-cells – would the sponsor assess and take care of the results to would they refer them to an expert to review them. The Chair also asked how much T-cell data would be available before dosing the participants. [redacted] responded that T-cell subsets will be analysed before the dosing.
3. The Chair informed [redacted] that on page 5 of 11 the information "study drug to the unborn foetus is unknown" may make the male participants think that this only applies to the female participants. [redacted] responded that it is Parexel's policy to recommend barrier contraception. The committee requested that this be added to the text on the PIS. [redacted] informed the committee that he would ensure that it became standard text in the PIS.
4. The Chair asked [redacted] what the procedure was if a serious illness was detected in a potential participant. [redacted] replied that in previous studies they had detected diabetes and leukaemia and they communicate the results to the participant and offer the services to help get the correct treatment. The Committee asked if they would offer a check up with an independent physician, obviously respecting confidentiality. [redacted] replied that they would at screening.
5. The Chair asked if they intended to screen for TB. [redacted] replied that it was not standard and did not think it necessary for this study. The Committee asked if the monoclonal antibody could cause a flare up of TB. [redacted] responded that there was a slight possibility that it could. [redacted] added that the majority of the volunteers tend to be South African travellers and they could add to the exclusion criteria that if they have been exposed to active TB in close family members then they may not take part. The Committee noted this point.
6. The Chair asked [redacted] if they would add HIV risk behaviour as an exclusion criterion. [redacted] replied that they carry out an HIV test at screening.
7. The Committee asked [redacted] to explain why the participation payment was higher for this study. [redacted] responded that the study was a totally novel drug and mode of action. [redacted] responded that the participation payment was higher as the follow up period was longer that usual at 3 months. In London, in comparison to other studies it has

to be worthwhile for the volunteers to join the study as 3-months is a long time to commit when most volunteers are travellers. The Chair requested a breakdown of the payment calculation. [redacted] noted this point.

8. The Chair informed [redacted] that parts of the COREC Application Form and the Participant Information Sheet were too technical and although the lay language has been addressed before the current application seems to have slipped back to more technical language. [redacted] noted this point.
9. The Committee asked [redacted] whether there was a case to have a lay title before the scientific title on the PIS. [redacted] noted this point.
10. The Chair asked [redacted] to submit to the committee a report from the immunologist along with a short CV for the immunologist. [redacted] responded that a toxicology report had been submitted as reviewed by [redacted]. The Committee asked [redacted] to access a specific clinical immunologist to review the toxicology report. [redacted] replied that they would contact [redacted] who was base at the Parexel unit in Berlin. The Committee noted. [redacted] informed the Committee that the MHRA approval was pending and would inform the Committee as soon as it was received. The Committee noted this point.

[redacted] and [redacted] left the meeting at 7.40 pm.

The Committee provisionally approved the Study subject to receiving satisfactory responses to the points of concern raised by the Committee, including revised information and consent forms (if appropriate). The Alternate Vice-Chair was given delegated authority by the Committee to approve the Study once satisfied that the Committee's queries/points had been satisfactorily answered and/or addressed in revised documentation.