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**Director: Professor J A Ledermann**

January 28, 2011

Ms Anna Bradnam  
Hertfordshire REC  
REC Office  
Victoria House  
Capital Park  
Fulbourn  
Cambridge  
CB21 5XB

Dear Ms Bradnam,

**Sponsor Name / Ref: UCL/05/134**

**EudraCT Number: 2005-003479-19**

**UK CTA Ref: 20363/0208/001**

**UK Main REC Ref: 05/Q0201/81**

**A Phase II Single Arm Study of the use of CODOX-M/IVAC with Rituximab (R-CODOX-M/IVAC) in the treatment of patients with Diffuse Large B-Cell Lymphoma (DLBCL) or Burkitt's Lymphoma (BL) of International Prognostic Index High or High – Intermediate Risk**

Please find enclosed a Notification of a Substantial Amendment detailing an urgent safety measure implemented on the above clinical trial.

The following urgent safety measures have been implemented;

- Chief Investigator was notified of the circumstances surrounding the decision of the urgent safety measure and the actions to be taken
- All relevant staff at the participating sites were notified of the urgent safety measure
- The MHRA medical assessor (Dr Israel) and the ethics committee coordinator were immediately informed by telephone of the urgent safety measure on 27<sup>th</sup> January 2011
- A new version of the protocol with the updated treatment schedule for R-CODOX-M has been sent out to sites, and should immediately supersede the current protocol being used

We have had a few sites call to clarify days to give intrathecal chemotherapy and IV vincristine. Though the protocol states that the National guidance for intrathecal chemotherapy should be followed at all times, the treatment schedule showed intrathecal drug to be given on the same day, day 1, as IV vincristine in the R-CODOX-M cycle.

To make it clear to sites that Vincristine should not be given on the same day as any intrathecal drug and also to make the treatment schedule table itself reflect these guidelines, it was decided to update the table. This was implemented on the 27<sup>th</sup> of January 2011.

Yours sincerely

Toyin Adedayo

*Clinical Trial Coordinator*

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Enclosed:

Substantial Amendment form - 28.01.2011  
List of detailed changes made to Protocol 7.0 -28.01.2011  
Protocol v7.1 - 25.01.2011 (tracked & untracked)

cc – MHRA