Cancer Research UK & UCL Cancer Trials Centre
University College London
Haematology Trials
90 Tottenham Court Road
London W1T 4TJ
Tel: +44 (0)20 7679 9538
Fax: +44 (0)20 7679 9861
E-mail: r-codox-mivac@ctc.ucl.ac.uk
Website: www.ctc.ucl.ac.uk

Director: Professor J A Ledermann

09 June 2011

Information Processing Unit
Area 6
Medicines and Healthcare products Regulatory Agency
151 Buckingham Palace Road
Victoria, London
SW1W 9SZ

Dear Sir/Madam,

Re: R-CODOX-M/IVAC Trial: 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

EudraCT Number: 2005-003479-19
Sponsor Name / Ref: UCL/05/134
REC Ref: 05/Q0201/81
Amendment No. 9.2 (IMP Labels) – 09.06.2011

Please find enclosed an application for a request for authorisation to the competent authority for a substantial amendment to the above mentioned trial.

The IMPs used in this study are Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Cytarabine, Methotrexate, Ifosfamide, Etoposide and Neulasta.

Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Cytarabine, Methotrexate, Ifosfamide and Etoposide will be taken from commercial stock for use in the trial and will not be segregated as clinical trial supply before use. Neulasta will be supplied for the trial.

We are proposing the following changes to the labelling for the IMPs.

Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Cytarabine, Methotrexate, Ifosfamide and Etoposide
We propose not to apply IMP labelling to Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Cytarabine, Methotrexate, Ifosfamide and Etoposide given as IV, as we believe their use falls under the

remit of Regulation 46(2) of the Medicines for Human Use (Clinical Trials) Regulations, for the following reasons:
1) The IMPs are marketed products, used broadly within their authorisations (i.e. cancer).

2) The IMPs will be dispensed to subjects in accordance with a prescription given by an authorised health care professional

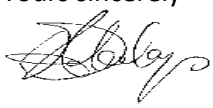
3) The IMPs will be labelled in accordance with the requirements of Schedule 5 to the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 that apply in relation to dispensed relevant medicinal products

Neulasta
We propose to change the labels for Neulasta that was submitted as a substantial amendment for this Clinical Trial on 17 September 2007, which was subsequently issued with a notice of acceptance on 10 October 2007.

Neulasta is given as IV and is supplied from Amgen Ltd. as commercial stock. It will be labelled on receipt at pharmacy to designate its use for the trial. The Neulasta labels have been amended to comply with Annex 13 requirements and the amended label wording is attached.

If you have any questions, please do not hesitate to contact me.

Yours sincerely



Toyin Adedayo

Clinical Trial Coordinator

On CD: 2005-003479-19 Reg 46 labellling exemption cover letter – 09.06.2011
2005-003479-19 Amendment 9.2 (IMP Labels) substantial amendment form - 09.06.2011
2005-003479-19 Neulasta label v2.0 RA submission form – 08.06.2011