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Centre Director: Dr J A Ledermann

Tuesday 28th August 2007

MHRA
Clinical Trials Unit
Market Towers
1 Nine Elms Lane
London
SW8 5NQ

Dear MHRA,

RE: Trial Name: R-CODOX-M/IVAC
Eudract Number: 2005-003479-19
MHRA Reference: 20363/0208/001-0001
Annex 2 Form Amendment 4.0

Please find enclosed, copies of the following: (all documents are on cd for your information)

Annex 2, notification of amendment 4.0 28.08.2007
Protocol 01.08.2007 Version 4.0 (tracked changes), incl Patient Information Sheet, Consent Form and GP letter Version 4.0 01.08.2007.
Protocol 01.08.2007 Version 4.0 (untracked changes)
Signed Part B NRES form (for information only- MREC notified) has been completed and signed by a medical expert from Nottingham University as the initial application pre-dated this requirement.

A list of amendments made to the main protocol, are as follows:

- International Prognostic Index has replaced the Age Adjusted IPI in Appendix 1 pg44 and reference made to this has changed throughout the protocol.
- The Declaration of Helsinki has been added, appendix 11 pg 63.
- Reference to Rasburicase has been removed pg 7,9 and 13.
- Information on who will be supplying what drugs has been added to pg 13.
- Rituximab is now to be given on day 11 as opposed to day 10 set out on page 15.
- Pg 32, section on safety reporting has had additions made to it, providing more comprehensive information to sites as well as a flow diagram on assessing and notifying the Lymphoma Trials Office of events**.**
- Pg 42, a reference has been removed.
- Appendix 3, pg 47, addition of information on prophylaxis has been added.
- Patient Information Sheet, pg 51, reference to 'age adjusted' has been removed as well as reference to Rasburicase .

- Consent form part I and II, pg 57 and 58, reference to ‘age adjusted’ has been removed.
- GP letter, pg59, reference to ‘age adjusted’ has been removed.
- Pg 62, contact details have changed for Cathy Burton.

Should you have any further queries, please do not hesitate to contact me at your earliest convenience.

Kindest regards,

Rachel Haley
Clinical Trial Coordinator