**Declaration of the End of Trial Form (cf. Section 4.2.1 of the *Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial*[1])**

**NOTIFICATION OF THE END OF A CLINICAL TRIAL OF A MEDICINE FOR HUMAN USE TO THE COMPETENT AUTHORITY AND THE ETHICS COMMITTEE**

*For official use*

| Date of receipt : | Competent authority registration number :<br>Ethics committee registration number: |
|---|---|

***To be filled in by the applicant***

**A MEMBER STATE IN WHICH THE DECLARATION IS BEING MADE :**

**B TRIAL IDENTIFICATION**

**B.1 EudraCT number :** **(2007-000379-41)**
**B.2 Sponsor's protocol code number:** **(..)**
**B.3 Full title of the trial :** **Liverpool Avastin Dose Response and Retreatment Study (Ladder Study) A new treatment for wet age related macular degeneration**

**C APPLICANT IDENTIFICATION** (please tick the appropriate box)

| | | |
|---|---|---|
| **C.1** | **DECLARATION FOR THE COMPETENT AUTHORITY** | ☐ |
| C.1.1 | Sponsor | ☐ |
| C.1.2 | Legal representative of the sponsor | ☐ |
| C.1.3 | Person or organisation authorised by the sponsor to make the application. | ☑ |
| C.1.4 | **Complete below:** | |
| C.1.4.1 | Organisation : **Royal Liverpool University Hospital Trust** | |
| C.1.4.2 | Name of person to contact : **Mr Heinrich Heimann** | |
| C.1.4.3 | Address : **St. Paul's Eye Unit, 2nd Floor , RLUHT, Prescot Street, Liverpool L7 8XP** | |
| C.1.4.4 | Telephone number : **0151 706 3970** | |
| C.1.4.5 | Fax number : **0151 706 5861** | |
| C.1.4.6 | E-mail **heinrich.heimann@rlbuht.nhs.uk** | |

| | | |
|---|---|---|
| **C.2** | **DECLARATION FOR THE ETHICS COMMITTEE** | ☐ |
| C.2.1 | Sponsor | ☐ |
| C.2.2 | Legal representative of the sponsor | ☐ |
| C.2.3 | Person or organisation authorised by the sponsor to make the application. | ☐ |
| C.2.4 | Investigator in charge of the application if applicable[2]: | |
| | • Co-ordinating investigator (for multicentre trial): | ☐ |
| | • Principal investigator (for single centre trial): | ☑ |
| C.2.5 | **Complete below :** | |
| C.2.5.1 | Organisation: **Royal Liverpool University Hospital Trust** | |
| C.2.5.2 | Name : **Mr Heinrich Heimann** | |
| C.2.5.3 | Address : **St. Paul's Eye Unit, 2nd Floor , RLUHT, Prescot Street, Liverpool L7 8XP** | |
| C.2.5.4 | Telephone number : **0151 706 3970** | |
| C.2.5.5 | Fax number : **0151 706 5861** | |
| C.2.5.6 | E-mail : **heinrich.heimann@rlbuht.nhs.uk** | |

**D END OF TRIAL**

| | | |
|---|---|---|
| **D.1** | **Date of the end of the complete trial in all countries concerned by the trial?** | |
| D.1.1 | (YYYY/MM/DD): 2010/11/19 | |

| | | |
|---|---|---|
| **D.2** | **Is it an early termination?**[3] | yes ☑ no ☐ |

[1] OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.
[2] According to national legislation.
[3] Cf. Section 4.2. of the detailed guidance CT-1.

D.2.1 If yes, give date (YYYY/MM/DD): 2010/11/19

D.2.2 Briefly describe in an annex (free text):

The justification for early termination of the trial: **Exudative age related macular degeneration (AMD) can now be treated with intravitreal injections of anti-VEGF agents. The recommended drug according to NICE recommendations is Lucentis (Ranibizumab), which is licensed in the UK for this treatment. Currently, this treatment is funded by local health authorities for all patients in need according to NICE guidelines, which was not the case when we initially planned this study. Avastin (Bevacizumab) is the "twin" drug of Lucentis that has been developed and licensed for the i.v. treatment of patients with colon cancer. Off-license use of Avastin demonstrated some efficacy in the treatment of exudative AMD. The proposed trial was planned to perform a dose-ranging study for this drug, which is cheaper than Lucentis, but has not been licensed for this use. Because it seems unethical to perform a trial with a drug that has not been licensed for this particular therapy whilst a licensed drug is available, we think that this trial has to be terminated.**

D.2.2.1 Number of patients still receiving treatment at time of early termination in the MS concerned by the declaration and their proposed management: **No patient has been recruited into the trial.**

D.2.2.2 The consequences of early termination for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product. **The drug is currently investigated in the UK in a large multicentre head to head trial Avastin vs. Lucentis (IVAN-trial) with Liverpool participating in this study.**

## E SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

E.1 I hereby confirm that/confirm on behalf of the sponsor that (delete which is not applicable):

- The above information given on this declaration is correct; and
- That the clinical trial summary report will be submitted within the applicable deadlines in accordance with the applicable guidance by the Commission.[4]

| E.2 | **APPLICANT TO THE COMPETENT AUTHORITY** (as stated in C.1) | ☑ |
|---|---|---|
| E.2.1 | Date : 2010/Nov/19 | |
| E.2.2 | Signature : | |
| E.2.3 | Print name: Mr Heinrich Heimann | |

| E.3 | **APPLICANT TO THE ETHICS COMMITTEE** (as stated in C.2) : | ☑ |
|---|---|---|
| E.3.1 | Date : 2010/Nov/19 | |
| E.3.2 | Signature : | |
| E.3.3 | Print name: Mr Heinrich Heimann | |

[4] Section 4.3. of the detailed guidance CT-1.

Safeguarding public health

MHRA

Dr H Heimann
ROYAL LIVERPOOL & BROADGREEN UNIVERSITY HOSPITALS NHS TRUST
PRESCOT STREET
LIVERPOOL
L7 8XP
UNITED KINGDOM

07/12/2010

Dear Dr H Heimann

**THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 S.I. 2004/1031**

| | |
|---|---|
| Our Reference: | 12155/0206/001-0003 |
| Eudract Number: | 2007-000379-41 |
| Product: | AVASTIN CONCENTRATE FOR SOLUTION FOR INFUSION 25MG/ML - 4ml vial |
| Protocol number: | RLBUHT3407 |

**ACKNOWLEDGEMENT OF END OF TRIAL**

Thank you for sending your end of trial declaration, received on 07/12/2010.

Yours sincerely,

**Submissions**
**MHRA**

PLEASE FORWARD TO
LINDA
HH 20/12/10

**Medicines and Healthcare products Regulatory Agency**
151 Buckingham Palace Road London SW1W 9SZ
T 0203 080 6000 www.mhra.gov.uk