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Medicines Health Regulation Authority
151 Buckingham Palace Road
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Dear Sir/Madam

Study Title: Can atorvastatin improve vascular function after preeclampsia? A randomised, double-blinded placebo-controlled crossover trial of atorvastatin in women with a history of preeclampsia (REC ref 10/H0604/58, EudraCT 2008-005759-21)

We are writing to inform you that we have made a decision to terminate the above study early. This is for the following reasons:

1. Primary endpoint (flow mediated dilatation): The primary objective of the study was '*to investigate whether 1 month treatment with atorvastatin (20mg/day) leads to improved conduit artery endothelial function in women 5-10 years following a pregnancy affected by preeclampsia, compared with placebo*'. This was based on previous data that suggested differences in endothelial function in women following preeclampsia [1-4]. Most of these studies were small scale and had enrolled women within the first two years after pregnancy. We have now completed the largest, current study of vascular phenotype in women 5-10 years following a pregnancy complicated by preeclampsia (Preeclampsia Vascular Study). Intriguingly, they do not demonstrate endothelial dysfunction (Lazdam, M. DPhil thesis University of Oxford). This is in itself of interest and is currently under further investigation but, critically, means our primary endpoint is no longer valid.
2. Secondary endpoints: We have reviewed our proposed secondary endpoints. Five of these are justified on the basis of variation in endothelial function being the primary measure of interest and are proposed in order to gather more detailed evaluation of vascular beds or circulating markers. The other endpoint relates to changes in lipid profile, which would be expected to alter with Atorvastatin.

Based on our observations with regard endothelial function late after preeclampsia, which negate our primary objective, we do not feel it is ethical anymore to continue recruitment of

women into this trial and therefore will terminate the trial early. We do feel it is important to make use of the data and blood samples that we have already collected and, the blood samples in particular, will be of value to develop new hypotheses to explain the long term increased cardiovascular risk of women following preeclampsia.

Yours sincerely

P Leeson