Reviewer's report

**Title:** A prospective randomised cross-over study of the effect of insulin analogues and human insulin on the frequency of severe hypoglycaemia in patients with type 1 diabetes and recurrent hypoglycaemia (the HypoAna Trial): Study rationale and design

**Version:** 1 **Date:** 31 March 2012

**Reviewer:** Dereck Hunt

**Reviewer's report:**

The manuscript describes the protocol for a randomized cross-over trial evaluating the effect of insulin analogue therapy on the frequency of severe hypoglycemia in patients with type 1 diabetes mellitus and a history of severe hypoglycemic episodes.

The paper is well written and addresses a very important, clinically relevant topic that has been under-studied to date.

The authors provide an excellent review of the literature in this area, and clearly identify the rationale for the study.

The methodology for the trial is clearly presented and is appropriate to address the stated objective. The study has been appropriately powered.

**Major Compulsory Revisions:**

- nil -

**Minor Essential Revisions:**

Page 2:
3rd last line in the “Background” paragraph, add “the” before the word “occurrence”

Page 4:
Line 5 under “Background”: add an “s” to the word “episode”
Line 6 under “Background”: change “much” to “, however, very”
Line 9 under “Background”: change “are” to “were” and change “in” to “with”
Line 14 under “Background”: change “less” to “decreased”

Page 5:
Last line: change “of” to “with”
Page 6:
Last line: change “in” to “with”

Page 8:
Line 8: change “at” to “on”

Page 12:
Line 7 under “Nocturnal hypoglycemia”: add “the” after the word “During”

Page 13:
First line under “HbA1c and plasma glucose”: change “totally” to “totaling”

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.