Reviewer's report

Title: Clinical Outcome of Preimplantation Genetic Diagnosis and Screening with the Use of Next Generation Sequencing

Version: 2
Date: 15 June 2014

Reviewer: Joris Vermeesch

Reviewer's report:

The authors went a long way in answering the reviewers comments. However, there remain two major and one extra comment they need to address.

1. In abstract: "Four embryos with false negative signals and 2 embryos with false positive signals in SNP array results were validated". This statement is wrong as it shows prejudice and should read: Following validation, four embryos were proven false negative and 2 false positive in SNP arrays. However, I still disagree with the answer provided: the qPCR is not the right method. Although the qPCR corroborates the sequencing results, it is no proof. Polymorphic marker analysis would proof that only maternal or only a paternal allele is present, rather than it being a SNP array artefact. Hence, either the authors perform additional work or they can be more modest in their claims: this could be removed from the abstract and the discussion could be more cautious.

2. Within the literature some confusion exists about the clinical validity of aneuploidy screening. The authors state that several reports exist of clinical practice of aneuploidy screeingin for AMA and refer to Munnué et al and Liang et al. I agree there are a lot of reports using the method, but the proof that it is clinically valid is lacking. Actually, there is no improved baby take home rate in randomized trials (for a review, see for example Harper et al., 2008, Human Reproduction; Harper and Sengupta, 2012) and randomized trials on blastocysts are lacking. Hence, the benefits of aneuploidy screening remain hypothetical and this should be stated as such.

Extra comments:

1. Table 3: In 99 couples no embryo transfer was possible because lack of euploid embryo’s. From a clinical perspective it is relevant to add this to table 3: No of couples participating, No of couples with embryos transferred.

Note to editor and authors

2. I disagree with reviewer 1 that NGS is the better wording: The sequencing is not next generation anymore but is massive parallel sequencing. The argument is circular. I would leave the choice to the authors.

Level of interest: An article of importance 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:**

see first review