Reviewer's report

Title: Two mechanisms of the enhanced antibody-dependent cellular cytotoxicity (ADCC) efficacy of non-fucosylated therapeutic antibodies in human blood

Version: 4 Date: 2 June 2008

Reviewer: Andreas Nechansky

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Regarding the revised manuscript, I have to say that I am still not convinced that this work deserves publication although, based on the changes made, I would up-grade the importance to 'interesting in the field'. If the vote is 3:1 for publication, I accept this decision because the manuscript is a nice piece of work which took a lot of effort and used cell-based methods. What I am questioning is the novelty of the work/conclusions draw.

Generally it has to be said, the authors did a good job regarding adaption of the paper to the reviewers comments. The point that within the introduction and discussion essential publications and issues (FcgPolymorphism, Assay variation) are missing/were not discussed, was handled by the authors (although the paper by preithner et al was not added). The method description and Fig.5 have been adapted and the quality of Fig.4 is ok.

The authors did not reply to comment: '... the determination of the percentage of non-fucosylated mAbs in endogenous (normally fucosylated) IgG is interesting but when looking on Figure 5 and comparing individuals 3 and 6, the percentage of non-fucosylated Fc oligosaccharide (Fig. 5c) does not correlate with cytotoxicity (Fig. 5d).’ The term 'validated' is obviously not correct (according to ICH guidelines) and requires therefore an exact definition what actually was done (was the method/assay validated?).

Language/grammar may be further improved.

Recommendation: Publish if 3 out of 4 reviewer agree to publication.