Mr Mark Taylor,
Appeals Committee Chair,
National Institute for Health and Clinical Excellence,
MidCity Place,
71 High Holborn,
London WC1V 6NA.

September 3rd 2008

Sent via email

Dear Mr Taylor,

Thank you for your letter dated 21st August 2008. We are grateful that you consider as valid the points that we raise around the BRAM model, and accepting the conclusions of this model to the exclusion of the other analyses.

We also welcome the opportunity to make further comments on our second and third appeal points. We note that you are initially minded to turn down our second appeal point, that is that the Appraisal Committee was perverse in giving insufficient consideration to the alternatives for patients failing their first anti-TNF therapy, because you consider this to be largely outside the scope of the appraisal. As we understand it, the scope of the Appraisal Committee was set by the Appeal Panel on 12th June 2007 (http://www.nice.org.uk/guidance/index.jsp?action=download&o=40342). The Appraisal Committee was asked to consider "a wider range of cost-effectiveness for standard disease modifying agents when used after anti-TNF therapy", and "a more complete examination of the minimum effectiveness that would be required of a second anti-TNF treatment for it to be marginally cost-effective." The Appeal Panel also required the Appraisal Committee, if they should still decline sequential anti-TNF, to "explain more fully its reasons for failing to recommend such treatment if there may be a reasonable possibility, on the evidence of the Committee, that the incremental cost-effectiveness ratios are within the range that it previously considered to be an effective use of NHS resources." In reaching the Final Appraisal Determination, the Appraisal Committee included rituximab as a new comparator, because it had been approved by NICE for use in patients failing their first anti-TNF. By including this new comparator, we believe it was the responsibility of the Appraisal Committee to follow the instructions given to them by the Appeal panel, and perform as complete an analysis of the available data as was expected for other comparators. The Appraisal

Committee acknowledge that rituximab is less likely to be effective in seronegative disease (4.3.20, pages 33 to 34, http://www.nice.org.uk/guidance/index.jsp?action=download&o=41284), but then fail to include this in their subsequent analyses. Having introduced rituximab as a comparator, we believe it was the responsibility of the Appraisal Committee to then scrutinise the data with as much rigour as the Appeal Panel had expected of them for other comparators, and that they have failed to do this. We believe that giving due consideration to the full range of comparators in the diverse disease subtypes, including those with seronegative disease for whom future treatment options are particularly limited, was very much within the scope that the Appraisal Panel had been given, and that this should be allowed to progress as a valid appeal point.

Our third appeal point was that the Appraisal Committee was perverse in concluding that there were significant limitations for the evidence base in this appraisal. The Appraisal Committee acknowledged in section 4.2.3 (page 17) that its Final Appraisal Determination was based in large part on the ReACT study, which in its own right was felt to be comprised of a sufficiently large sample to enable an analysis of primary (i.e. no response to their first anti-TNF) and secondary failures (i.e. reduction of initial response to their first anti-TNF), and yet no further analysis was performed on these sub-groups to be included in sensitivity analyses. We contend that the numbers of patients available to scrutinise the differential experiences of primary and secondary non-responders could have been bolstered by data from other sources (e.g. the British Society for Rheumatology Biologics Register), and that this would have enabled a cost effectiveness analysis to be performed. ARMA acknowledges that some patients may have a form of RA that is not driven by TNF, and may not respond to any version of blocking this cytokine and ARMA would not wish to see NHS resources being used in primary non-responders. However, secondary non-responders show a significant response to a second version of anti-TNF. We believe that the current FAD does not give an opportunity for these patients to have fair representation when the data is available to include this in health economic modeling, and that this is in breach of the instructions given by the Appeal Committee to give "a more complete examination of the minimum effectiveness that would be required of a second anti-TNF treatment for it to be marginally cost-effective" and to "explain more fully its reasons for failing to recommend such treatment if there may be a reasonable possibility, on the evidence of the Committee, that the incremental cost-effectiveness ratios are within the range that it previously considered to be an effective use of NHS resources." We believe that this should be allowed to progress as a valid appeal point.

We look forward to your ruling on these further comments, and hope that they will yet be included as valid appeal points.

Yours sincerely,