HEALTH TECHNOLOGY APPRAISAL: NICE Health Technology Appraisal - Assessment Report (AR) On Bevacizumab, sorafenib, sunitinib and temsirolimus for renal cell carcinoma	
TO: NICE	**FROM: NHS Quality Improvement Scotland**

Bevacizumab and Sunitinib – first line

The review has used their own model of baseline disease progression (figure 11, page 135). This is in contrast with the modelling of baseline disease progression provided by Pfizer (figure 6, page 109). The review appears to have used data from the Escudier 2007 study published in the Lancet. The control group in this study which received Interferon alpha survived for much longer than previous reports of such treatment and this is probably due to improved supportive care and second line therapy offered such patients in the form of tyrosine kinase inhibitors and Temsirolimus.

By using this estimate of baseline progression to examine whether Bevacizumab or Sunitinib should be available to the NHS for first line therapy the review group have assumed that these drugs would be available second line, therefore giving the improved survival compared with historical report in this group. As these drugs are not available on the NHS on second line therapy, this makes the calculation of cost-effectiveness invalid.

Sorafenib - second line

The data on the activity of Sorafenib versus best supportive care in second line therapy for patients with renal cancer has also been examined in an invalid manner. The trial was stopped early on the advice of the independent data monitoring committee as the activity of Sorafenib was seen to be so much better than supportive care and patients in the control arm crossed over to receive Sorafenib.

The analysis of this health economic data in this manner I think will prejudice future trials. If investigators run a trial of a highly effective drug versus supportive care and reach a stopping rule for the trial because of improvements, then they are faced with a difficult choice of either continuing recruitment in an unethical

manner in order to obtain health economic data to get the drug funded, or making the ethical decision and allowing patients in the control arm to cross over to the drug that failed to make the health economic case for the drug.

Cytoreductive nephrectomy

Two controlled clinical trials have shown an overall survival benefit for performing cytoreductive nephrectomy followed by Interferon therapy. Given the activity of Sunitinib, Bevacizumab, Sorafenib and Temsirolimus that have been demonstrated in the primary tumour, it seems likely that performing a cytoreductive nephrectomy can be avoided by using these agents. Any health economic analysis should take this into account and this does not appear to have been considered in this review.

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18 June 2008