Royal College of Physicians
Setting higher medical standards

11 St. Andrews Place
Regent's Park, London NW1 4LE

Telephone +44(0) 20 7935 1174
Textphone +44(0) 20 7486 5687
Facsimile +44(0) 20 7487 5218

www.rcplondon.ac.uk

[redacted]

Telephone extension [redacted]
Direct facsimile [redacted]

Chris Feinmann
Project Manager Single Technology Appraisals
National Institute for Health and Clinical Excellence (NICE)
Peter House
Oxford Street
Manchester
M1 5AN

19th June 2008

Dear Mr Feinmann

Re: Bevacizumab, sorafenib, sunitinib and temsirolimus for renal cell carcinoma - Assessment Report

I write to submit the joint response of the NCRI Renal Cancer Clinical Studies Group, RCP, RCR, ACP and JCCO to the above Assessment Report. We are grateful for the opportunity to comment and would like to make the following comments, which have been coordinated by [redacted], [redacted] of the Renal Cancer Clinical Studies Group:

We have received comment from several expert colleagues. There are strong reservations about the model used for producing QALY values, particularly with sunitinib. Some assumptions are incorrect – interferon has been the standard of care for metastatic RCC in the UK with marginal benefits; toxicity is different, not equivalent, to sunitinib and similar agents; patients completing treatment do continue to see the oncologist; and also the IFN curve from AVOREN is not an appropriate comparator. QALY values are difficult to interpret with short survivals and where cross-over occurs (because one arm proves obviously superior in progression free survival whilst the trial is still running). This is particularly relevant in view of the new data from the sunitinib randomised controlled trial presented at this year's American Society for Clinical Oncology (ASCO) meeting where, even with cross-over, there is borderline significant overall survival benefit for sunitinib. An analysis in which patients who crossed over or received 2nd line treatment with other agents was presented confirming a huge median overall survival benefit (increased from 14months to 28 months). This is the "purest" population in which it is possible to establish the survival benefit of sunitinib. We also note that no account has been taken of the new pricing structure for sunitinib.

The PenTAG QALY analysis inevitably penalizes uncommon tumours where existing treatments are inexpensive, and the R &D costs of developing a new drug in this scenario are the same as for common cancers but the potential returns reduced. Also, in using the AVOREN interferon data the QALY value from the analysis for first-line sunitinib is only valid if tyrosine kinase inhibitors are available second line.

We would re-emphasize that these drugs (particularly sunitinib) are considered to be a major advance in all of the countries with health services with which we like to compare ourselves, for a clinical situation (advanced renal cell cancer) where there is no other effective treatment (interferon has been used but is of marginal benefit). Many PCTs in the UK have already agreed to funding sunitinib for suitable patients. These basic facts must be taken into account and cost should not be the sole consideration in such difficult clinical circumstances. The overwhelming clinical opinion is, therefore, that sunitinib, in particular, should be approved by NICE.

I trust these comments will be of use but please get back to me if clarification is required.

Yours sincerely

[redacted]