Multiple Technology Appraisal (MTA)
Cetuximab (mono- or combination chemotherapy), bevacizumab (combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy (review of technology appraisal 150 and part-review of technology appraisal 118)

Personal statement by Professor Mohammad Ilyas (Professor of Pathology and clinical specialist in gastrointestinal pathology)

Metastatic colorectal cancer
This technology appraisal evaluates a number of new targeted therapies against currently used chemotherapies in the treatment of metastatic colorectal cancer (CRC) when first line therapy has failed. Tumour metastasis is usually the cause of death in colorectal cancer and thus, in my view, any promising new therapy should be evaluated once clinical trials have shown that it may be superior to standard therapies being used at that time.
The number of people requiring therapy for may change in the near future. Prior to the introduction of the NHS Bowel Cancer Screening Program (NHSBCSP) approximately 25% of patients with CRC presented with advanced (i.e. Stage IV) disease. Early evidence suggests that NHSBCSP is causing a dramatic shift in the stage at presentation with a marked reduction in the frequency of stage IV disease in screening detected cancers. However, the incidence of stage III (i.e. Dukes' stage C) tumours may not be altered by the NHSBCSP and since up to 70% of these may develop recurrence, it is likely that metastatic CRC will continue to represent a significant health burden.

Development of targeted therapies
The technologies being appraised are therapies targeted specifically to the Epidermal Growth Factor Receptor (Cetuximab and Panitumumab) and the Vascular Endothelial Growth Factor Receptor (Bevacizumab). In the former case the therapies are only effective if the tumours do not contain a Kras mutation and thus this requires testing of tumour prior to therapy in order to stratify patients into the appropriate groups. There may also be a better response to Bevacizumab in Kras wild type tumours although this relationship is not quite as straightforward.
Increasing numbers of specifically targeted therapies are being developed for use in the treatment of both cancer and other diseases (such as Infliximab in Crohn's disease). Targets include not only specific molecules but also specific pathways. As technologies are developing, it is becoming easier to interrogate tumours tissues to identify molecules/pathways which can be targeted and which will ultimately lead to the holy grail of bespoke therapy for each patient. The technologies being appraised here represent a step towards this goal although I wonder whether they should be considered as first line therapies.

Impact on the role of the Pathologists
Traditionally the role of the Pathologist has been to provide a diagnosis prior to surgery and to stage tumours following surgery. The technologies being appraised will have an impact on the role of Pathologists in two ways. Firstly, they will have to become involved in the delivery of the molecular diagnostic tests which are required for patient stratification. The exact role of that Pathologist in the delivery of these tests is a moot point but, as a minimum, it will involve evaluation of tumour blocks to ensure the presence of sufficient tumour material prior to testing. Far more preferable, in my opinion, would be a central role for the Pathologist as the person co-ordinating and interpreting molecular tests together with the morphology. Secondly, should treatment with these therapies be followed by surgery, then evaluation of the resection specimen may require a different approach with more attention paid to features of therapeutic intervention such as tumour regression or tumour vascularity. Some of the effects on tumours may be therapy-specific may therefore need to be interpreted accordingly.

Summary
Should the MTA of these technologies lead to approval of their use as second line agents in metastatic CRC, it will increase the choices available for treatment of a significant number of patients. It will have an impact on the role of Pathologists but, given the development of new anti-cancer therapies and the patient stratification, the role of the Pathologist is changing anyway and it is likely that Pathologists will adapt appropriately.