The additional analyses requested

As requested the economic model has been modified as follows:

1. A PFS HR of 1 has been applied for the indirect comparison of erlotinib and gefitinib
2. The PFS utility value estimated for erlotinib has been applied in both arms
3. Functionality has been added to enable the user to change the proportion of patients receiving erlotinib or gefitinib at day 60 (same proportion applied in both arms)

In order to allow the implementation of this 60 day proportion input within the model an 'IF' statement was placed in the model so that if the proportion of patients yet to cease treatment at day 30 was any lower than that inputted for day 60 the higher day 60 value would be used.

In order to remain consistent with the assumption of equivalent PFS utility values for each treatment it was additionally assumed that the incidence of Rash and Diarrhea in each arm was equivalent. The inclusion of the cost of these adverse would have minimal impact upon the results estimated as both AEs are relatively inexpensive to manage and occur at approximately the same incidence for both agents.

The proportion of patients 'activating' the gefitinib PAS and receiving erlotinib on day 60 of the model was varied in the range requested.

These results demonstrate that erlotinib is cost-effective compared to gefitinib so long as more than **91%** of patients 'activate' the gefitinib PAS (i.e. more than 91% of patients are still receiving gefitinib on day 60 of their treatment). Given the evidence currently available (summarized in the bullet points below) this appears highly likely:

- In all four of the gefitinib RCTs the proportion of patients in PFS on day 60 was above 91% (IPASS = **95%**, WJTOG = **96%**, First-SIGNAL = **92%**, NEJSG = **92%**)
- A review of EU patient case records (n=273, Kantar Health 2011) demonstrates that in EU clinical practice **99**% of patients who receive gefitinib do so for more than 60 days (**100%** in the 51 UK samples)
- This is further supported by a patient case note audit undertaken in 8 English centers which found that **97**% of patients 'activated' the gefitinib PAS (n=32) (medeConnect, 2012)
- Clinical experts in the first Committee meeting for this appraisal indicated that *'***nearly all**' patients remain on treatment beyond 60 days (a view shared by our own clinical advisors)

Table 1: Additional analyses requested in ACD

Proportion of patients receiving erlotinib or gefitinib on day 60	Gefitinib Drug Costs	Gefitinib PAS Costs	Erlotinib Drug Cost	Incremental Cost (E vs G)	Incremental QALYs (E vs G)
1	£12,200	£448	[redacted]	[redacted]	[redacted]
0.99	£12,078	£447	[redacted]	[redacted]	[redacted]
0.98	£11,956	£447	[redacted]	[redacted]	[redacted]
0.97	£11,834	£446	[redacted]	[redacted]	[redacted]
0.96	£11,712	£445	[redacted]	[redacted]	[redacted]
0.95	£11,590	£445	[redacted]	[redacted]	[redacted]
0.94	£11,468	£444	[redacted]	[redacted]	[redacted]
0.93	£11,346	£443	[redacted]	[redacted]	[redacted]
0.92	£11,224	£443	[redacted]	[redacted]	[redacted]
0.91	£11,102	£442	[redacted]	[redacted]	[redacted]
0.9	£10,980	£442	[redacted]	[redacted]	[redacted]
0.89	£10,858	£441	[redacted]	[redacted]	[redacted]
0.88	£10,736	£441	[redacted]	[redacted]	[redacted]
0.87	£10,614	£441	[redacted]	[redacted]	[redacted]
0.86	£10,492	£440	[redacted]	[redacted]	[redacted]
0.85	£10,370	£440	[redacted]	[redacted]	[redacted]
0.84	£10,248	£439	[redacted]	[redacted]	[redacted]
0.83	£10,126	£439	[redacted]	[redacted]	[redacted]
0.82	£10,004	£439	[redacted]	[redacted]	[redacted]
0.81	£9,882	£438	[redacted]	[redacted]	[redacted]
0.8	£9,760	£438	[redacted]	[redacted]	[redacted]