Comments on the ACD Received from the Public Through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I think this is a good proposal that balances clinical need and funding.
Section 2 (clinical need and practice)	
Section 3 (The technology)	good summary
Section 4 (Evidence and interpretation)	very clear
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/5/2009 9:08:00 AM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	yes
Notes	I am a member of the Shering Plough National Advisory Board I was invited to the Abbot National Advisory but at the time of the meeting was unable to attend My Unit has received a small educational grant from SP for nurse led service development and research
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	It is good that NICE has recognised the need for maintenance therapy in this Guidance, however it goes against the principle of clinician (and Patient) choice. If cost is going to be the primary argument against choice then the argument should be for local negotiation to secure best price for best practice so that both drugs are available for all indications. I am not certain how adulimumab is cheaper in maitenance as in my experience high induction doses and weekly maitenance is often necessary for clinical effect. Particularly on switching. We have no evidence to show that reverse switching from Adulibumab to

	Infliximab will be effective and I do not understand how primary failure is to be defined. The principle of the guidance is incorrect: we need choice and locally negotiated best possible cost.
Section 2 (clinical need and practice)	There is a clinical need to use biologics in a top down fashion: this is a matter of clinical judgement and will be based on expert opinion and some retrospective data. The evidence to support this will only come from longer term studies and follow up but it is well recognised that patients need to be stratified not just on severity of disease but on poor prognostic features of diesease (in the future this will be seroloically and genetically and clinically based). The opportunity to use these drugs intelligently needs to be preserved. The current emerging data on Immunosuppression is that eventually after 20 years of increased volume of use we are seeing an effect on disease progression
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	The most difficult decision for clinicians is when to stop biological therapy. Proper endoscopic and biomarker asessment is essential but few clinicians would stop drug if there was evidence of mucosal relapse and rising serum markers even in the face of a asymtomatic patient. Intuitively I think with proper predictors about 20% only would be able to stop drug.
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	6.7 the is most comprehensive and sensible of these. Robust longitudinal data would properly inform decision making for the future and NICE would do well to help leverage (and support) the formation of such a register, deferring its final advice until the regiseter data allowed a better informed opinion
Section 7 (related NICE guidance)	I have tried to submit my comments three times but have had problems with the website - this is my final attempt. You may have recieved earlier attempts already which will have been better phrased!- I have changed my email address to see if this makes a difference
Section 8 (proposed date of review of guidance)	
Date	10/5/2009 7:52:00 AM

Name	[redacted]
Role	[redacted]
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	If a young patient who has previously responded well to infilximab,a year or so later having flare up but now is adult, would you go for adalimumab or go back on infliximab?
Section 2 (clinical need and	In 2.3 regarding the pattern of crohns, there was no mention of perianal involvement as defined by Montreal classification?

practice)	
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/4/2009 8:02:00 PM

Name	[redacted]
Role	[redacted]
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	1.3 Surely if there is evidence of ongoing active disease at 12 months then, by definition, response has been lost and treatment should be stopped or switched. For maintenance decisions at 12 months the issue is whether treatment should be continued in those that have evidence of ongoing benefit (remission or partial response). The guidance needs to make this clear. Are we to stop treatment at 12 months in those who are doing well simply to see if they relapse?
Section 2 (clinical need and practice)	
Section 3 (The technology)	3.1 and elsewhere. Somtimes azathioprine, 6MP and methotrexate are referred to as immunosuppressants and sometimes as immunomodulators. This might be confusing to some readers and I would recommend that one of these terms is used consistently.
Section 4 (Evidence and interpretation)	I cannot see any recommendation about switching from infliximab to adalimumab (or vice versa) for patients who fail to respond to the first anti-TNF therapy. I understand that the evidince base is small, but can some view be taken? Patients will undoubtedly ask.
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	

Date	10/4/2009 2:36:00 PM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	England
Conflict	no
Notes	I have received unconditional research support from SP, but not for several years, in the context of ulcerative colitis and pyoderma gangrenosum, but not Crohns disease.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The ability to prescribed maintenance antiTNF therapy for CD, with NICE support, for the first time is to be welcomed. The previous restrictions were hard to justify in light of RCT data. However, the decision to use adalimumab over infliximab is impossible to justify on the basis of clinical trails. Both drugs work equally well. There have been no head-to-head comparison. Such a trial is unlikely to take place. The perception amongst my peers is that infliximab works faster than adalimumab. Consequently, it is potentially preferable to sick inpatients with Crohns disease, while adalimumab might be preferred for initiation of induction for outpatients. I would favour having the ability to use BOTH agents, the caveats the infliximab be used for induction in in patients, and adalimumab be reserved for outpatients, who will be the majority of recipients.
Section 2 (clinical need and practice)	The points are well made.
Section 3 (The technology)	The differences between infliximab and adalimumab are small. As mentioned above, infliximab appears to work faster. As a result, it ought to save the cost of bed days when given to sick inpatients. Adalimumab is ideal for initiation of induction for outpatients. The saving of inpatient bed days is likely to mean the apparent saving when prescribing adalimumab are more than offset.
Section 4 (Evidence and interpretation)	The drugs can and should be used in different ways, for in and outpatient induction which will undermine both companies Markov models.
Section 5 (implementation)	No comment
Section 6 (proposed recommendations for further research)	It is unlikely that these studies will be funded!
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/3/2009 12:29:00 PM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	Wales
Conflict	yes
Notes	These comments are submitted on behalf of the Welsh Association for Gatroenterology and Endoscopy (WAGE)representing all specialties involved with GI disorders in Wales
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Response on behalf of the Welsh Association of Gastroenterology and Endoscopy (WAGE) Oct 1st 2009 WAGE is the association representing gastroenterologists, GI endoscopy and GI specialist nurses, GI surgeons and GI pathologists and radiologists in Wales. 1) It is noted that published studies show that efficacy of Infliximab and Adalimumab are similar in severe active non-fistulizing Crohn?s disease, and in maintenance of remission. Most clinicians? experience of using the two drugs confirms that overall efficacy is similar. 2) The decision to recommend Adalimumab as the first-line choice in severe active non-fistulizing Crohn?s appears to be based entirely on costs. It is noted however that the various health economic models presented to the Appraisal Committee produce widely divergent results. These models are dependent on extrapolation from the epidemiological model of Silverstein et al, which may not be directly applicable to UK populations. There are significant gaps in the published health economic data for the two drugs. Infusion costs are included for Infliximab, but not for Adalimumab. For acute treatment with Adalimumab, it is noted that most patients will receive training and support from specialist nurses, and support costs should be included. In view of the ambiguity and contention surrounding these data, a decision to recommend one drug as first-line should not be based solely on cost. 3) Patients should be offered a choice of which anti-TNF treatment they receive, provided the difference in cost is not excessive. Clinicians therefore should be permitted to make a decision based on a) what is most convenient for the patient, b) availability of local facilities and experience, as well as c) the estimated costs of therapy (factoring in the weight of the patient). 4) Provision should be made for patients switching from Adalimumab to Infliximab (or vice versa) because of intolerance or secondary loss of response
Section 2 (clinical need and practice)	
Section 3	Although IV administration is not required for adalimumab,

(The technology)	patients require training in S-C administration, and this requires specialist nursing support. These costs should be included, at least for the initial administration with 2 visits to a specialist nurse clinic.
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/3/2009 12:06:00 PM

Name	[redacted]
Role	[redacted]
Other role	
Location	England
Conflict	no
Notes	I have accepted hospitality within ABPI guidelines from both Schering Plough and Abbott.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	
Section 2 (clinical need and practice)	
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	The committee state that the economic models presented by the pharmaceutical companies are not directly comparable. The conclusion that Adalimumab is more cost effective as maintaince therapy compared to infliximab is therefore not sound. There are other patient factors not taken into consideration by the analysis such as patient adherence with self administration of the drug is not clear. In addition there are a group of patients who are reviewed by their IBD team at the time of administration of Infliximab which is of benefit to the patient as well as reducing the utilisation of out-patient clinic appointments. A pragmatic approach of leaving the choice of agent for maintenance to the clnician in charge of the patients care would allow optimisation of the individual patients care, rather than a blanket approach of "One size fits all". [redacted] Southampton General Hospital

Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/3/2009 11:47:00 AM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	
Section 2 (clinical need and practice)	2.7 Insert the word antibiotics into the first line as a current treatment.
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/2/2009 10:16:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	I have attended advisory boards sponsored by manufacturers of both adalimumab and infliximab
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The choice of which agent is most cost effective is an individual calculation, depending on several factors including patients weight and which dose of adalimumab is selected. Induction with adalimumab 160mg, 80mg then 40mg is more effective

	than induction with 80mg and 40mg, but is moore expensive. The higher doses have been shown to have a lower rate of dose escalation subsequently.
Section 2 (clinical need and practice)	
Section 3 (The technology)	The paragraphs above deal with doses for infliximab but not adalimumab.
Section 4 (Evidence and interpretation)	I feel that the need to acheive optimal induction efficacy by using the optimal dose of adalimumab has not been factored in to the above calculations and it would substantially increase the cost of adalimumab. I am also concerned that there may be compliance issues with treatment deliviered to patients homes rather than administered at hospital.
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	Randomised trials aimed at identifying a strategy for withdrawal of anti TNF treatment in patients in remission should be performed.
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/2/2009 6:14:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	no
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I strongly reject adalimumab as first line treatment. There is far more experience and positive evidence with infliximab. In a vast group of patients there is the need to closely monitor the therapy response in the hospital setting and as I mentioned in my previously sent comments, these recommendations ignore the patients who cannot self-inject. These recommendations will only show, once again how far and delayed UK is compared with the strong evidence comming from leading european and american centres. These recommendations are onec again, not taking into account primarily patients benefit as they are supposed to do.
Section 2 (clinical need and practice)	
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	

Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/2/2009 1:41:00 PM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	England
Conflict	yes
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	1.1. There should be the option to use Adalimumab in patients with fistulaising crohns disease. Currently adalimumab is being used in patients who have failed/intolerant to Infliximab. 1.2. I do not agree with using Adalimumab as a first line treatment , as this is against what is currently happening in clinical practice. Infliximab is used as a first line biological as there is currently more evidence for its use and clinicans have more experience with this agent. Furthermore there is no evidence to say how patients will fare if there are initally started on Adalimumab and then transferred on to Infliximab (if intolerant/failed). Ultimately meaning that this is a non evidence based pratice.
Section 2 (clinical need and practice)	Corticosteroids are not a long term medical option owing to the number of side effects associated with their use. Surgery does occur in Crohns disease but again is not a long term option, as Crohns disease will always re-occur at another site in the GI tract. Patients who have multipal surgeries will be at risk of short bowel, which has significant morbibity and mortality.
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	There is no evidence to privde us with data on how patients fair once they are transferred from Infliximab to Adalimumab.
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	10/1/2009 12:37:00 PM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	England
Conflict	no
Notes	I have received Educational support from both Abbott and Scherring Plough and have sat on advisory boards for Scherring plough. I have had previous reasearch supported by NACC.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Generally I am very supportive of these recommendations but think they should be worded in such a way that should the relative costs of the two agents change there should be the option of using the cheeper alternative in those situations where either agent is licenced, there being no clear evidence of differing efficacy. This would also promote comercial competition.
Section 2 (clinical need and practice)	These drugs in my experience have revolutionized selected patients lives for the better and have got them back to tax paying employment and high quality lives. The need and practice section does not alude to seronegative arthritis other than commenting on extra intestinal manefestations which in my experience is a not uncommon cross over area with rheumatological indications for anti-tnf therapy.
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	There is a lot of support in the profession for a UK biologics registry, which if possible from an eithical and data protection point of view, i believe should be mandatory. This would support local and national audit and research.
Section 6 (proposed recommendations for further research)	Information on employment, tax income and benifit payments to patients should be collected as part of 6.5
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/30/2009 11:30:00 AM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	yes
Notes	Abbott are funding part of the work of the international IBD genetics consortium
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	This is a great improvement on the last consultation document - and NICE are to be commended for that. Im not sure of the logic of using adalimumab 1st line for all patients: it might be

	reasonable to issue this as a recommendation but not a rule - Id rather see flexibility to allow use of infliximab at clinicians discretion as 1st line (for example in patients whose adherence to medication is poor or who lead a disorganized life - who may find self-administration difficult and who benefit from the closer hospital supervision of their treatment). Further while there is a significant literature on how to manage people with severe Crohns who have lost response to infliximab (and the benefits of adalimumab in this context) there is much less data the other way round.
Section 2 (clinical need and practice)	Anti-TNF therapies should be reserved for those with severe disease - a raised CRP or endoscopic evidence of activity
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	There is a major issue as children grow up: for those who have been well maintained on infliximab it is counter-intuitive to switch them to adalimumab at some arbitrary age - much better to allow them to continue on the medication known to work for them (again with yearly review). After one year we stretch th einterval from 8 weekly to 10 weekly then 12 and 14 weekly then stop if patient remains well.
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/24/2009 7:08:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	This looks surprisingly reasonable 1.2 should include secondary failure to infliximab
Section 2 (clinical need and practice)	
Section 3 (The technology)	Adalimumab enables more care in the community. This, though, should be supported by expansion of IBD specialist nurses to liaise with the patients. Also (a small point), these days TNF-a is just called TNF
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	

Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/24/2009 4:32:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	Scotland
Conflict	no
Notes	I have previously received research support and consultation fees from Abbott and Schering-Plough.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I am very pleased that NICE now recognises the need for maintenance therapy. However, the positioning of adalimumab ahead of infliximab in this way is counter to current UK practice which has evolved over several years - the majority of UK physicians use infliximab as first-line therapy, and have developed a knowledge of the product. I do not see a logic in essentially making infliximab the second-line drug, on current evidence. If this has been done on economic grounds, I think the reasoning in this document is FLAWED as the quoted induction costs for adalimumab assumes 80/40mg not 160/80mg, and the maintenance costs overlook the fact that a very high proportion of patients need to increase dosage to 40mg weekly. There are no trial data to support infliximab after adalimumab failure - indeed all data available support adalimumab in infliximab failure. Patients need to have had an opportunity to respond to therapy with steroids and a thiopurine, before exposure to the toxicity of anti-TNF therapy, and this needs to be explicit, as previously. Whilst I strongly favour the need for trials of exit strategies, these draft recommendations for stopping treatment lack an evidence basis.
Section 2 (clinical need and practice)	
Section 3 (The technology)	Adalimumab escalation to weekly therapy is frequent in severe disease and essentally doubles costs of maintenance therapy. Trial data supports 160mg/80mg as induction regimen. Demyelination and malignancy are complications that need be discussed.
Section 4 (Evidence and interpretation)	The modelling is very confusing. I would advice equipoise is the correct approach in comparing these therapies.
Section 5	

(implementation)	
Section 6 (proposed recommendations for further research)	There is an urgent need for a trial of exit strategies - this is not attractive for the industry, but vital for doctors and patients.
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/24/2009 9:41:00 AM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	Scotland
Conflict	no
Notes	I have sat on advisory boards for both Abbott and Schering Plough in the past. Schering plough have funded a study day that we run but I do not receive a personal fund from this.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	I found the conclusions in this interim document very strange. Our experience is that many patients who receive adalimumab require dose escalation. Ho GT et al, alimentary pharmacology and therapeutics. This calls in to question the cost effectiveness analysis that I assume has caused the preference to adalimumab. There are other points to consider. 1. The edinburgh experience (one of the largest in the UK) suggests infliximab use is cheaper overall. 2. Most UK physicians are most familiar with infliximab. This confidence is important with these potentially toxic drugs. 3. The agents are of equal efficacy. 4. Prior treatment with (and failure of) steroids and immunosuppressants is mandatory before anti-TNFs are used. 5. There is no evidence base for the use of adalimumab in infliximab failures. All of the evidence is the other way round. In my opinion the first line agent should be the choice of the treating physician. The other agent used for non-response. this will not lead to escalating costs but probably to a more effective use of these. [redacted] I would entirely agree with guidance for review of the treatment plan.
Section 2 (clinical need and practice)	
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	

Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/23/2009 8:36:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Once again, for reasons completely incomprehensible, the committee has taken an absolutist approach. The first time around, everyone was to have infliximab. This time around adalimumab is the "treatment of choice". I have grave concerns about the safety of this approach. Working in a deprived area with a patient population that is perhaps less well-educated and less well-motivated than others, I would be reluctant to offer essentially unsupervised home treatment with a biological. For many of our patients, "directly-observed treatment" (that is, with infliximab) is the safer option AND, more often than not, the patients choice. People with Crohns disease severe enough to warrant treatment with a biological are often frightened by both the disease and the treatment. And, when informed of the risks associated with biological treatment, many are even more frightened and specifically ASK for the treatment that is given in hospital under direct supervision. The other patient cohort about whom I would have grave concerns about treating wtih adalimumab are those in whom compliance/concordance are major issues.
Section 2 (clinical need and practice)	
Section 3 (The technology)	The costs of infliximab can be reduced significantly if units adopt vial-sharing, as ours has done.
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8	

(proposed date of review of guidance)	
Date	9/19/2009 9:26:00 AM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	Anti TNF treatment i believe should be a decision made with the clinician and the patient. the delivery is very different as well as the time interval because of this it suits different types of people.professionals do take into account of cost in all they do. both should be available to be used jointly.
Section 2 (clinical need and practice)	the need is to have choice with both being available
Section 3 (The technology)	adalimumab is good for patients who wish to administer their own medication and have limitations with work life balance. or poor venous access. infliximab is iv and the response is normally more rapid, you also know the patient has had the medication
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/18/2009 7:21:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	The appraisal and economic analysis do not appear to have taken account of the dose escalation required for some patients. This will increase opportunity cost (weekly doses will double treatment cost) and will make the intervention less cost-effective when given as a weekly dose compared to the recommended starting dose of once every 2 weeks. Some consideration of the dose used (as in NICE appraisal of

	etanercept for RA, for example) would be helpful. Ho GT. Aliment Pharmacol Ther 2009 29:527 - 34. Reports that 30% and 55% of patients require dose escalation to weekly therapy at 1-and 2-year follow-up, respectively. Russo EA. Eur J Gastroenterol Hepatol 2009 June 12 (epub). Reports that at follow up of 8 months, 13% of patients on 40mg weekly.
Section 2 (clinical need and practice)	
Section 3 (The technology)	Not comments above about dose escalation with time.
Section 4 (Evidence and interpretation)	Note comments above about dose escalation over time which must have a bearing on cost-effectiveness (since treating weekly will double the cost of treatment) and should be accounted for in economic model.
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	9/16/2009 4:48:00 PM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	England
Conflict	
Notes	On behalf of the Gastroenterology team at St Mark's/Northwick Park and Central Middlesex Hospitals I would like the Committee to consider the following comments in response to the Appraisal Committee's preliminary recommendation for the use of biological agents in Crohn's disease: 1) The committee recommends Adalimumab as the first biological agent. There is no guidance as to the next course of action when patients either loose response or experience adverse events to Adalimumab. There is evidence from the GAIN study for patients who lost response to Infliximab given as a first line agent: the study shows that switching to Adalimumab is clinically effective. However there is no evidence for the reverse situation. The lack of evidence for using Infliximab as a second line biological agent leaves both patient and physician without a further therapeutic tool to manage the disease. 2) The decision to continue maintenance therapy only for patients who are showing a clinical response at regular review is justified considering the costs of these agents. However there statement pertaining to the 12 month limit is very ambiguous. The committee states that at 12 months 'maintenance treatment

	should only then be continued if there is clear evidence of ongoing active disease, as determined by clinical symptoms and investigation, including endoscopy if necessary'. This statement implies that only non-responders should continue maintenance therapy as only this group will exhibit features of active disease whilst on therapy. Responders to biologicals would not be expected to show signs of active disease whilst on therapy. Responders, will only develop active disease once therapy is discontinued. Patients may find stopping therapy whilst in remission unacceptable. Clinicians would be concerned about restarting therapy after a drug-free period as this may be associated with an attenutated response to biologicals and a higher risk of infusion reactions. A more appropriate evidence-based therapeutic approach would be to routinely review of clinical state at 12 months whereby responders should continue therapy and any non-responders should have the treatment stopped.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	
Section 2 (clinical need and practice)	
Section 3 (The technology)	
Section 4 (Evidence and interpretation)	
Section 5 (implementation)	
Section 6 (proposed recommendations for further research)	
Section 7 (related NICE guidance)	
Section 8 (proposed date of review of guidance)	
Date	5/10/2009