NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ustekinumab for treating active psoriatic arthritis (rapid review of technology appraisal guidance 313)

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Definitions:

Consultees – Organisations that accept an invitation to participate in the appraisal including the companies, national professional organisations, national patient organisations, the Department of Health and the Welsh Government and relevant NHS organisations in England. Consultees can make a submission and participate in the consultation on the appraisal consultation document (ACD; if produced). All non-company consultees can nominate clinical experts and/or patient experts to verbally present their personal views to the Appraisal Committee. Company consultees can also nominate clinical experts. Representatives from NHS England and clinical commissioning groups invited to participate in the appraisal may also attend the Appraisal Committee as NHS commissioning experts. All consultees have the opportunity to consider an appeal against the final recommendations, or report any factual errors, within the final appraisal determination (FAD).

Clinical and patient experts and NHS commissioning experts – The Chair of the Appraisal Committee and the NICE project team select clinical experts and patient experts from nominations by consultees and commentators. They attend the Appraisal Committee meeting as individuals to answer questions to help clarify issues about the submitted evidence and to provide their views and experiences of the technology and/or condition. Before they attend the meeting, all experts must either submit a written statement (using a template) or indicate they agree with the submission made by their nominating organisation.

Commentators – Commentators can participate in the consultation on the ACD (if produced), but NICE does not ask them to make any submission for the appraisal. Non-company commentator organisations can nominate clinical experts and patient experts to verbally present their personal views to the Appraisal Committee. Commentator organisations representing relevant comparator technology companies can also nominate clinical experts. These organisations receive the FAD and have opportunity to report any factual errors. These organisations include comparator technology companies, Healthcare Improvement Scotland any relevant National Collaborating Centre (a group commissioned by NICE to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups such as the NHS Confederation, the NHS Commercial Medicines Unit, the Scottish Medicines Consortium, the Medicines and Healthcare Products Regulatory Agency, the Department of Health, Social Services and Public Safety for Northern Ireland).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would be otherwise inappropriate.

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comments received from consultees

Consultee	Comment	Response
Janssen	We are very pleased to hear that the Appraisal Committee has recommended ustekinumab for active psoriatic arthritis (PsA) for those patients for whom a TNF-alpha inhibitor is contraindicated, and also for those who have had treatment with 1 or more TNF-alpha inhibitors. The Committee's recommendation supports Janssen's view that ustekinumab offers value-for-money to the NHS as well as being clinically valuable. We are delighted that patients living with this condition will soon have access to another treatment option beyond currently available TNF-alpha inhibitors.	Thank you for your comments.
	For those patients for whom TNF-alpha inhibitor is not suitable As stated in our patient access scheme (PAS) submission (August 2014) and also noted in the ACD, there is a considerable unmet need in patients for whom TNF-alpha inhibitors are unsuitable. Whilst contraindication to a TNF-alpha inhibitor is clearly an important factor, there are other reasons why TNF-alpha inhibitor may not be suitable for some patients with active PsA. For such patients, a more frequent dosing regimen with a TNF-alpha inhibitor may not be suitable and these patients may benefit from ustekinumab's infrequent 12 weekly regimen. Examples of such patients include: • those who are needlephobic, • those who are unable to self-inject due to arthritis in fingers, • those who have difficulties complying with a more frequent dosing regimen due to their co-morbid physical or mental condition, or due to their professional requirement (e.g. frequent travel). It must be noted that the nurse-led homecare service, provided free-of-charge to the NHS, ensures that any nervous or concerned patients can receive ustekinumab treatment safely, and supports their adherence to treatment. As far as we are aware, a similar nurse-led homecare service is not provided by manufacturers of TNF-alpha inhibitors. In summary, we believe there are a small number of patients for whom a TNF-alpha inhibitor may not strictly be contraindicated, yet is otherwise unsuitable, and thus may	Comments noted. The Committee understood that people for whom tumour necrosis factor (TNF) alpha inhibitors are contraindicated have a considerable unmet need. It noted that ustekinumab appeared to be less effective than TNF-alpha inhibitors in the TNF-alpha inhibitor-naive population, and that ustekinumab is not a cost-effective option compared with TNF-alpha inhibitors in this group (see sections 4.7 and 4.18 of the final appraisal determination [FAD]). The Committee therefore concluded that ustekinumab could be recommended for treating psoriatic arthritis in people who have not previously had TNF-alpha inhibitors, only if TNF-alpha inhibitors are contraindicated.

Consultee	Comment	Response
	benefit from having ustekinumab as a treatment option.	
	Costs associated with the implementation and operation of the PAS Paragraph 3.31 of the ACD states: "The company estimated the additional costs associated with the patient access scheme to be £33 per patient; it considered these costs irrelevant and did not include them in the economic analyses." We would like to clarify this point as the additional costs associated with the PAS are clearly relevant to the economic analyses. However, as we stated in our PAS submission, the cost (£31 per ustekinumab patient) is very small and therefore can be considered immaterial. Since incremental QALY gains for ustekinumab is 1 or above in most of the incremental analyses, the impact of the PAS-related costs on the ICER is £30 per QALY gained or below, and therefore is inconsequential to the Committee's decision-making.	Comment noted. The FAD notes that the company considered that the additional costs associated with the patient access scheme were small and would not affect the appraisal (see FAD section 3.31).
Psoriasis and Psoriatic Arthritis Alliance	Thank you for the opportunity to comment on the above appraisal consultation document. We are pleased to see that the company has reconsidered the cost of ustekinumab, so it can be made available to the NHS, therefore providing a further option of care for people with psoriatic arthritis. We also welcome the opportunity for those who weigh more than 100kg to have equal access to the drug. As an organisation, we are aware that cost-effectiveness is an important issue in these decisions and are glad to see that this revised decision, will not be to the detriment of other users of the health service.	Thank you for your comments.
Psoriasis Association	The Psoriasis Association welcomes this Rapid Review from NICE looking at Ustekinumab for active psoriatic arthritis and supports the recommendation that it should be recommended as an option for those contraindicated to TNF alpha inhibitors, or have had treatment with one or more TNF alpha inhibitor. We feel that these are sound and provide a suitable basis for guidance to the NHS, as offer a treatment option to people who may otherwise remain un-treated or on suboptimal therapies owing to them having exhausted other forms of treatments.	Thank you for your comments.
Royal College of Nursing	**Introduction** The Royal College of Nursing (RCN) was invited to review the Appraisal Consultation Document (ACD) for Ustekinumab for treating active psoriatic arthritis (Rapid Review of	Thank you for your comments.

Consultee	Comment	Response
	TA313) [ID819] Nurses caring for people with active psoriatic arthritis reviewed the documents on behalf of the RCN. **Appraisal Consultation Document – RCN Response** The Royal College of Nursing welcomes the opportunity to review this document. The RCN also supports the recommendations set out in this technology Appraisal. **Has the relevant evidence has been taken into account?** The evidence considered seems comprehensive. **Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?** We would ask that the summaries of the clinical and cost effectiveness of this appraisal should be aligned to the clinical pathway followed by patients with **active psoriatic arthritis**. The preliminary views on resource impact and implications should be in line with established standard clinical practice. **Are the provisional recommendations sound and a suitable basis for guidance to the NHS?** Nurses working in this area of health have reviewed the recommendations of the Appraisal Committee and do not have any other comments to add. The RCN would welcome guidance to the NHS on the use of this health technology. **Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?** **Are there any equality-related issues that need special consideration that are not covered in the appraisal consultation document?** We are not aware of any specific issue at this stage. We would ask that any guidance issued should show that an equality impact analysis has been considered and that the	

Consultee	Comment	Response
	guidance demonstrates an understanding of issues relating to all the protected characteristics where appropriate	

Comments received from clinical experts and patient experts

No comments received

Comments received from commentators

Commentator	Comment	Response
AbbVie	AbbVie welcomes the opportunity to comment on the Appraisal Consultation Document (ACD) prepared by the Committee for the appraisal of ustekinumab for the treatment of active psoriatic arthritis (PsA). AbbVie's detailed comments are set out under section headings containing the questions NICE asks consultees to comment on for the ACD consultation.	Thank you for your comments.
	1. Do you consider that all of the relevant evidence has been taken into account? AbbVie consider that the majority of relevant evidence has been taken into account by the Appraisal Committee in preparing provisional recommendations detailed in the ACD. However, and as presented in Abbvie's previous response to the first ACD, we emphasize that there are notable data relating to the efficacy of a second-line anti-TNF in a PsA population previously exposed to anti-TNF.	Comments noted.
	a. Clinical effectiveness of biologic therapy in an anti-TNF exposed PsA population Abbvie would like to remark the evidence presented in a RCT showing of similar response in both sub-groups anti-TNF therapy in PsA patients with and without prior anti-TNF exposure[1]. Further, results from an observational trial[2], examined the safety and efficacy of adalimumab in patients with active PsA in real-life clinical practices including patients who had been treated unsuccessfully with other anti-TNF agents, showing that patients previously exposed to anti-TNF achieved a good response with adalimumab, albeit numerically lower than biologic-naïve patients. In an open-label extension study[3] show responses to adalimumab in patients with active psoriatic arthritis who have not adequately responded to prior therapy and in another open-label study[4]	The Committee understood that there is some evidence for the effectiveness of TNF-alpha inhibitors in people who have had previous TNF-alpha inhibitor therapy (the TNF-alpha inhibitor-exposed population). However, it was aware that there was not enough evidence to compare ustekinumab and TNF-alpha inhibitors in this population. The Committee concluded that there is still uncertainty about the relative effectiveness of ustekinumab and TNF-alpha inhibitors in people who have previously had TNF-alpha inhibitors (see

Commentator	Comment	Response
	studied the effectiveness and safety of adalimumab in patients with ankylosing spondylitis or psoriatic arthritis and history of anti-tumor necrosis factor therapy patients with a prior history of anti-TNF therapy had a high response rate, similar to the population without anti-TNF exposure Further, The British Society of Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) Guideline for the treatment of PsA with biologics look at biologic switching in PsA patients, referencing a body of evidence, and state: *"Multiple open-label studies and registry data have confirmed the potential benefits of switching anti-TNF therapies in patients with PsA. There are no RCTs of sufficient quality to confirm this benefit. Studies of patients with PsA, taken from cohorts and registries of psoriasis and SpA patients, have generally shown a lower response rate to second and subsequent anti-TNF therapies when compared with a first drug, but nevertheless have shown a significant response."* [5,6,7,8,9,10,11] The second sentence relating to RCT data has since been made redundant (see above). Despite the limitations of not having head-to-head randomised controlled data comparing ustekinumab with anti-TNF therapies in a PsA population and with no formal network meta-analysis of the results presented in this section, AbbVie consider the available evidence suggests that an anti-TNF therapy in an anti-TNF exposed PsA population is likely to be more effective on arthritis symptoms than ustekinumab in the same PsA population.	section 4.8 of the FAD).
	2. Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate? AbbVie consider the summaries of clinical and cost-effectiveness from the manufacturer and the ERG to be, on the whole, reasonable interpretations of the evidence. Both manufacturer and ERG addressed several limitations of the economic model and tested it further is sensitivity analyses. However, there are still important limitations in both model structure and parameter. These limitations have been considered by the Appraisal Committee and reflected in the provisional recommendations but AbbVie would like to discuss further the following points in relation to the derivation of cost-effectiveness in the manufacturer's submission:	Comments noted.

Commentator	Comment	Response
	a. HAQ-DI progression over time in ustekinumab treated patients The Committee consider in the last ACD that the assumption of a maintained fixed improvement in HAQ-DI over time might not the most appropriate, because of the different mechanism of action of ustekinumab. Further, the Committee's acknowledgment of the differences in radiographic progression presented and the possibility of some worsening of HAQ-DI score during treatment with ustekinumab, leading to a decrease in the cost effectiveness. However, it is noted that the model assumptions were sufficient for the Committee to make a decision. AbbVie do not consider the data presented to be comparable with radiographic progression data for the licensed anti-TNFs in PsA, and therefore do not consider that the same modelling assumptions are appropriate when evaluating cost-effectiveness. Further, AbbVie do not consider this to be an appropriate assumption for the anti-IL 12/23 ustekinumab based on its different mechanism of action and on the radiographic progression results presented from PSUMMIT 1 and PSUMMIT 2 Randomized Controlled Trials (RCT's).[12] AbbVie consider it clinically plausible to assume that an increase in radiographic progression score over time in ustekinumab treated PsA patients will be associated with an increase in functional disability and therefore an increase in HAQ-DI score over time. This assumption is based on the studied relationship between HAQ-DI and radiographic progression in patients with rheumatoid arthritis (RA) investigated in several studies[13,14,15].	The Committee noted that uncertainty remains as to how well the model assumptions regarding Health Assessment Questionnaire Disability Index (HAQ-DI) scores apply to ustekinumab. It also noted that differences in radiographic progression results between studies of ustekinumab and TNF-alpha inhibitors provide some evidence to suggest care is needed when applying assumptions based on TNF-alpha inhibitors to ustekinumab. However, the Committee understood that the radiographic progression results should be interpreted with caution, and noted evidence from the PSUMMIT 1 study that did not suggest a substantial worsening of HAQ-DI over time. The Committee concluded that the assumptions in the model were a sufficient basis on which to make a decision (see sections 4.6 and 4.11 of the FAD).
	b. No PASI improvement in conventional management arm In the first economic model presented it was assumed that patients treated with conventional management do not experience any PASI improvement, i.e. there are no benefits on the skin from conventional management strategies. As PASI response rates are used within the economic model to generate health state utilities and costs in the base case analysis, AbbVie consider this assumption to overestimate the likely incremental benefits of ustekinumab compared to conventional management in PsA patients. RCT data suggest that patients in the conventional care arm can be expected to have a modest improvement in skin clearance which should be taken into consideration within the model.[16] This assumption of zero benefit of conventional management on PASI improvement is contrary to previous modelling of anti TNF therapy in PsA patients which have used the PASI response rates from placebo arms in the available trials.[17]	The Committee noted that the company's original, post-clarification and post-consultation models assumed that conventional management strategies did not affect skin symptoms, and that the model was updated in the rapid review to incorporate the effect of conventional management on skin symptoms. The ERG noted some inconsistencies in the score to which people are assumed to rebound when they stop biological treatment, but considered the modelling to be mostly reasonable. The Committee concluded that it was appropriate to include the effect of

Commentator	Comment	Response
	This assumption was corrected in the economic model, where skin symptoms from conventional therapy were added and PASI scores and response rates for conventional management was taken from the placebo arm of the mixed treatment comparison and SUMMIT 1 and 2 studies. However, the ERG highlighted the differences in PASI score between people assumed to rebound when they stop biological treatment and the average PASI score for people having conventional treatment.	conventional management on skin symptoms in the economic model (see sections 3.38 and 4.12 of the FAD).
	c. Choice of comparator in different sub-groups AbbVie consider that the appropriate comparator(s) when ustekinumab is evaluated as a biologic option in an anti-TNF exposed PsA population is other licensed and recommended anti-TNF therapies for the treatment of active PsA including adalimumab, etanercept, golimumab and infliximab. When evaluating ustekinumab in an anti-TNF exposed PsA population, AbbVie **do not** consider the incremental comparison versus conventional management to be reflective of clinical practice in the management of PsA patients in the UK based on current NICE Guidance and clinical guidelines in PsA[18]. Recommendations made in NICE TA's 199 and 220 do not preclude the use of more than one anti-TNF in PsA patients and AbbVie consider it would be routine clinical practice to offer eligible PsA patients more than one anti-TNF if appropriate. In addition, The British Society of Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) Guideline for the treatment of PsA with biologics make the following recommendations in relation to biologic switching in PsA patients: *"In the case of failure of an anti-TNF treatment either due to inefficacy or adverse events, an alternative anti-TNF therapy should be considered and response to treatment assessed as for the first anti-TNF agent."* The only scenario in which conventional management strategies would be the appropriate comparator(s) in an anti-TNF exposed population is in those patients who have had an inadequate response with anti-TNF therapies **as a class** (i.e. **all four** currently available anti-TNFs). This is likely to represent a very small patient sub-group.	The Committee considered that the most appropriate comparators in most people in the TNF-alpha inhibitor-exposed population would be TNF-alpha inhibitors (see FAD section 4.2). Conversely, it heard from the clinical experts and the patient expert that the availability of second-line TNF-alpha inhibitors varies across the UK (FAD section 4.1). Consequently, for people who have had a TNF-alpha inhibitor and for whom treatment with a subsequent TNF-alpha inhibitor is appropriate, the Committee based its decision on a sequencing analysis comprising an incremental comparison of ustekinumab, TNF-alpha inhibitors and conventional management (see FAD section 4.20). The Committee considered that in people whose condition failed to respond to TNF-alpha inhibitors as a class, conventional management was the most appropriate comparator (see FAD section 4.3). For this population, the Committee based its decision on a comparison of ustekinumab and conventional management (see FAD section 4.21).
	d. Withdrawal rates for ustekinumab patients The manufacturer's economic model assumes an annual withdrawal rate of 16.5% for ustekinumab patients in both anti-TNF naïve patients and anti-TNF exposed patients. This withdrawal rate has been used in previous anti-TNF appraisals in PsA[19] but is based on withdrawal rates for PsA patients treated with anti-TNF agents.	The Committee heard that the rate of withdrawal from ustekinumab in clinical trials was lower than that included in the model, although the long-term withdrawal rate for ustekinumab is unknown. The Committee considered that if the withdrawal rate were

Commentator	Comment	Response
	Given the different mechanism of action of an anti-IL/12 23 such as ustekinumab, AbbVie consider it would be appropriate for the manufacturer to assess the impact on cost-effectiveness of using the actual withdrawal rates observed in ustekinumab patients from PSUMMIT 1 and 2 in a series of one-way sensitivity analyses. Currently, the manufacturer has assessed the impact on the ICER of varying the assumed 16.5% annual withdrawal rate by an arbitrary +/- 25%, which may or may not reflect the range of withdrawal observed in PSUMMIT 1 and 2.	lower than 16.5%, the cost effectiveness of ustekinumab might be expected to improve by a small amount. The Committee concluded that the withdrawal rate was not a key driver of the economic model (see FAD section 4.15).
	3. Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS? AbbVie do not agree with the provisional recommendations made by the Appraisal Committee. Based on the evidence provided by the manufacturer, ustekinumab is unlikely to be a cost-effective use of NHS resources when used in the treatment of active PsA patients either as a first-line biologic option or as an option for PsA patients who have previously been exposed to anti-TNF therapy. AbbVie consider there are relevant and important differences in radiographic progression data between the classes of biologic therapies in PsA which suggest that using similar modelling assumptions over a lifetime horizon may not be appropriate. AbbVie consider that the results from the data presented do not support the link between radiographic progression and quality of life compared with TNF-alpha inhibitors. Further, results show that ustekinumab is less effective than TNF-alpha inhibitors for PASI75, PASI90 and PsARC response. Finally, the diminishing effectiveness of ustekinumab in an anti TNF-alpha treated population supports the conclusion of continuous treatment with TNF-alpha inhibitors might be a better approach for the treatment of PsA.	Comments noted.
	4. Are there any equality related issues that may need special consideration? AbbVie are not aware of any equality related issues that may need special consideration in the preliminary recommendations. **References** [1] Mease et al. ACR 2013 abstract [2] F van den Bosch et al. (2006). Adalimumab (HUMIRA®) is Effective and Safe in Treating Psoriatic Arthritis (PsA) in Real-Life Clinical Practice Preliminary Results of the STEREO Trial.	Noted.

Commentator	Comment	Response
	[3] Gladman DD et al. Responses to adalimumab in patients with active psoriatic arthritis who have not adequately responded to prior therapy: effectiveness and safety results from an open-label study. J Rheumatol 2010; 37(9): 1898–1906. [4] Effectiveness and safety of adalimumab in patients with ankylosing spondylitis or psoriatic arthritis and history of anti-tumor necrosis factor therapy. Rudwaleit M, Van den Bosch F, Kron M, Kary S, Kupper H. JournalArthritis Res Ther. 2010;12(3):R117. doi: 10.1186/ar3054. Epub 2010 Jun 16. [5] Coates LC, Cawkwell LS, Ng NW et al. Sustained response to long-term biologics and switching in psoriatic arthritis: results from real life experience. Ann Rheum Dis 2008;67:717 9. [6] Conti F, Ceccarelli F, Marocchi E et al. Switching tumour necrosis factor alpha antagonists in patients with ankylosing spondylitis and psoriatic arthritis: an observational study over a 5-year period. Ann Rheum Dis 2007;66: 1393 7. [7] Gomez-Reino JJ, Carmona L. Switching TNF antagonists in patients with chronic arthritis: an observational study of 488 patients over a four-year period. Arthritis Res Ther 2006;8:R29. [8] Mazzotta A, Esposito M, Costanzo A et al. Efficacy and safety of etanercept in psoriasis after switching from other treatments: an observational study. Am J Clin Dermatol 2009;10:319 24. [9] Papoutsaki M, Chimenti MS, Costanzo A et al. Adalimumab for severe psoriasis and psoriatic arthritis:an open-label study in 30 patients previously treated with other biologics. J Am Acad Dermatol 2007;57:269 75. [10] Spadaro A, Punzi L, Marchesoni A et al. Switching from infliximab or etanercept to adalimumab in resistant or intolerant patients with spondyloarthritis: a 4-year study. Rheumatology 2010;49:1107 11. [11] Wick MC, Ernestam S, Lindblad S et al. Adalimumab (Humira) restores clinical response in patients with secondary loss of efficacy from infliximab (Remicade) or etanercept (Enbrel): results from the STURE registry at Karolinska University Hospital. Scand J Rheumatol 2005;34:353 8. [12] Available at http://www.eurekalert.org/pub_releases/2013-10/tlcu-nsd102413.php [13] Odegard S, Landewe R, van der Heijde D, Kvien T, Mowinckel P, Uhlig T. Association of Early Radiographic Damage With Impaired Physical Function in Rheumatoid Arthritis. Arthritis & Rheumatism 2006;54(1):68-75. [14] Van der Heijde D, Landewe R, van Vollenhoven R, Fatenejad S, Klareskog L. Level of	

Commentator	Comment	Response
	radiographic damage and radiographic progression are determinants of physical trial function: a longitudinal analysis of the TEMPO trial. Annals of Rheumatic Disease 2008;67:1267-1270. [15] Van Vollenhoven, Cifaldi M, Ray S, Chen N, Weisman M. Improvement in Work Place and Household Productivity for Patients With Early Rheumatoid Arthritis Treated With Adalimumab Plus Methotrexate: Work Outcomes and Their Correlations With Clinical and Radiographic Measures From a Randomised Controlled Trial Companion Study. Arthritis & Care research 2010;62(2):226-234. [17] NICE TA199 ERG report available at http://guidance.nice.org.uk/TA199 (last accessed Jan 2014) [18] Coates et al. (2012). The 2012 BSR and BHPR guideline for the treatment of psoriatic arthritis with biologics. doi:10.1093/rheumatology/ket187 [19] Yang et al. (2012); Schering-Plough (2010); Bojke et al. (2011); Rodgers (2011).	
MSD	Thank you for giving MSD the opportunity to comment on the Appraisal Consultation Document for 'Psoriatic arthritis (active) - ustekinumab (Rapid Rev TA313) [ID819]'. MSD believes that the preliminary recommendation by the appraisal committee is appropriate given the evidence presented and has no further comments	Thank you for your comments.

Comments received from members of the public

No comments received

The following organisations stated that they had no comments on the draft guidance:

- British Association of Dermatologists
- Department of Health
- Pfizer