National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

Virtual Touch Quantification to diagnose and monitor liver fibrosis

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from KiTEC to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 4pm, **29 August 2014** using the proforma comments table below. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the assessment report.

27 August 2014

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P10 Our statement 'Earlier identification of fibrosis…'	The final point …*quote* …depends on easier access to fibrosis assessment by VTq versus the comparators.	was made on the basis that we believe that the barrier to VTq will be lower than TE (or biopsy) as VTq can be an 'add on' test to an existing procedure (diagnostic ultrasound) and will have lower cost implications.	The following edit has been made: The EAC was uncertain about the final point (*'Earlier identification of fibrosis in patients with viral hepatitis should allow earlier intervention with anti-viral drugs, which can reverse the course of early disease'*), as it is not clear why VTq should allow earlier intervention as compared to TE. However the sponsor clarified that this statement was made on the basis that they believed that access to VTq would be easier than to TE (or liver biopsy). This is primarily because VTq is an 'add on' test to an existing procedure.

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P19	Anthony Stevens		Edit made; apologies.

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Liver biopsy referred to in a number of places as the gold standard	Replace 'gold standard' with comparator. Indicate at the outset that LB is not a true 'gold standard'	We highlighted that LB had limitations and therefore is not a 'true' gold standard. This is well documented.	The sponsor states on page 15 of the submission that "Liver biopsy is considered the gold standard for assessing liver fibrosis for both hepatitis B and C." The first mention of liver biopsy as a gold standard in the EAC's submission has been edited as follows: "The sponsor refers to liver biopsy as the current gold standard (although it is acknowledged there are well documented limitations with this technique) and discusses the accuracy of elastography methods (VTq and TE) in comparison to liver biopsy."

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
P57/70/79 insufficient emphasis given to the cost of TE in low	in low patient scenarios (1000 tests per year) the cost of TE will be significantly higher.	The cost of TE is very sensitive to workload as noted by ourselves and	The EAC agrees with the sponsor that the cost of TE will be significantly higher

patient scenarios.		EAC. This was insufficiently highlighted.	in low patient scenarios (1000 tests per year). In the EAC's revised model, this was estimated to be £42.06. The EAC subjected this cost in the sensitivity analysis and found that it did not alter the cost-saving conclusions of the base-case analysis. This has been sufficiently highlighted in section 4.6. The EAC feels that no further change is required to the report.

Issue 5

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 62	Acknowledged	'seems to have acknowledged' that TE and VTq levels are equivalent. We clearly acknowledged this - page 32 EAC document. P142 submission.	This has now been amended in the report.

Issue 6

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 82 obesity and VTq technique. A sentence should be added for balance.	The clinical evidence indicates that the failure rate of TE in obese patients is far higher than that for VTq.	The EAC comments on obesity and issues with VTq. We understand that this was the question posed to the advisor however it could imply that the performance of VTq is unfavourable. We highlighted on page 82 of our submission issues	Edit made: These are factors highlighted earlier in this report that could not be accounted for in the EAC's meta-analysis using the current available clinical evidence **and are applicable to TE as well as VTq**. In

		with TE and obesity. Our conclusion was that TE was less able than VTq to deal with obese patients or those with ascites. We cited a failure rate of 7% for TE versus 3% for VTq. We calculated that there would be an additional cost of biopsy associated with each technique of these failures.	light of this, the EAC believes that a study using a UK population to **compare VTq, TE and liver biopsy** would be beneficial, appropriately allowing for such confounding factors, potentially through suitable sub-group analysis.

Issue 7

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Page 8 but does not provide any estimates for the proportion of patients within these categories who have liver fibrosis, or the distribution of Metavir scores within these patients.	Delete and insert at end of para The sponsors were unable to identify UK evidence as to the proportion of hepatitis patients with liver fibrosis and the distribution of Metavir score. The EAC is in agreement that this information is not available.	We discuss that this is a limitation and suggest this as an area for further study. Both our and the EAC advisors also highlighted that evidence was limited or non-existent. We feel the current wording implies that we were remiss.	Edits made: The sponsor was unable to provide estimates for the proportion of patients within these categories who have liver fibrosis, or the distribution of Metavir scores within these patients. The EAC searched for this information and is in agreement with the sponsor that this information is not currently available.