Computed tomography (CT) scanners for cardiac imaging – Somatom Definition Flash, Aquilion One, Brilliance iCT and Discovery CT750 HD. – Response to stakeholder comments.

Background information and typographical errors – There were a number of comments noting typographical errors of inconsistencies/inaccuracies in the technical descriptions of the instruments provided in the background section. These will be corrected prior to publication in the HTA monograph series and do not affect the overall conclusions of the report.

Should NGCCT be appraised and is evidence on improved accuracy sufficient to justify adoption of a new technology? – One stakeholder questioned the justification for assessment of NGCCT, given the current state of evidence on earlier CT technologies. The absence of evidence for patient benefit was noted and two previous HTAs, which reported accuracy of 64-slice CT for diagnosis of CAD and noted the absence of any evidence on changes to patient management or outcome, were cited. Both of these assessments also noted that there were some patient groups in whom the diagnostic performance of these scanners was inadequate or unknown. These groups form the focus and justification for the current assessment. As noted by the stakeholder, the current assessment offers evidence of improved accuracy in these patients. However, we agree that, as stated in our report, no evidence of patient benefit (changes to patient management/outcome) was identified. We agree that such evidence is highly desirable, arguably essential, when considering the introduction of any new health intervention (including diagnostic tests). However, the current reality is that diagnostic studies reporting such outcomes are extremely rare. In the absence of direct evidence of patient benefit, evidence of test accuracy combined with evidence of effective treatment for the target condition may sometimes be considered an adequate surrogate. Where, as in this case, accurate methods of diagnosis are already available, potential for reduced harm may also be an important consideration in justifying the assessment a new test.

Definition of 'NGCCT' and 'equivalence' of the instruments under assessment – A number of stakeholders make the point that there is no clear definition of NGCCT and that the instruments assessed have a number of differences and 'unique features', which mean that they cannot be considered equivalent. This issue was discussed extensively and acknowledged at the scoping workshop and the decision to include all these instruments in the same assessment (despite some potential problems) was clear and was agreed by participants. Because, there is no clear unique feature which is common to all of these instruments, the EAG aimed rather to consider representative latest technologies from the listed manufacturers and this is reflected in the broad search strategies and the inclusion of studies of dual source Somatom Definition, as well as those (one abstract only), which explicitly reported use of Somatom Definition FLASH; we acknowledge that this could have been made clearer in the report. It should be noted that no studies of single source Somatom definition were included. It is frequently unclear (from publications) exactly what model of scanner was used in a study. However, those details that were reported are clearly recorded in the data extraction tables provided in Appendix 4 of the report.

Inclusion of studies using Dual Source Somatom Definition in addition to those including Somatom Definition FLASH – A number of stakeholders queried the inclusion of studies using Dual Source Somatom Definition. Somatom definition FLASH is the most recent CT model produced by Siemens, however, data explicitly for this model are very sparse (one abstract). The main differentiations (made by the manufacturer) between Somatom Definition FLASH and Somatom Definition are reduced scan time and reduced radiation dose; radiation dose reduction was not found found to be a significant factor in determining cost-effectiveness and the inclusion of an earlier generation of machine might be expected to produce more conservative estimates of diagnostic performance. However, the paucity of data in Somatom Definition FLASH do mean that no advantage for this machine (under the terms of this assessment) over the earlier Dual Source Somatom Definition; we acknowledge that this point could have been made more clear in the report. We would argue that the inclusion of Dual Source Somatom Definition studies increases the relevance of the report to decision makers. Had we limited our report to studies which explicitly named one of the specified instrument models, we would have included only one abstract and one full paper.

Could earlier generation instruments from other manufacturers have been inappropriately omitted? – A number of stakeholders made the point that earlier generations of scanner from other manufacturers may have been inappropriately excluded from the assessment. We would argue that, given the apparent heterogeneity of these technologies, our use of broad search strategies using technical description terms associated with newer CT technologies, e.g. 'high definition', 'dual source', and terms for slice/detector row number provided the best approach possible to identifying studies of relevant instruments. In addition, although search terms for specific products were included, absence of these terms was not used to exclude studies (they were combined with the technical description terms using 'OR', rather than 'AND'). Every effort was therefore made to identify studies of relevant instruments, and manufacturers were given the opportunity (during the scoping phase and through submissions) to suggest both other instruments that they considered relevant to this assessment and specific studies which they considered may be relevant. We did not search using terms for 64-slice scanners, as this approach would have identified a very large volume of studies of earlier technologies, which it would not have been practical to screen within the time frame of the assessment. It should be noted that, of the 140 studies excluded at the full paper screening stage, in only seven instances was 'index test' given as the reason for exclusion (Appendix 5); re-examination of these seven studies showed that four clearly failed other inclusion criteria and the remaining three used single source 64-slice scanners.

Variation of radiation dose between different instruments and patients – A number of stakeholders questioned the estimated reduction in radiation dose given for NGCCT and pointed out the potential for variation between instruments and patient groups. We acknowledge that this issue could have been discussed in more detail. However, the estimates of reduction in radiation dose were based on expert opinion (the best practical option available to us within the time frame of the assessment) of the likely radiation dose associated with different imaging strategies in the relevant populations. It should also be noted that reduced radiation dose was not a key driver of the cost-

effectiveness results, as indicated in the discussion section of the report: 'The inclusion of the reduced radiation effects achievable using NGCCT versus ICA has only very minimal impact on the outcomes.'

Suggested additional studies – The stakeholders highlighted a number of specific studies for potential inclusion. Some of these studies were included in initial submissions from manufacturers. None of the studies listed met the inclusion criteria of the review. Given the comments above, it should also be noted that none of these studies failed the inclusion criteria solely because they were conducted in instruments other than those specified in the title of the report.

Use of estimates based on expert opinion – A number of stakeholders questioned the use of expert opinion and, in particular, the small number of experts involved. We acknowledge that a more formal and wide ranging expert elicitation process would be preferable, but this was not possible within the scope and time frame of this assessment. We feel that the opinion of experts in specialist centres, which was used, represents the best option available to us.

Assumption that 'difficult to image' patient groups could not be imaged using current CT technologies – Two comments queried the assumption that the 'difficult to image' patient groups specified in the assessment could not be imaged using current CT technologies, and one comment queried the range of high heart rates at which patients might be considered 'difficult to image'. This issue was discussed and the assumption agreed at the scoping workshops for this assessment. It was not part of the objectives of this assessment to assess the accuracy of CT in general in these patient groups; such an assessment would have involved a much larger systematic review, which would not have been practical within the time frame of this assessment. A previous health technology assessment (reference 15 in our report) of 64-slice and above (all but one of the studies included were in 64-slice instruments) highlighted patients with high heart rates, obesity, or high coronary calcium as potentially problematic to image and noted the paucity of data in these patients. Where reported the mean heart rate of patients in the studies included in the Mowatt et al HTA were between 58 and 72 b.p.m. It should be noted that, where reported, the mean heart rates for the HHR study populations included in our review ranged from 76 to 89 b.p.m.

Assumption of equivalence in sensitivity and specificity between suspected and known CAD populations – One stakeholder queried the validity of this assumption. Whilst we acknowledge that variation in test performance might be expected between these two populations, the accuracy data included in this assessment support the validity of our assumption.

Should cost savings from reduced β-blocker use be included in cost-effectiveness modelling? – One stakeholder suggested that cost-savings from reduced β-blocker use could be included in cost-

effectiveness modelling. Because NGCCT is not being compared to an imaging scenario where β-blockers might be used (current 64-slice technologies), this potential cost-saving is not relevant to our cost-effectiveness models.

The specificity of NGCCT is lower than its sensitivity – One comment noted that the specificity estimates for NGCCT may mean that numbers of 'false positive' patients would undergo unnecessary interventions if this imaging technology were used. In practice, it is unlikely that patients would undergo surgical procedures without further investigation (ICA) of a positive imaging result.