NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of Diagnostics Guidance [DG6]; Depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M

Final recommendation post consultation
Transfer the guidance to the static guidance list.

1. Background

This guidance was issued in November 2012

At the GE meeting of 09 February 2016 it was agreed that we would consult on the recommendations made in the GE proposal paper. A four week consultation has been conducted and the responses are presented below.

2. Proposal put to stakeholders

Transfer the guidance to the 'static guidance list'.

3. Rationale for selecting this proposal

No significant changes to the care pathway or the technologies have been identified since the publication of diagnostics guidance 6. Further, no evidence has been found through the updated literature searches that will materially impact the recommendations made in diagnostics guidance 6. It is therefore proposed that this guidance is placed on the static guidance list.

4. Summary of consultation comments

Comments received during 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 comments received, and are not endorsed by NICE, its officers or advisory committees.

Respondent: The Royal College Of Anaesthetists **Response to proposal:** The Royal College of Anaesthetists wishes to express some concern at several levels in relation to this proposed guidance on the use of depth of anaesthesia (DOA) monitors. In its report, there seems to be an over-reliance by NICE on randomised controlled trials (RCTs) and this is to the apparent exclusion of all other forms of publication types. This leads to a skewed interpretation of the data. Accidental awareness during general anaesthesia (AAGA) is a rare complication and like all rare complications, AAGA is particularly poorly suited to study by RCT, due to its rarity. What results is guidance that is at best potentially confusing to practicing anaesthetists and at worst likely to be ignored by most practicing anaesthetists, especially as it is not consistent with very clear advice they will have already received from both the outputs from the NAP5 project, and also from the AAGBI's recent document on minimum standards of monitoring. We would have liked to have seen guidance from NICE that is more explicitly consistent with that existing specialty guidance. Both these sources emphasised the central role of neuromuscular blockade (NMB) in the genesis of accidental awareness during general anaesthesia (AAGA), which this current NICE guidance fails adequately to do. For example, in the list of patients considered at high risk, the first mention is of patients with high opiate or alcohol usage (for which current evidence is in fact extremely sparse) and it is only later that NMBs are mentioned at all. Indeed, we would question this entire table of 'risk' (bottom page 2). Older patients and those with comorbidities are not in fact at higher risk of AAGA as NICE suggests: NAP5 found the highest risk was in middle age, whereas at the extremes of age (peadiatric and elderly), the risk was proportionately lower. There was no increased risk in ASA 3 or 4	**Comments from the Diagnostics Assessment Programme** Thank you for your comments, which have been considered by NICE. Diagnostics Guidance 6 (DG6) on depth of anaesthesia monitors has not been changed since its publication. The review proposal document considers any new evidence or changes since the publication of the guidance and if there is a need to update the existing guidance. The existing guidance (DG6) was released for public consultation during its development and all comments were considered by the Diagnostics Advisory Committee at that time. Therefore, only comments relating to the potential update of Diagnostics Guidance 6 will be considered for this consultation on the review proposal. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance.

patients as NICE claims. Yet, in addition to neuromuscular blockade (which is by far the biggest risk) missing from this list are factors like: obstetric caesarean section, rapid sequence induction of anaesthesia, cardiothoracic surgery, obesity, emergency surgery performed out of hours by grades other than consultant or specialist staff, use of certain agents such as thiopental for induction. Moreover, in this table and elsewhere, the cause of AAGA is stated to be the use of lower levels of anaesthetic to reduce cardiovascular side effects. While this may be the case in specific types of surgery this of course does not apply to obstetrics for example, and the mechanisms of AAGA here are entirely different. Furthermore it completely overlooks the fact that the majority of AAGA events occurs at induction and at emergence, when it is the balance of anaesthesia depth and paralysis that is the cause, and not some implicit or explicit desire to avoid cardiovascular compromise. Obesity is a risk for AAGA and should also be on this list: it is simply incorrect to state (as the next paragraph in the NICE report does) that obese patients are at risk of excessive anaesthesia - any evidence for such is sparse. Most evidence in this field of awareness in fact indicates that obese patients are at risk of insufficient anaesthesia. At bottom, page 2, the words “unless these patients are also paralysed with neuromuscular blockade” should be added to the line “Patients receiving total intravenous anaesthesia are not considered at higher risk of adverse outcomes from general anaesthesia than patients receiving inhaled anaesthesia”. This makes the statement correct. In other words, there is already strong evidence to show that patients receiving total intravenous anaesthesia (TIVA) with paralysis are at much higher risk of AAGA than if undergoing an inhalational technique, and NAP5 data confirms this. This revised statement we propose also encapsulates the additional risk of TIVA during the transfer of paralysed patients (eg, from theatre to intensive care or from theatre to scan, etc).	In the event that Diagnostics Guidance 6 is updated, stakeholders will be contacted for input through the normal diagnostics guidance development process. The existing NICE guidance on depth of anaesthesia monitors (DG6) was developed before the recent specialty guidance from Association of Anaesthetists of Great Britain and Ireland (AAGBI), and does not therefore include reference to the AAGBI guidance. The review proposal on DG6 noted the draft AAGBI recommendations for standards of monitoring during anaesthesia and recovery and the final report of the NAP5 audit. A link will be added to the recent AAGBI specialty guidance from the landing page for Diagnostics Guidance 6 on the NICE website to highlight the specific recommendations for depth of anaesthesia monitoring made by the AAGBI.
We are concerned about Recommendation 7.1. NICE missed an opportunity to encourage further research when this guidance was first published some years ago, and this is now compounded by the revised document. The current paragraph will actively discourage funding of research in this area. We cannot see how an organisation like NICE to imply that uncertainty can ever justify adopting any technology. Our view, and the view of those	

actually undertaking the research nationally and internationally, is that the current uncertainty mandates a delay in general or indiscriminate adoption of the technology. Specifically, the bundling together of BIS with entropy and Narcotrend was not justified in the first NICE report and remains unjustified: this is an area where specific research can be recommended and will be invaluable. --- The repeated use of the term 'recommended as an option' by NICE is unhelpful to practicing anaesthetists. There is either evidence to recommend the use of these monitors in defined situations, or there is not. Our colleagues already know these monitors 'are an option' and will be looking for more specific guidance. The last words in this section 7.1 (and particularly, the wording "to patients") are clearly redundant. Who else is likely to benefit or not in this discussion, other than patients? --- Under 4 Rationale (and repeated elsewhere) it is stated that "No significant changes to the care pathway or the technologies have been identified since the publication of Diagnostics Guidance 6". We consider this at best misleading and at worst simply incorrect. As the majority of anaesthetists now know, novel care pathways were published by NAP5 in the management and treatment of AAGA patients (see http://www.nationalauditprojects.org.uk/NAP5-Anaesthetia-Awareness-Pathway#pt) and are being widely used. The AAGBI monitoring guidelines (which also provide explicit guidance on the use of DOA monitors) are correctly regarded also as a care pathway, so this sentence in the NICE report will be regarded as incorrect by the majority of anaesthetists. --- The Section 6.3 New Studies raises numerous concerns. We are surprised that some important literature is omitted, that could usefully inform the guidance. Most importantly, the NAP5 Report is not even referenced, which most readers will find very surprising and a glaring omission. Then, some references are mis-quoted. The correct quotation from the AAGBI guidance is:	NICE agrees that the NAP Anaesthesia Awareness support Pack constitutes a change to the care pathway for people reporting accidental awareness during general anaesthetic, and should be included in the review proposal document.

"….commence from induction of anaesthesia and be continued at least until the completion of surgical and anaesthetic interventions": the words that NICE has used appear to be from an earlier, unpublished draft of that AAGBI guidance. Overall the descriptions of the new studies seems to add little. It is stated that these new studies 'tested the effect of BIS monitoring' (page 8). This has little meaning unless we know exactly how the monitors were used in these studies, ie, with what limits, whether the alarms were on, and what action was taken if readings drifted outside the limits. Description of each of the studies should specify whether they were funded by a manufacturer. Some methodologies seem targeted to such unique populations as to make it difficult or impossible to generalise (eg, the developmentally delayed paediatric population of Sargin et al., 2015 and the elderly Asian population of Shafiq et al., 2012). The inclusion of Jiang et al., 2013, of monitor use in infants (reporting a significant reduction in 'intraoperative awareness') suggests some indiscriminate use of the literature by NICE that would, to most anaesthetists, appear surprising, if not amusing. Yet, important studies missing from the list includes the study by Schneider et al. 2014 which underlines the importance of combining pEEG readings with other information in an algorithmic way. In other words, the correct guidance should make clear that information from DOA monitors alone is arguably of little value, and potentially misleading: it must be combined in a transparent and reproducible manner with other data to make sense. Then, there are the very important papers from Russell 2013 that show that pEEG readings simply fail to correlate with actual patient awareness (as measured by a positive response to command during apparent anaesthesia). If Russell's work is correct then it is unclear why NICE is making the recommendation it is. Then, there is the striking and very potent result of Schuller et al. 2015 that underlines Russell's work. They administered neuromuscular blockade to awake volunteers yet discovered BIS readings as low as 50, even when the volunteers were responding to command (isolated forearm technique). In other words, pEEG readings consistently fail to correlate with the awake state. Our point is that if NICE's methodology for accepting studies is so restrictive that it filters out such highly relevant work, then any conclusions are at serious risk of being regarded by the	However, as this new care pathway is implemented after the depth of anaesthesia monitoring is used it is unlikely to substantially impact the effectiveness of monitoring. In addition, although this new care pathway may impact on the incidence of post-traumatic stress disorder, the care pathway is recently implemented and no evidence of its impact has been identified in literature searches. New evidence that is generated can be considered in a future update of NICE guidance if appropriate. The NAP5 report is referred to in section 6.2 and section 7 of the review proposal. Thank you for highlighting that this report was not also included in the reference list. Thank you for highlighting the updated wording in the AAGBI guidance. At the time of writing the review proposal only the draft guidance was available. The review proposal noted that the final publication was scheduled for early 2016. The review proposal updated the searches done for the original diagnostics assessment report which were designed to update an existing systematic review. Studies were included if they were a prospective controlled trial and non-RCT evidence was considered for relevant

anaesthetic community as unsafe or irrelevant. We suggest that a wider and more appropriate literature base is taken into account before NICE re-issues its recommendation. (As an aside, all the work by Schneider, Russell and Schuller that we cite were officially classed as registered clinical trials). In summary, we would like to see NICE make recommendations that are reflect the understanding of anaesthetic practitioners, as they are informed from other authoritative sources. Otherwise, there is the risk of confusion and, at worst, a complete disregard for the work of NICE by the wider anaesthetic community. This would be unfortunate, since NICE has so much to offer. Therefore a recommendation would be welcome that: a) Stresses the positive role of pEEG monitoring in TIVA with neuromuscular blockade b) Acknowledges that with inhalational anaesthesia with neuromuscular blockade, there is probably no advantage of pEEG technology over and above end-tidal monitoring (with a lower limit alarm set) c) Lists high risk groups more consistent with published evidence, especially from the largest ever study in the field (NAP5) d) Ensures that any recommendation is consistent in terminology with the latest AAGBI guidelines on monitoring e) Makes clear that, where no neuromuscular blockade is used there is unlikely to be a serious risk of AAGA making any additional monitoring technology redundant f) Emphasises the need for research as essential to develop clearer algorithms for use of the available technology, which is a prerequisite for wider adoption. This emphasis from NICE would be a much valued source of support as anaesthetists seek grant funding to support quality improvement research.	parameters where RCT evidence was not available. Thank you for the references. There were a number of uncertainties in the evidence base of Diagnostics Guidance 6 and the cost effectiveness analyses showed that the ICERS for depth of anaesthesia monitoring were sensitive to changes in the probability of awareness during surgery and in the quality-of-life decrement applied to post-traumatic stress disorder. The NAP5 audit data on awareness during surgery is welcomed but no new evidence on quality of life, particularly relating to post-traumatic stress disorder, has been identified during the literature searches. The Committee considered that the impact of post-traumatic stress disorder on a patient's life and the cost of treating this disorder were likely to have been underestimated in the analyses. The inclusion of non-randomised studies is unlikely therefore to address the key uncertainties in the evidence base to an extent which is likely to have a material effect on the recommendations in the existing guidance. It is proposed that the guidance is transferred to the static list until further evidence becomes available. NICE considered the existing guidelines from other bodies during the development

References Pandit JJ, Andrade J, Bogod DG, Hitchman JM, Jonker WR, Lucas N, Mackay JH, Nimmo AF, O'Connor K, O'Sullivan EP, Paul RG, Palmer JH, Plaat F, Radcliffe JJ, Sury MR, Torevell HE, Wang M, Cook TM. 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors. British Journal of Anaesthesia 2014; 113: 549-59. Checketts MR, Alladi R, Ferguson K, Gemmell L, Handy JM, Klein AA, Love NJ, Misra U, Morris C, Nathanson MH, Rodney GE, Verma R, Pandit JJ. Recommendations for standards of monitoring during anaesthesia and recovery 2015 : Association of Anaesthetists of Great Britain and Ireland. Anaesthesia 2016; 71: 85-93. Russell IF. The ability of bispectral index to detect intra-operative wakefulness during total intravenous anaesthesia compared with the isolated forearm technique.Anaesthesia 2013;68:502-11. Russell IF. The ability of bispectral index to detect intra-operative wakefulness during isoflurane/air anaesthesia, compared with the isolated forearm technique.Anaesthesia 2013;68:1010-20. Schneider G, Jordan D, Schwarz G, et al. Monitoring depth ofanesthesia utilizing a combination of electroencephalographic andstandard measures. Anesthesiology2014;120:819–28. Schuller PJ, Newell S, Strickland PA, Barry JJ. Response of bispectral index to neuromuscular block in awake volunteers.Br J Anaesth. 2015;115, Suppl 1:i95-i103.	of its guidance on depth of anaesthesia monitors. Although NICE guidance recommends the use of depth of anaesthesia monitors as an option in a broader population than that specified in the recently published AAGBI guidance, it does not preclude their use in TIVA with NMB and as such is consistent with the AAGBI guidance. In addition, NICE considers both the clinical effectiveness and cost effectiveness of technologies used in the NHS and independent NICE committees may therefore consider different or additional factors in its decision making to those used by other national bodies. NICE notes that final guidance on recommendations for standards of monitoring during anaesthesia and recovery has been published by the Association of Anaesthetists of Great Britain and Ireland (AAGBI). A link will be added to this guidance from the landing page for Diagnostics Guidance 6 to highlight the specific recommendations made by the AAGBI.

Respondent: The Royal College Of Anaesthetists **Response to proposal:** 'Older patients … are also considered at higher risk of unintended awareness. This is because they are at greater risk of haemodynamic instability during surgery. In these patients, lower levels of anaesthetic are often used to prevent adverse effects on the cardiovascular system and these levels can be inadequate.' This statement might be worth reviewing, as it (wrongly) links awareness to haemodynamic instability. NAP5 showed that older patients were among the least likely patient group to experience accidental awareness under anaesthesia [1]. There may be a case to be made for older patients receiving general anaesthesia to have depth-of-anaesthesia monitoring, for the purpose of avoiding excessively deep anaesthesia but it is not at all clear that any of these monitors have been designed for this purpose [2, 3]. Indeed, they are primarily marketed and designed to prevent accidental awareness, which is a different thing. References [1]. Table 11.1 + paragraph 11.42, http://www.nationalauditprojects.org.uk/download.php/?fn=NAP5%20full%20report.pdf&mime=application/pdf&pureFn=NAP5%20full%20report.pdf) [2]. Jack JM, White SM. Older surgical patients--under-aware or overanaesthetised?Anaesthesia 2015; 70: 109-10. [3].Page 89, Association of Anaesthetists of Great Britain and Ireland Safety Guideline Perioperative Care of the Elderly 2014https://www.aagbi.org/sites/default/files/perioperative_care_of_the_elderly_2014.pdf, Anaesthesia 2014;69 s.1: 81-98.)	**Comments from the Diagnostics Assessment Programme** Thank you for your comments, which have been considered by NICE. The existing guidance (DG6) was released for public consultation during its development and all comments were considered by the Diagnostics Advisory Committee at that time. Therefore, only comments relating to the potential update of Diagnostics Guidance 6 will be considered for this consultation on the review proposal. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. In the event that DG6 is updated stakeholders will be contacted through the normal diagnostics guidance development process. No new evidence on the effects of excessively deep levels of anaesthesia, particularly in the longer term, has been identified. New data from the NAP5 audit in older patients, while helpful, is therefore unlikely to have a material effect on the

	recommendations in the existing guidance.
Respondent: The Royal College Of Anaesthetists **Response to proposal:** 2 'Original objective of guidance. To assess the clinical and cost effectiveness of BIS, E-Entropy and Narcotrend for assessing depth of anaesthesia in individuals undergoing general anaesthesia' 3.1.1 'The use of … depth of anaesthesia monitors is recommended as an option during any type of general anaesthesia in patients considered at higher risk of adverse outcomes'. 3.1.2 'The use of … depth of anaesthesia monitors is also recommended as an option in all patients receiving total intravenous anaesthesia.' Although we understand that the guidance relates to general anaesthesia, there is a problem with elderly, high-risk patients receiving sedation. The recent UK National Sprint Audit of Practice (ASAP) [4] found that 45% of 11, 085 elderly (high-risk) patients received spinal anaesthesia for hip fracture surgery. 85% of these received additional sedation during the surgery. However, separate research by Sieber et al. [5] in 40 patients > 65 years undergoing hip fracture repair with spinal anaesthesia and propofol-based sedation found that 15 patients receiving routine anaesthesia care spent 32.2% of their surgical time at BIS levels consistent with general anaesthesia, compared with just 5% in 25 patients receiving sedation titrated to a sedation score. This indicates that some patients are receiving relative overdoses of sedation, such that they are effectively receiving general anaesthesia. This has an important safety implication, because these patients are not receiving simultaneous airway support. Patients are	**Comments from the Diagnostics Assessment Programme** Thank you for your comments which have been considered by NICE. Patients receiving sedation are outside the scope of Diagnostics Guidance 6, which was 'people undergoing general anaesthesia'. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. In the event that DG6 is updated, stakeholders will be contacted for input through the normal diagnostics guidance development process.

therefore at avoidable risk in two ways: 1. From haemodynamic instability (and/or death [6]), caused by relative overdosage of sedation/general anaesthesia; 2. From aspiration of gastric contents into the lungs caused by receiving general anaesthesia with an unsupported airway. We suspect that Sieber's study [5] reflects UK practice. Extrapolating incidence data from ASAP, ~ 12 500 patients annually in the UK are exposed to this potential risk. In other words, there is potential scope for considering whether older patients should have EEG-based depth of anaesthesia monitoring when sedated (rather than anaesthetised) for higher risk surgeries, because of the high risk of unintended general anaesthesia occurring? Thus, whereas the benefits of EEG-based monitoring in the anaesthetised, paralysed patient are highly questionable, there may be more benefits in the sedated, unparalysed patient, as the monitor serves as a useful early warning, supplemented later by patient response. References [4]. Royal College of Physicians and the Association of Anaesthetists of Great Britain and Ireland. National Hip Fracture Database. Anaesthesia Sprint Audit of Practice 2014. http://www.nhfd.co.uk/20/hipfractureR.nsf/4e9601565a8ebbaa802579ea0035b25d/f085c664881d370c80257cac00266845/$FILE/onlineASAP.pdf [5]. Sieber FE, Gottshalk A, Zakriya KJ, Mears SC, Lee H. General anesthesia occurs frequently in elderly patients during propofol-based sedation and spinal anesthesia.Journal of Clinical Anesthesia 2010; 22: 179-83. [6]. Brown CH 4th, Azman AS, Gottschalk A, Mears SC, Sieber FE. Sedation depth during spinal anesthesia and survival in elderly patients undergoing hip fracture repair.Anaesthesia and Analgesia 2014; 118: 977-80.	

We suspect that Sieber's study [5] reflects UK practice. Extrapolating incidence data from ASAP, ~ 12 500 patients annually in the UK are exposed to this potential risk. In other words, there is potential scope for considering whether older patients should have EEG-based depth of anaesthesia monitoring when sedated (rather than anaesthetised) for higher risk surgeries, because of the high risk of unintended general anaesthesia occurring? Thus, whereas the benefits of EEG-based monitoring in the anaesthetised, paralysed patient are highly questionable, there may be more benefits in the sedated, unparalysed patient, as the monitor serves as a useful early warning, supplemented later by patient response. References [4]. Royal College of Physicians and the Association of Anaesthetists of Great Britain and Ireland. National Hip Fracture Database. Anaesthesia Sprint Audit of Practice 2014. http://www.nhfd.co.uk/20/hipfractureR.nsf/4e9601565a8ebbaa802579ea0035b25d/f085c664881d370c80257cac00266845/$FILE/onlineASAP.pdf [5]. Sieber FE, Gottshalk A, Zakriya KJ, Mears SC, Lee H. General anesthesia occurs frequently in elderly patients during propofol-based sedation and spinal anesthesia.Journal of Clinical Anesthesia 2010; 22: 179-83. [6]. Brown CH 4th, Azman AS, Gottschalk A, Mears SC, Sieber FE. Sedation depth during spinal anesthesia and survival in elderly patients undergoing hip fracture repair.Anaesthesia and Analgesia 2014; 118: 977-80.	

Respondent: The Royal College Of Anaesthetists **Response to proposal:** The description of anaesthesia alluded to is not really a recognisable UK technique. Midazolam is not usually described as an anaesthetic agent. We question the relevance of this study at all. There appears to be a typographical error in the last sentence of the paragraph: "…a significant difference for awareness and breathings."	**Comments from the Diagnostics Assessment Programme** Thank you for your comments, which have been considered by NICE. Thank you for highlighting that this study may not be relevant.

Respondent: The Royal College Of Anaesthetists **Response to proposal:** The guidelines do not seem to take into consideration some important practical aspects of this technology; for example the fact that battery powered mobile monitors are not widely available. This would be a problem in emergency situations prior to induction in obstetric cases and if patients need to be transferred, as these are less likely to have undergone TIVA and are particularly high risk. Note that NAP5 discovered by far the highest incidence of AAGA is at induction.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. The review proposal document considers any new evidence or changes since the publication of the guidance and if there is a need to update the existing guidance. The existing guidance (DG6) was released for public consultation during its development and all comments were considered by the Diagnostics Advisory Committee at that time. Therefore, only comments relating to the potential update of Diagnostics Guidance 6 will be considered for this consultation on the review proposal. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. In the event that DG6 is updated, stakeholders will be contacted for input through the normal diagnostics guidance development process

Respondent: The Royal College Of Anaesthetists **Response to proposal:** We wonder if NICE is aware that there is a major international trial currently ongoing exploring the benefits of depth of anaesthesia monitoring. There are several NHS hospitals participating in this. NICE have previously elected to publish guidance whilst the definitive trials were still ongoing and this is not at all helpful. Perhaps the GDG could wait for the evidence from this study before issuing definitive guidance. Information about the BALANCED trial can be found here: http://balancedstudy.org.nz/	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. NICE notes that the final data collection date for the primary outcome measure in the BALANCED Anaesthesia Study is January 2019 (https://clinicaltrials.gov/ct2/show/NCT02073357). NICE may review guidance before the expected review date when there is significant new evidence that it considers is likely to change the recommendations. NICE is keen to hear about any new evidence that becomes available before the review date (please send information to diagnostics@nice.org.uk). NICE will assess the likely impact of the new evidence on the recommendations and will propose an update to the published guidance if required.

Respondent: GE Healthcare **Response to proposal:** GE agrees with the recommendations of the review proposal and the decision to transfer the guidance to the static list.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: GE Healthcare **Response to proposal:** GE requests that the text is modified to read: “Although the number of outcome studies conducted for the E-Entropy and NarcoTrend-Compact M depth of anesthesia monitors is fewer than for the BIS monitor, the Committee concluded that the E-Entropy and Narcotrend-Compact M monitors are broadly equivalent to BIS.”	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. The review proposal document considers any new evidence or changes since the publication of the guidance and if there is a need to update the existing guidance. The existing guidance (DG6) was released for public consultation during its development and all comments were considered by the Diagnostics Advisory Committee at that time. Therefore, only comments relating to the potential update of Diagnostics Guidance 6 will be considered for this consultation on the review proposal. As the text referred to is in the recommendations of the existing guidance, it cannot be changed if the guidance is transferred to the static list.

Respondent: Association of Anaesthetists of Great Britain and Ireland **Response to proposal:** The AAGBI remains concerned about several aspects of this guidance:	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE.

Respondent: Association of Anaesthetists of Great Britain and Ireland **Response to proposal:** 1. Practising anaesthetists will find this guidance at best, confusing but at worse will most likely ignore it, as it is inconsistent with very clear advice that they have already received in 2 recent outputs from within the speciality, the NAP5 project, and the AAGBI's recent guideline on 'Standards of Monitoring during Anaesthesia and Recovery, 2015'	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. NICE notes that final guidance on recommendations for standards of monitoring during anaesthesia and recovery has been published by the Association of Anaesthetists of Great Britain and Ireland (AAGBI) since the publication of DG6. A link will be added to the AAGBI guidance from the landing page for Diagnostics Guidance 6 on the NICE website to highlight the specific recommendations made by the AAGBI.

Respondent: Association of Anaesthetists of Great Britain and Ireland **Response to proposal:** 2. The current DoA guidance only refers to and has quoted from the draft version of the AAGBI guideline on 'Standards of Monitoring during Anaesthesia and recovery'. This document has now been published (2015) and this guidance needs to be correctly referenced. The NICE panel should read this final document.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. Thank you for highlighting this error in the review proposal. At the time of writing the review proposal only the draft guidance was available. The review proposal noted that the final publication was scheduled for early 2016.

Respondent: Association of Anaesthetists of Great Britain and Ireland **Response to proposal:** 3.This table of risk factors for unintended awareness during general anaesthesia (p2), needs updating to reflect the findings from the recent NAP 5 report (eg obesity, Neuromuscular Blockade, tyoe of surgery, type of anaesthetic used etc)	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. In the event that DG6 is updated, stakeholders will be contacted for input through the normal diagnostics guidance development process.

Respondent: Association of Anaesthetists of Great Britain and Ireland **Response to proposal:** 4. We would like to see this document reinforce the role of pEEG monitoring in TIVA with NMB, point out that with inhalational anaesthesia with NMB there is probably no advantage of pEEG, and that where no NMB is used, there is unlikely to be any need for DoA	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Although NICE guidance recommends the use of depth of anaesthesia monitors as an option in a broader population than that specified in the recently published AAGBI guidance, it does not preclude their use in TIVA with NMB and as such is consistent with the AAGBI guidance. In addition, NICE considers both the clinical effectiveness and cost effectiveness of technologies used in the NHS and independent NICE committees may therefore consider different or additional factors in its decision making to those used by other national bodies. A link will be added to the AAGBI guidance from the landing page for Diagnostics Guidance 6 on the NICE website to highlight the specific recommendations made by the AAGBI.

Respondent: Association of Anaesthetists of Great Britain and Ireland **Response to proposal:** The AAGBI therefore supports option 2: An accelerated update of the guidance to correctly reflect the guidance from NAP 5 (2015) and the 2015 SoM guideline from the AAGBI. This will provide a robust, up to date and consistent guidance for practising anaesthetists of all grades.	**Comments from the Diagnostics Assessment Programme** Thank you for your comment, which has been considered by NICE. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance.

Paper signed off by: Carla Deakin, 21 April 2016

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