NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Pressurised intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis**
Name of Specialist Advisor:	Anthony Antoniou
Specialist Society:	British Society of Gastroenterology

1 Do you have adequate knowledge of this procedure to provide advice?

x Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

x Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

x Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

x I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

I am currently involved in a trial with Imperial College, London, to ascertain the efficacy of this procedure. Although I perform Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) as part of the Complex Cancer Service at my institution, we do not perform PIPAC. PIPAC has been taken on by only a handful of units, with one dedicated unit in London.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

x I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

There are strict referral criteria for inclusion of patients for PIPAC. These patients have a high Peritoneal Cancer Index (PCI) that is not eligible for Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) and, by definition, have disseminated peritoneal malignancy. They must have a life expectancy of > 6months and have a Performance Status of 0 or 1.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

x I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

x I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

x Other (please comment)

Comments: I am currently involved in a trial of PIPAC utilisation in conjunction with Imperial College, London and The Bart's Cancer Institute, London. The investigative team have submitted the following paper for publication:
Safety and Efficacy of Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) for Peritoneal Metastases: A Systematic Review and Pooled Analysis.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

x Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

St Mark's Hospital, Harrow has been designated a Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) centre after collaboration with The Peritoneal Malignancy Institute, Basingstoke. This is a recognised technique in the treatment of colorectal peritoneal metastases. Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) is currently only available in a trail setting in the UK.

3.2 What would be the comparator (standard practice) to this procedure?

Maintenance/ palliative systemic chemotherapy is currently offered to patients with inoperable peritoneal metastatic disease. This is used in a palliative setting with poor outcomes.

Sadeghi B, Arvieux C, Glehen O, Beaujard AC, Rivoire M, Baulieux J, Fontaumard E, Brachet A, Caillot JL, Faure JL, et al. Peritoneal carcinomatosis from non-gynecologic malignancies: results of the EVOCAPE 1 multicentric prospective study. Cancer. 2000;88:358–363.
Chu DZ, Lang NP, Thompson C, Osteen PK, Westbrook KC. Peritoneal carcinomatosis in nongynecologic malignancy. A prospective study of prognostic factors. Cancer. 1989;63:364–367.

Köhne CH, Cunningham D, Di Costanzo F, Glimelius B, Blijham G, Aranda E, Scheithauer W, Rougier P, Palmer M, Wils J, et al. Clinical determinants of survival in patients with 5-fluorouracil-based treatment for metastatic colorectal cancer: results of a multivariate analysis of 3825 patients. Ann Oncol. 2002;13:308–317.

Bloemendaal AL, Verwaal VJ, van Ruth S, Boot H, Zoetmulder FA. Conventional surgery and systemic chemotherapy for peritoneal carcinomatosis of colorectal origin: a prospective study. Eur J Surg Oncol. 2005;31:1145–1151.

Verwaal VJ, van Ruth S, de Bree E, van Sloothen GW, van Tinteren H, Boot H, Zoetmulder FA. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal cancer. J Clin Oncol. 2003;21:3737–3743.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

x Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) is offered in a very small number of hospitals in the UK. The introduction of Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) will be confined to even fewer centres.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

1) No access rates into the peritoneal cavity vary from 0-17%. This may increase with repeated interventions.

C. B. Tempfer, G. Winnekendonk, W. Solass et al., “Pressurized intraperitoneal aerosol chemotherapy in women with recurrent ovarian cancer: a phase 2 study,” Gynecologic Oncology, vol. 137, no. 2, pp. 223–228, 2015.

G. Nadiradze, U. Giger-Pabst, J. Zieren, D. Strumberg, W. Solass, and M. A. Reymond, “Pressurized intraperitoneal aerosol chemotherapy (PIPAC) with low-dose cisplatin and doxorubicin in gastric peritoneal metastasis,” Journal of Gastrointestinal Surgery, vol. 20, no. 2, pp. 367–373, 2015.

C. Demtroder, W. Solass, J. Zieren, D. Strumberg, U. Giger-Pabst, and M. A. Reymond, “Pressurized intraperitoneal aerosol chemotherapy (PIPAC) with oxaliplatin in colorectal peritoneal metastasis,” Colorectal Disease, vol. 18, no. 4, pp. 364–371, 2015.

M. Robella, M. Vaira, and M. De Simone, “Safety and feasibility of pressurized intraperitoneal aerosol chemotherapy (PIPAC) associated with systemic chemotherapy: an innovative approach to treat peritoneal carcinomatosis,” World Journal of Surgical Oncology, vol. 14, no. 1, p. 128, 2016.

2) Intraoperative complications with surgical access.

G. Nadiradze, U. Giger-Pabst, J. Zieren, D. Strumberg, W. Solass, and M. A. Reymond, “Pressurized intraperitoneal aerosol chemotherapy (PIPAC) with low-dose cisplatin and doxorubicin in gastric peritoneal metastasis,” Journal of Gastrointestinal Surgery, vol. 20, no. 2, pp. 367–373, 2015.

3) The majority of patients will develop an inflammatory response to the intraperitoneal chemotherapy also seen in HIPEC (Hyperthermic Intra-Peritoneal Chemotherapy). Patients can also develop renal and hepatic dysfunction.

Robella M, Vaira M, De Simone M. Safety and feasibility of pressurized intraperitoneal aerosol chemotherapy (PIPAC) associated with systemic chemotherapy: an innovative approach to treat peritoneal carcinomatosis. *World journal of surgical oncology*. 2016;14:128.

2. Anecdotal adverse events (known from experience)

There is a potential for wound infection and pain from port site insertions. One potentially serious adverse event is extravasation of chemotherapy from port sites during the post-operative period.

3. Theoretical adverse events

Intra-operative mortality is potential risk from this procedure Also, disease progression with Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) is possible indicating a failure of the technique.

4.2 What are the key efficacy outcomes for this procedure?

This procedure has two key outcomes which would indicate efficacy.

1) Patient tolerability

2) Evidence of disease remission objectively looking at histological and radiological response to treatment. Histology can be obtained at the time of the PIPAC procedure and interval radiology can be carried out in conjunction with PIPAC treatments.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

The main uncertainty of this procedure is whether a patient that has been deemed palliative gains any benefit from this intervention. Patients will be subjected to repeated surgeries to undergo Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC). The procedure is repeated in 6 to 8 weekly intervals. A further uncertainty is after how many procedures will the patient expect to reveal any benefit? Does this procedure need to be repeated indefinitely akin to 'maintenance chemotherapy'?

4.4 What training and facilities are needed to do this procedure safely?

The main concern is the exposure of the theatre team and surgeons to aerosol chemotherapy. Safety measures should include:

1) the PIPAC procedure should be remote-controlled i.e. no one remains in theatre during the PIPAC application

2) zero flow of CO_2 should be ensured so that the system remains airtight and no leaks occur.

3) the procedure should be performed in a theatre with laminar flow and, at the end of the procedure, the chemotherapy aerosol should be exhausted into the hospital's air-waste system.

As with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) surgeons must take precautions to prevent contact with the chemotherapeutic agent.

1) The surgical team should double glove, wear protective glasses/ visors and wear disposable, non-absorbent gowns.

2) Similar precautions need to be undertaken by the theatre staff involved in the case.

3) Remote monitoring should be employed during the PIPAC procedure. This will limit the potential exposure to the anaesthetic team.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

There are two major trials:

1) PIPAC for peritoneal metastases for colorectal cancer - Netherlands
ISRCTN89947480 a Phase II study
Currently recruiting – target of 20 patients

2) PIPAC for the treatment of colorectal metastases – Imperial College, UK
This is the study I am currently involved in. A phase II interventional study.
ClinicalTrials.gov Identifier: NCT03868228
Currently recruiting – target of 30 patients

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

None

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

At present the procedure is being offered within a trial setting. Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) is only being offered in recognised centres.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Outcome measures can be divided in to Primary and Secondary.

Primary Outcome Measures include:

1) progression free survival as measured by laparoscopy and cross-sectional imaging.

2) morbidity. The measurement of adverse events using the Clavien-Dindo grading of surgical complications. This should be carried out after each PIPAC-procedure up to 4 weeks after the last PIPAC-procedure.

Secondary Outcome Measures include:

1) Quality of life assessments - QLQ-C30 questionnaire [Time Frame: Repeated 6-8 weekly before each PIPAC treatment and European Organisation for Research and Treatment of Cancer (EORTC) Quality of life questionnaire (QLQ-C30 Verison 3).

2) PIPAC related safety regulation breaches / adverse events in theatre. This should be assessed following each PIPAC treatment 6-8 weekly.

3) Costs derived from the NHS costing guidelines at the time of analysis.

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

Major morbidity as measured by the Clavien-Dindo classification III, IV and V include:

III – Patient requiring surgical, radiological or endoscopic intervention

IIIa – intervention under regional/ local anaesthesia

IIIb – intervention under general anaesthetic

IV – Life threatening complication requiring intensive care management

IVa – single organ dysfunction

IVb – multiorgan dysfunction

V - Patient death

The Clavien-Dindo score should be measured after each PIPAC procedure up to 4 weeks after the last PIPAC procedure.

Organ specific adverse outcomes should be measured:

1) Organ-specific toxicity, based on bone marrow, liver, and kidney functions measured at baseline, each postoperative day, and four weeks after each PIPAC procedure

2) Readmissions, defined as any hospital admission after initial discharge, up to four weeks after the last PIPAC procedure

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

Once again, the procedure will only be carried out in centres offering Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC). PIPAC is considered a palliative procedure at present and will only be offered by a few centres.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

x Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☐ Moderate.

x Minor.

Comments:
This is a palliative procedure that is repeated every 6 to 8 weeks. The number of patients eligible will be small.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

Publications involving Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) are limited in number and number of patients treated. To date, we have identified only 16 studies from 7 countries covering 582 patients undergoing 1327 PIPAC deliveries. The use of PIPAC in a trail setting is the way forward to evaluate the efficacy of this procedure.

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

X ☐ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares	☐	**YES**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

of the healthcare industry	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Pressurised intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis**
Name of Specialist Advisor:	Jamie Murphy
Specialist Society:	Association of Coloproctology of Great Britain and Ireland

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

☒ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

The expertise in the UK at present with this technique is limited – I have performed the procedure 5 times on two patients, under the auspices of a clinical trial. The only other centre in the UK who has any experience of this procedure is University of Wales who have a similar level of experience as I do.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☒ I take part in patient selection or refer patients for this procedure regularly.

Comments:

As lead clinician for the Imperial College Peritoneal MDT I have been involved in the selection of patients for PIPAC since December 2018 when approval was granted for our clinical trial to begin.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☒ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

My group are in the process of publishing a review article that concludes - 'In a terminally ill population, PIPAC may be able to offer localised histopathological regression of peritoneal metastases whilst remaining relatively safe and well tolerated, assuming a given patient's baseline performance status is sufficient to allow for repeated procedures. Correlation with longer term clinical outcomes is not yet available and there is an absence of controlled or randomised studies.'

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

PIPAC is definitely a novel procedure but a number of further studies will be necessary to establish the role of this procedure in the hierarchy of treatments available for peritoneal cancer. However, the published literature is clear that it is safe for both patients and their caregivers, assuming the appropriate training has been received.

It is important to remember that PIPAC is being used to treat a cohort of patients who are unlikely to be cured of their metastatic cancer and thus the most appropriate outcome measures for future studies investigating PIPAC are likely to be quality of life, complication rates, overall survival and as part of the NICE appraisal cost must inevitably be considered.

To my mind the main outstanding issues that should guide future trials assessing PIPAC are: what is the most efficacious chemotherapy regimen for PIPAC; what the dose(s) of the PIPAC chemotherapy agent(s) should be; what additional benefit PIPAC confers above systemic chemotherapy; how PIPAC compares to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy; if patients with low peritoneal cancer index scores or high scores more likely to benefit from PIPAC; the role of PIPAC in patient cohorts with low volume extra abdominal metastases;

and, the inclusion / exclusion criteria that should be used to select patients for PIPAC.

3.2 What would be the comparator (standard practice) to this procedure?

Systemic chemotherapy with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy being used for a small proportion of these patients also.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

At the present time only 2 centres in UK offer this treatment – Imperial College and University of Wales.

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

I have attached a table from our forthcoming systematic review – I would appreciate if this was not made public yet as has not been accepted for publication.

2. Anecdotal adverse events (known from experience)

From my experience thus far the only complications the patients I have treated have had were constipation and nausea for one patient each; however, the patients reported that they had previously suffered from these symptoms after general anaesthesia and chemotherapy, respectively.

3. Theoretical adverse events

Complications related to accessing the peritoneum (bleeding or injury to viscera) that might mandate laparotomy either at the time of the procedure or as an emergency, complications relating to the chemotherapy agents (anaphylaxis, extravasation into tissues), life threatening massive tumour lysis (thus far only reported for mesothelioma) that is best thought of as being equivalent to reperfusion injury after

ischaemia, safety breaches in theatre causing exposure of staff to chemotherapy agents.

4.2 What are the key efficacy outcomes for this procedure?

I have outlined these in 3.1

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Yes – the efficacy of this procedure at present is uncertain. I have outlined the major issues in 3.1

4.4 What training and facilities are needed to do this procedure safely?

A laminar flow operating theatre is generally required for this procedure, although there is a French publication outlining a technique to use this procedure in theatres that do not have this. At present there is only one supplier (Capnomed) of the device needed for PIPAC and in order to buy this device a named surgeon is needed who has attended a company approved 3-day training course. I am aware of at least one manufacturer who is developing a similar device but as yet the training programme that will be required to buy that device has not been established.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Imperial College has established a clinical trial to investigate the efficacy of PIPAC for patients with colorectal cancer - ClinicalTrials.gov Identifier: NCT03868228, which the University of Wales group is likely to join. A group of surgeons from different institutions around UK have recently formed a group named 'PIPAC-UK', with the express aim of establishing further PIPAC trials which will require a number of other centres to be able to offer this procedure in order that patient recruitment to future trials occurs in a timely fashion. This group is also proposing to establish a UK PIPAC registry. An international PIPAC registry already exists – PIPACRegis ClinicalTrials.gov Identifier: NCT03210298.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

There is a case series (n=3) that will be reported in near future indicating that PIPAC in the presence of luminal stents may result in perforation and peritonitis and that this should be an exclusion criterion.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Electrostatic precipitation is a modification of PIPAC. The additional benefit of this over 'conventional' PIPAC is thus far untested.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

This would be best undertaken by a committee of experts who would design the proposed UK registry. From my perspective a minimum dataset would include: age; gender; sex; disease process; radiological and laparoscopic peritoneal cancer index; prior lines of systemic chemotherapy; concomitant systemic chemotherapy; presence of extra peritoneal metastases; chemotherapy agent(s) utilised for PIPAC; number of PIPAC procedures per patient before this discontinued; primary and secondary non access rates; morbidity as per CTCAE complication scores; procedure related mortality (will require careful definition given terminally ill population); quality of life scores; peritoneal progression free survival; and, overall survival.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Previously outlined in 3.1

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

90 day CTCAE complication scores

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

I believe the procedure will not significantly spread out with the existing established Peritoneal Malignancy centres – Imperial, Cardiff, Christie, Basingstoke, Birmingham. The reason for this is expert peritoneal disease MDT decision making will be required to identify which patients may be PIPAC candidates, as opposed to other treatment options.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☒ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

As above

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☒ Major.

☐ Moderate.

☐ Minor.

Comments:
It potentially could be the case that thirty percent of gastric cancer, ten percent of colorectal cancer, forty percent of ovarian cancer, twenty percent of pancreatic cancer and all patients with peritoneal mesothelioma could be PIPAC candidates.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

X I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☒	**YES**
	☐	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Comments:
My only decleration in that I have a PhD student who is studying this technology and that he will soon publish his systematic review

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 **Personal family interest**

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 **Personal non-pecuniary interests**

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

Before completing this questionnaire, please read Conflicts of Interest for Specialist Advisers. Certain conflicts exclude you from offering advice, however, please return the questionnaire to us incomplete for our records.

Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Pressurised intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis**
Name of Specialist Advisor:	Professor Jared Torkington
Specialist Society / Royal College:	Association of Coloproctology of Great Britain and Ireland

1 Do you have adequate knowledge of this procedure to provide advice?

x Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

x Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

x Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

Relevant to gynaecology and general surgery

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☐ I have never done this procedure.

x I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

To my knowledge there are only two units in the UK with experience of doing this procedure – ourselves (5 cases) and Imperial (2 cases)

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

x I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

x I have done bibliographic research on this procedure.

x I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

X Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Safety is established – efficacy requires further research

3.2 What would be the comparator (standard practice) to this procedure?

Weak comparator but intravenous/systemic chemotherapy or intraperitoneal chemotherapy via a catheter

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

x Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

There is wide interest and we have established a PIPAC UK working group

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Those related to any form of laparoscopic surgery

Allergic reactions

2. Anecdotal adverse events (known from experience)

Sclerosing peritonitis

(case reports)

3. Theoretical adverse events

Theatre contamination affecting staff

4.2 What are the key efficacy outcomes for this procedure?

Survival; morbidity and mortality, Quality of life

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

There are uncertain – one

4.4 What training and facilities are needed to do this procedure safely?

Courses for training, preceptorship
Laminar flow theatre, high pressure injector and currently capnopen

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Numerous worldwide (all registered on Clinicaltrials.gov)
Only one in UK based at Imperial College

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

Nil else

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

No

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

Progression free survival

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

No abdominal access possible
Surgical related and chemotherapy related morbidity

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

quickly due to patient demand

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

x Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

x Moderate.

☐ Minor.

Comments:
Difficult to predict expansion beyond peritoneal disease but may have a role in neo-adjuvant and protection against recurrence

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

nil

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

xI have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above. For more information about how we process your personal data please see our privacy notice.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

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Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	**X**	**YES**
	☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	**X**	**YES**
	☐	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	X	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	X	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	X	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	X	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	X	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:
I have been involved in the development of an instrument called Ultravision that is used for clearing smoke in laparoscopic surgery. This has led to a spinout company in which I have a very very small sharehold. This instrument has attracted interest to be used regularly as part of the PIPAC procedure

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional **Mark Campbell**
Acting Programme Director

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Procedures Advisory Committee Chair Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

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2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

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3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

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5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Specialist Adviser questionnaire

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Please respond in the boxes provided.

Please complete and return to: azad.hussain@nice.org.uk and IPSA@nice.org.uk

Procedure Name:	**Pressurised intraperitoneal aerosol chemotherapy for peritoneal carcinomatosis**
Name of Specialist Advisors:	Sanjeev Dayal & Alexios Tzivanakis
Specialist Society:	British Society of Gastroenterology (BSG)

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

Comments:

In 2018-19 we had **738** peritoneal malignancy referrals which were discussed in our weekly CRAM and SMDT meetings and patients where cytoreduction surgery and hyperthermic chemotherapy (CRS and HIPEC) was likely to benefit were offered this procedure. We performed **322** CRS and HIPEC procedures in 2018-19. In our SMDT we do come across patients who are unlikely to benefit from CRS and HIPEC but where PIPAC could be a treatment option. Ours is a unit where we have performed over 2500 peritoneal malignancy operations to date.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next 2 questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure, please answer question 2.2.2.

2.2.1 If you are in a specialty that does this procedure, please indicate your experience with it:

☒ I have never done this procedure.

☐ I have done this procedure at least once.

☐ I do this procedure regularly.

Comments:

We have completed the PIPAC course and are trained to perform the procedure.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☒ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have done bibliographic research on this procedure.

☐ I have done research on this procedure in laboratory settings (e.g. device-related research).

☐ I have done clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☒ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Safety has been proven in literature within the confines of a Registry or a Trial.

3.2 What would be the comparator (standard practice) to this procedure?

Cytoreduction Surgry and Hyperthermic Peritoneal Chemotherapy.

3.3 Please estimate the proportion of doctors in your specialty who are doing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What is the potential harm of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Adverse events reported in the literature (if possible please cite literature)

Grass et al 2017: Systemic Review of Literature-Complication rate (CTCAE). Most common abdominal pain and nausea - CTCAE (Grade 1-2) 0-12%; Grade 3-5 0-37%; however highest rate of complications described when CRS was combined with PIPAC.

Kurtz et al 2018: Reported on the registry data – 2.8% intraoperative complication rate and 4.9% postop complication rate.

Peritoneal Sclerosis (Graveresen M et al 2018, reported 2 cases)

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Potential efficacy on disseminated Ovarian, Colorectal, Mesothelioma, Appendix and Gastric peritoneal malignancy.
Giger-pabst U et al 2018 Mesothelioma
Tempfer C et al 2018 Ovarian
Demtrodr C et al 2016 Colorectal
Sgarbura O et al 2019
Grass F et 2017 Systemic Review

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

The evidence is based on Registry and Phase 1 & 2 trails and small numbers of patients. Randomized trails are ongoing.

4.4 What training and facilities are needed to do this procedure safely?

Standardized PIPAC courses which are now readily available. These courses are organised and the training provided by the pioneers of the procedure. It is mandatory to do the course before given access to the equipment needed to perform it. There is also now a standardized safety check list that has to be completed before the procedure can be undertaken.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

15 trials listed on www.clinicaltrials.gov (accessed 6.6.19)

Registry: PIPAC-ICH GCP NCT 03210298

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, for example PUBMED? (This can include your own work). If yes, please list.
Please note that NICE will do a literature search: we are only asking you for any very recent or potentially obscure abstracts and papers. Please do not feel the need to supply a comprehensive reference list (but you may list any that you think are particularly important if you wish).

No

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

No

5 Audit Criteria
Please suggest a minimum dataset of criteria by which this procedure could be audited.
As set out in the Registry.

5.1 Outcome measures of benefit (including commonly used clinical outcomes, both short and long - term; and quality-of-life measures). Please suggest the most appropriate method of measurement for each:

As set out in the Registry.

5.2 Adverse outcomes (including potential early and late complications). Please state timescales for measurement e.g. bleeding complications up to 1 month post-procedure:

As set out in the Registry.

6 Trajectory of the procedure

6.1 In your opinion, how quickly do you think use of this procedure will spread?

Procedure should be limited to centres who have experience treating peritoneal malignancy patients.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☒ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

☒ Moderate.

☐ Minor.

Comments:

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8. Data protection, freedom of information and conflicts of interest

8.1 Data Protection

The information you submit on this form will be retained and used by the NICE and its advisers for the purpose of developing its guidance and may be passed to other approved third parties. Your name and specialist society will be published in NICE publications and on the NICE website. The specialist advice questionnaire will be published in accordance with our guidance development processes and a copy will be sent to the nominating Specialist Society. Please avoid identifying any individual in your comments.

☑ I have read and understood this statement and accept that personal information sent to us will be retained and used for the purposes and in the manner specified above and in accordance with the Data Protection Act 1998.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Nothing in your submission shall restrict any disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

Please submit a conflicts of interest declaration form listing any potential conflicts of interest including any involvement you may have in disputes or complaints relating to this procedure.

Please use the "Conflicts of Interest for Specialist Advisers" policy as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if needed from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares	☐	**YES**

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

of the healthcare industry	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds that include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – for example have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements, please describe the nature of the conflict(s) below.

Comments:

Thank you very much for your help.

Dr Tom Clutton-Brock, Interventional Procedures Advisory Committee Chair

Mark Campbell
Acting Programme Director
Devices and Diagnostics

June 2018

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.