NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name: **Preoperative high dose rate brachytherapy for rectal cancers (342/2)**

Name of Specialist Advisor: **Dr Andrew Weaver**

Specialist Society: **Royal College of Radiologists**

Please complete and return to: azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

CONFIDENTIAL

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 two 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 which does this procedure, please indicate your experience with it:

☒ I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

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 undertaken bibliographic research on this procedure.

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

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

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

☐ Other (please comment)

Comments:

CONFIDENTIAL

General interest in the local therapy of rectal cancers by surgery, radiotherapy (EBRT, contact and HDR Brachytherapy)

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 that procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

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

Local surgical excision (TEM) +/- external beam radiotherapy

3.3 Please estimate the proportion of doctors in your specialty who are performing 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:

CONFIDENTIAL

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

Rectal pain during and after procedure - 36% experience moderate to severe pain

Rectal or bladder perforation ~ 10%

Mucosal damage causing ulceration and bleeding 10%

Stenosis of the rectal lumen or small bowel ~ 10%

Fistula formation between the rectum and the bladder or the vagina, ~ 15%

Skin Changes on perineum.5%

2. Anecdotal adverse events (known from experience)

Small bowel stricture

Persisting proctitis

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

Rectal pain, rectal bleeding, rectal fistula formation, small bowel obstruction and perforation, proctitis, anastomotic stricture, cerebrovascular accident.

4.2 What are the key efficacy outcomes for this procedure?

Sphincter preservation rate compared with conventional therapy, quality of life (including long-term bowel function), local recurrence rates, disease-free survival and overall survival

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

Unclear how safe the procedure is in terms of local recurrence, disease free and overall survival, compared with conventional therapy

4.4 What training and facilities are required to undertake this procedure safely?

A radiotherapy centre requires specialized equipment – High dose rate machine and specific rectal applicators. Clinicians need to undergo training both in terms of endoscopy and identifying the rectal tumours and the use of the rectal applicators

CONFIDENTIAL

which will be inserted into the patient, as well as prescribing the treatment and understanding the physics of brachytherapy treatments

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

I am not aware of any currently in the UK. There is a proposal for the few centres who have contact radiotherapy available to undertake randomised trials to help provide a stronger evidence base for this type of therapy (OPERA and CONTEM-5)

CONFIDENTIAL

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, e.g. PUBMED? (This can include your own work). If yes, please list.

The experience of pain and anxiety in rectal cancer patients during high-dose-rate brachytherapy. Néron, Perez, Benc, Bellman, Rosberger , Vuong . Curr Oncol. 2014 Feb;21(1):e89-95. doi: 10.3747/co.21.1741

HDR brachytherapy of rectal cancer using a novel grooved-shielding applicator design. Webster MJ1, Devic S, Vuong T, Han DY, Scanderbeg D, Choi D, Song B, Song WY. Med Phys. 2013 Sep;40(9):091704. doi: 10.1118/1.4816677.

Salvage high-dose-rate interstitial brachytherapy for locally recurrent rectal cancer: long-term follow-up results.
Morimoto M1, Isohashi F, Yoshioka Y, Suzuki O, Seo Y, Ogata T, Akino Y, Koizumi M, Ogawa K. Int J Clin Oncol. 2014 Apr;19(2):312-8. doi: 10.1007/s10147-013-0567-0. Epub 2013 Jun 1.

Dynamic modulated brachytherapy (DMBT) for rectal cancer.
Webster MJ[1], Devic S, Vuong T, Yup Han D, Park JC, Scanderbeg D, Lawson J, Song B, Tyler Watkins W, Pawlicki T, Song WY. Med Phys. 2013 Jan;40(1):011718. doi: 10.1118/1.4769416.

Short-term outcome after neoadjuvant high-dose-rate endorectal brachytherapy or short-course external beam radiotherapy in resectable rectal cancer.
Hesselager C1, Vuong T, Påhlman L, Richard C, Liberman S, Letellier F, Folkesson J. Colorectal Dis. 2013 Jun;15(6):662-6. doi: 10.1111/codi.12193.

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):

Sphincter preservation, local recurrence and distant recurrence. Disease free and overall survival

5.2 Adverse outcomes (including potential early and late complications):

Incidence of bleeding, perforation, bowel obstruction, perineal skin chages

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

CONFIDENTIAL

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:

Many centres already have a HDR machine but few will have the rectal applicators

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:

CONFIDENTIAL

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

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

CONFIDENTIAL

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required 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:

---

[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).

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 which include investments in the healthcare industry	☐ **YES** ☒ **NO**
Do you have a **personal non-pecuniary** interest – eg 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:

I undertake a regular private practice clinics

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

CONFIDENTIAL

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

CONFIDENTIAL

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

CONFIDENTIAL

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.

CONFIDENTIAL

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Preoperative high dose rate brachytherapy for rectal cancers (342/2)**
Name of Specialist Advisor:	**Ayan Banerjea**
Specialist Society:	**Association of Coloproctology of Great Britain and Ireland**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

CONFIDENTIAL

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: I have agreed to contribute to this topic after discussion with Professor Campbell. This is a Colorectal Surgeon's view of a technology delivered by Oncologists.

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:

This procedure is used in the management of rectal cancer

The next two 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 which does this procedure, please indicate your experience with it:

X I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

Use of HDR brachytherapy for rectal cancer is described for therapy in conjunction with surgery, or in some cases without. I perform surgery – local and radical – in patients that may have had radiotherapy but I have no direct experience of patients treated with this type of radiotherapy.

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.

X 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:

I am part of our Colorectal Cancer MDT. I have also established our Early Rectal Tumour MDT and we have an established Contact radiotherapy service. However, we have no Endorectal HDR brachytherapy service.

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

☐ I have undertaken bibliographic research on this procedure.

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

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

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

CONFIDENTIAL

☐ 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 that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

None of the above apply.
This is not a new procedure but has not been practised widely in the UK. It is more than a minor variation on standard radiotherapy commonly used for rectal cancer in the UK.
There is limited published literature largely emanating from the US.

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

HDR Brachytherapy may have a number of different roles:

1. Treatment for rectal cancer in those unfit for any surgical or endoscopic intervention, who have already had pelvic radiotherapy.
2. Treatment for rectal cancer in a neo-adjuvant setting instead of long or short course external beam radiotherapy, with or without chemotherapy.
3. HDR brachytherapy might be used to boost standard radiotherapy given to rectal cancer not immediately amenable to curative surgical resection at the time of diagnosis and staging. Radiotherapy is given to improve resectability. This may yield a complete clinical response, the management of which is uncertain. The concept of "watch & wait +/- salvage surgery" in this setting should be compared with immediate surgery.
4. Treatment for early rectal cancer in those who are fit but in whom radical surgery may be over-treatment. Here, HDR brachytherapy (perhaps in combination with Transanal Endoscopic local excision) should be compared with radical resection: Anterior resection or abdominoperineal excision. Such comparison should include cancer disease-free survival and overall survival, but perhaps more importantly Quality of life measures that include stoma rates and urine, bowel and sexual dysfunction.

CONFIDENTIAL

3.3 Please estimate the proportion of doctors in your specialty who are performing 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.

X Cannot give an estimate.

Comments:

I am not aware of this technique being used in the UK.

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

No deaths reported/no rectal perforation reported that I am aware of.

2. Anecdotal adverse events (known from experience)

I have no experience.

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

Adverse effects might be largely consistent with those of standard radiotherapy: radiation proctopathy, altered bowel habit and rectal bleeding. HDR brachytherapy alone may yield fewer side effects than standard radiotherapy alone due to localisation effect – standard radiotherapy irradiates a larger field.

Hesselager et al (Colorectal Dis. 2013 Jun;15(6):662-62013) report higher rates of cardiovascular problems compared to short course radiotherapy but not compared to a group that had no radiotherapy at all.

CONFIDENTIAL

4.2 What are the key efficacy outcomes for this procedure?

See 3.2 – this treatment may be used in different settings.

Complications of surgery
Histopathological outcomes of surgery
Disease control – local recurrence, distant recurrence, disease-free survival, overall survival.
Permanent stoma rate
Bowel, urinary and sexual function.
Quality of life.

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

Not all rectal cancers respond to this treatment initially and this cannot be predicted – also true of standard radiotherapy.
Long term control rates using this treatment requires wider study as current literature is limited.
There is wide variation in the use of radiotherapy for rectal cancer in the UK already – the role of HDR brachytherapy needs to be evaluated within this context.

4.4 What training and facilities are required to undertake this procedure safely?

I am unable to comment.

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

I am not aware of any in the UK.

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, e.g. PUBMED? (This can include your own work). If yes, please list.

No

CONFIDENTIAL

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

There is uncertainty about the role because of a lack of high-quality evidence. There are many unanswered questions currently about the role of radiotherapy in rectal cancer, and HDR brachytherapy is one branch of a wider debate. However, it is a promising modality that needs further evaluation in a few centres with good audit. The heterogeneity of patient factors, disease properties and treatment modalities shall make clean comparisons in randomised trials difficult to attain.

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):

Overall and disease free survival
Reduction of stoma/stoma complications
Reduction of complications from resectional surgery
Reduction of disturbance in:
    Bowel function: continence and frequency
    Urinary function: continence and frequency
    Sexual function: impotence and sensation
Faster return to normal activity
Lower rates of depression/anxiety/poor body image

5.2 Adverse outcomes (including potential early and late complications):

Complications after surgery
Local recurrence
Systemic recurrence

CONFIDENTIAL

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Slow until further evidence available.

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:

Initially, this should be evaluated in a few centres only to clarify its role. Thereafter, between 10 and 20 centres will be required across the UK to provide adequate service provision.

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:

X Major.

☐ Moderate.

☐ Minor.

Comments:

Rectal cancer is common.

CONFIDENTIAL

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?

No.

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required 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:

[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).

CONFIDENTIAL

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐ X	YES 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	☐ X	YES NO
Investments – any funds which include investments in the healthcare industry	☐ X	YES NO
Do you have a **personal non-pecuniary** interest – eg 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?	☐ X	YES NO

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

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

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

CONFIDENTIAL

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

CONFIDENTIAL

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

CONFIDENTIAL

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.

CONFIDENTIAL

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Preoperative high dose rate brachytherapy for rectal cancers (342/2)**
Name of Specialist Advisor:	**Prof Sun Myint**
Specialist Society:	**Association of Coloproctology of Great Britain and Ireland**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

CONFIDENTIAL

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?

☐ Yes.

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

Comments:

We should drop the word 'Pre-operative' and just say 'High dose rate brachytherapy for rectal cancers'
Although it initially started as pre-operative procedure, we now (more commonly) use this for non-operative treatment for more advanced rectal tumours in elderly and medically unfit patients. Contact x-ray brachytherapy (Papillon) is normally use for early stage rectal cancers.

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?

X☐ 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:

See my comments below

The next two 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 refer patients for the procedure please answer question 2.2.2.

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

☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

X☐ I perform this procedure regularly.

Comments:

We have performed this procedure at Clatterbridge for over 20 years. First with Novi Sad rectal applicator then with OncoSmart @ applicator.
Approximately over 200 patients radical (RT alone), Palliative and pre-operative.

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.

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

Comments:

There are 4 centres in the UK offering this procedure. Apart from our centre at Clatterbridge, Prof Peter Hoskin at Mount Vernon in London, Prof Sebag Montefiore from Leeds and Dr Alex Stewart at Guildford also offer this procedure. I refer patients to them who live closer home to these centres after I reviewed them for second oncology opinion for consideration of this procedure

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

☐ I have undertaken bibliographic research on this procedure.

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

CONFIDENTIAL

X☐ I have undertaken 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:

BRACA -2 was a small non randomised trial done at Clatterbridge to evaluate the efficacy of this procedure prior to surgery

Sun Myint et al Colorectal Disease (2010); 12:30-36

Under the auspices of GEC ESTRO we are planning a trial of HDR rectal brachytherapy for elderly, medically unfit patients with advanced rectal cancer

Several papers from Dr Te Vuong (Montreal) Single Institutional experience

Danish randomised trial

Int J Radiat Oncol Biol Phys. 2012 Nov 15;84(4):949-54. doi: 10.1016/j.ijrobp.2012.02.006. Epub 2012 May 15.

3 Status of the procedure

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

☐ Established practice and no longer new.

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

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

Rectal brachytherapy is not new but there is revival of interest in this procedure due to production of new applicators by Nucletron (Elekta). There are few centres around the world offering this procedure apart from the UK (mainly in Denmark, Canada and Holland)

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

1. Pre-operative external beam radiotherapy prior to Surgery

2. Contact x-ray brachytherapy (Papillon) suitable only for early rectal cancer and small minimal residual disease following external beam chemo radiotherapy (good responders) for advanced rectal cancers

CONFIDENTIAL

3.3 Please estimate the proportion of doctors in your specialty who are performing 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:

See my other comments

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

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

1. Theoretical adverse events

Proctitis (rectal inflammation)

Rectal perforation

Rectal ulceration

2. Anecdotal adverse events (known from experience)

Rectal fistulation (rare)

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

Proctitis

Bleeding

Rectal Pain

Please see publications submitted

HDR chapters in Clinical Oncology (2007);19: 9711-719 ; 701-705; 706-710

CONFIDENTIAL

4.2 What are the key efficacy outcomes for this procedure?

Improve R0 resection rates in CRM involved or threatened rectal cancer in patients fit for surgery

Improve local control following external beam radiotherapy especially in patients not medically fit for surgery

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

There is only one randomised trial from Denmark not showing Improve pCR (complete pathological response) which was its end point but show some benefit in T3 tumours in terms of improved Ro resection rates. . The brachytherapy boost dose was inadequate in this trial.

Others including our own study at Clatterbridge showed increased in pCR (30%) compared to external beam alone (15-20%)

4.4 What training and facilities are required to undertake this procedure safely?

There are brachytherapy courses at Clatterbridge, Montreal and Leiden for clinicians who wish to be trained up in rectal brachytherapy

HDR brachytherapy machine is available in most centres which offer gynaecological brachytherapy. There are two types of rectal brachytherapy applicators one flexible (OncoSmart@) and the other rigid rectal applicator with or without central shielding.

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

A randomised trial funded by Industry currently ongoing in USA

A randomised trial proposed by Montreal group for elderly medically unfit patients

HERCULES (UK proposed trial on hold)

A randomised trial

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, e.g. PUBMED? (This can include your own work). If yes, please list.

CONFIDENTIAL

A special issue on 'Radiotherapy in early rectal cancer' was commissioned by Prof Peter Hoskin on behalf of the Royal College of Radiologists and I was the editor of this special issue. I invited all the world leading experts in rectal brachytherapy to contribute. Dr Te Vuong from Montreal and Prof Corrie Marijnen from Leiden contributed in addition to my own review article on this subject. The Special edition was published as volume 19 Number 9 in November 2007.
A full list of recent publications on rectal HDR brachytherapy has been submitted to IP Team 342/2 at NICE (Oct- December) 2014.

Dose searching study from Leiden known as HEBBERT trial evaluate the optimal dose for HDR brachytherapy. They recommended 7Gy in 3 fractions as optimal dose. The result were only published as abstracts and no data has been published, so far.

A randomise Danish trial has been carried out and results published in 2012.

Int J Radiat Oncol Biol Phys. 2012 Nov 15;84(4):949-54. doi: 10.1016/j.ijrobp.2012.02.006. Epub 2012 May 15.

Dose-effect relationship in chemo-radiotherapy for locally advanced rectal cancer: a randomized trial comparing two radiation doses.

Jakobsen A[1], Ploen J, Vuong T, Appelt A, Lindebjerg J, Rafaelsen SR.

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

Most colorectal MDT in the UK does not offer HDR brachytherapy in the UK. There are only few centres that have this facility –Clatterbridge, Mount Vernon, Guildford and Leeds. Most so called colorectal oncologist in the UK are not trained to use this procedure as this is not part of the standard of care for rectal cancer and not recommended in any of the colorectal guide lines including those of NICE (2011) Most colorectal oncologist offer external beam alone for advanced rectal cancer in elderly and medically unfit patients with short term benefit. In most cases local recurrence occurred within 12-18 moths and they are referred to palliative care services. Some patients survive for many years resulting in agonising death from local progression which puts extra burden on palliative care services

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):

Patients who had surgery

1. R0 (clear resection margins) rate
2. Complete pathological response (pCR) or minimal residual disease (both has shown to improve disease free survival)

Patients who do not have surgery

CONFIDENTIAL

1. Local control
2. Progression free survival
3. Quality of Life

5.2 Adverse outcomes (including potential early and late complications):

Early complications

1. **Proctitis**
2. **Frequency of bowel movements**
3. **Bleeding**

Late complications

1. **Pain in the rectum**
2. **Bleeding**
3. **Rectal stricture**
4. **Rectal fistula (rare)**

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

We are training HDR brachytherapy to all centres who attended contact x-ray (Papillon) training. HDR machines are available in most radiotherapy centres offering gynaecological brachytherapy and no additional machines are required for rectal brachytherapy. There are reusable rigid rectal applications which are commercially available and flexible multichannel ones are single use for each patient which cost around 2-3K.
The Royal College of Radiologists run annual brachytherapy courses and I teach on this course. Those clinicians who wish to be trained up can contact me for period of clinical attachment.

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:

All centres offering contact x-ray brachytherapy should have this facility for more advanced rectal cancers (See my comments below)

CONFIDENTIAL

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:

There are many elderly patients with advanced rectal cancer. Average age of patient with rectal cancer is above 70 years and many have comorbidities. Most patients with mid low rectal cancer were offered APER. (Unacceptable variations in APER rates for rectal cancer: Time to intervene? Morris et al. Gut (2008); 57:1690-1697.Many patients are just offered external beam radiotherapy alone with poor outcomes. HDR brachytherapy boost if offered can improve local control but this is not recommended as standard of care. Therefore, most patients when relapse are referred to palliative care services with increased financial and logistic burden on provider services in the NHS.

Approximately, 1000-2000 additional potential patients can benefit from this procedure. We need about 10-15 centres with this facility around the country. All centres offering contact x-ray brachytherapy should have HDR brachytherapy facility for more advanced rectal tumour not suitable for contact x-ray brachytherapy.

CONFIDENTIAL

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?

The concept of rectal cancer management has changed drastically in the last few years with more colorectal units adopting a watch and wait approach rather than offering surgery upfront. HDR brachytherapy when it was first available about 10 years ago, initially used this as pre-operative treatment for locally advanced rectal cancer which were still bulky or involving more than half the circumference or still threatening CRM following preoperative chemo radiotherapy. The current practice is to use this modality to improve local control in patients who are not offered surgery upfront because of advancing age or medical comorbidities. Therefore, the term pre-operative HDR brachytherapy should not be use and this treatment should simply be referred to as ‘HDR rectal brachytherapy’.

This treatment should not be confused with contact x-ray brachytherapy (Papillon) which is use for much earlier staged rectal cancers (T1/T2) and some T3a and T3b cancers which are responders with minimal residual disease (2cm) following chemo-radiotherapy (good responders).

There are number of publications on surgical 30 days, 6 months and one year mortality showing increased death rates in elderly patients up to 50% in some reports. Many surgeons are reluctant to offer these patients surgery even with advanced disease when they respond well to chemo radiotherapy or radiotherapy alone and adopt a ‘Watch and wait ‘policy. There are several publications from Sao Paulo and Maastricht on this subject. Many UK publications on this subject from MERCURY group, Clatterbridge brachytherapy group and Northwest Colorectal group are expected this year

CONFIDENTIAL

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information

is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

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

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required 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**
	X ☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	X ☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	X ☐	**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 which include investments in the healthcare industry	☐	**YES**
	X ☐	**NO**
Do you have a **personal non-pecuniary** interest – eg 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**

[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).

CONFIDENTIAL

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:

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

CONFIDENTIAL

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, pension 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

CONFIDENTIAL

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 healthcare industries 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

CONFIDENTIAL

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.

CONFIDENTIAL