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:	**Transcatheter valve-in-valve implantation for aortic bioprosthetic valve dysfunction**
Name of Specialist Advisor:	Uday Trivedi
Specialist Society:	The Society for Cardiothoracic Surgery in 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:

This procedure is performed in patients who have had previous cardiac surgery where a tissue heart valve has been implanted in the aortic position. The standard procedure is a repeat operation, but in higher risk cases this valve-in-valve TAVI is now an option. The long term outcome of TAVI valves remain unknown and as such this procedure should not be offered to young patients.

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:

It is a straightforward TAVI type procedure but cannot be used with all types of TAVI valves.

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:

Referrals are always made through a MDT process.

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:

The procedure sits somewhere in-between these descriptions. For the elderly and high risk it is effective and safe but one cannot say this for all patients. It still has a big risk of patient-prosthesis mismatch. Repeat surgery will remove the older valve and replace it with one of the same size. It also allows one to make the annulus larger to implant a bigger valve. The valve-in-valve procedure will put a smaller valve in than with open surgery.

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

Repeat cardiac surgery

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)

The complications are similar to TAVI, access issues, para-valvar leaks, stroke and pacemaker need. In addition there is a risk of PPM as the TAVI valve has to fit into the old tissue valve. Coronary artery occlusion.

2. Anecdotal adverse events (known from experience)

Femoral & iliac vessel injury. Pacemaker implantation. Coronary ostium occlusion.

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Avoidance of repeat surgery and associated mortality and morbidity

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

May not be effective in the small valve sizes. High risk of mismatch and residual symptoms and cardiac failure.

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

Neds to be done in a TAVI centre with cardiac surgery on-site. All cases need to go through a formal MDT meeting.

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

Data is collected as part of the TAVI dataset by BCIS.

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 sufficient literature already published.

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

Long-term outcomes are not known. Younger patients may be falsely reassured into have the wrong valve implanted in the hole that future surgery will not be required.

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:

Mortality, major morbidity such as stroke, bleeding, resolution of symptoms, improvement in myocardial performance, improvement in quality of life and life expectancy.

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:

Valve failure, residual stenosis, para-valvar leak, valve embolization,

6 Trajectory of the procedure

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

Nearly all TAVI centres have done these procedures.

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?

This procedure should not be used in determining the valve choice at the time of the first procedure. The mid and long -term results remain uncertain, particularly in younger patients.

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 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:
I have not had much time to complete this form and had to do it today in less than an hour.

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

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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:	**Transcatheter valve-in-valve implantation for aortic bioprosthetic valve dysfunction**
Name of Specialist Advisor:	Marjan Jahangiri
Specialist Society:	The Society for Cardiothoracic Surgery in 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.

X☐ 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 performed by cardiologists. However, treating a failed bioprosthetic valve can also be done by redo cardiac surgery. This latter has been the norm practice worldwide before the advances made in TAVI.

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:

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.

X☐ 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.

☐ 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: I have reviewed articles on this procedure.

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:

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

Redo cardiac surgery for failed bioprosthetic valve.

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:

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)

Thrombosis, reduction of valve area giving rise to patient prosthesis mismatch, need for dual anti-platelet therapy and possibly anti-coagulation and its side effects.

2. Anecdotal adverse events (known from experience)

3. Theoretical adverse events

4.2 What are the key efficacy outcomes for this procedure?

Potentially lower morbidity and mortality compared to redo surgery

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

See 4.1.1.

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

As per standard TAVI procedure.

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

Only case series.

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).

TVT registry (comparing valve-in-valve with surgery); 5 yr follow-up of Partner II

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

The morbidity and the complications of the procedure have to be assessed properly. Not just comparing it with surgery. But, analysing the actual procedure and its complications in detail. The reason is that many younger patients undergoing first time heart valve surgery are now being promised a tissue valve as opposed to a mechanical valve, in the hope that they can have 'redo' procedure of TAVI valve-in-valve when the bipoprosthetic tissue valve fails. The risk and benefits of all this have to be properly assessed with appropriate informing and consenting of patients.

5 Audit Criteria

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

Reviewing the current literature. The current UK database is too small to produce any meaningful results.

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:

Procedural outcomes: length of procedure, paravalvular leak, valvar gradient, management of concomitant coronary artery disease, the number of procedures patient subjected to, any coronary occlusion problems

Short and long term outcomes: success of the procedure as assessed by valve function, paravalvar lead, PPM, bleedings, thrombosis and panus formation on the prosthesis, QOL measured by standard cardiac testing.

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 above

6 Trajectory of the procedure

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

3-5 years

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

☐ Most or all district general hospitals.

☒ **X** A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

The selection of patients and the risk and benefits have to weighed against surgery.

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:

I believe that this is a very important guideline, since it would determine the use of type of vale in first time aortic valve surgery patients.

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?

Please see above.

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.

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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 - NO

☐ **NO**

Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice- NO**

☐ **YES**

☐ **NO**

Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry - NO

☐ **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 **-NO**

☐ **YES**

☐ **NO**

Investments – any funds that include investments in the healthcare industry - NO

☐ **YES**

☐ **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).

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? NO

☐ **YES**

☐ **NO**

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

Fellowships endowed by the healthcare industry - NO

☐ **YES**

☐ **NO**

Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts - NO

☐ **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:	**Transcatheter valve-in-valve implantation for aortic bioprosthetic valve dysfunction**
Name of Specialist Advisor:	John Rawlins
Specialist Society:	**British Cardiovascular Intervention Society (BCIS)**

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

Yes.

1.1. Does the title used above describe the procedure adequately?

Yes.

Comments:
Conventionally this procedure is termed Valve-in-valve TAVI

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.

Comments:
There are cardiac surgeons involved in TAVI programs across the UK, and some perform TF TAVI (including valve in valve implantation). However, in all centers there is close working relationships between surgeons and cardiologists and there is little evidence of inter-specialty controversy.

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 do 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 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.

Comments:

3. Status of the procedure

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

Established practice and no longer new.

Comments:
Valve in valve TAVI has become established practice in TAVI.

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

Re-do aortic valve surgery requiring repeat sternotomy.

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.

Comments:

This statement assumes that the term specialists encompasses an Interventional Cardiologist with a specialist interest in TAVI. This comprises around 20% of the interventional cardiology community in the UK.

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);

   There are two major adverse events that are increased in likelihood during a valve-valve TAVI:

Coronary Obstruction - depending upon the original valve implanted, there is an increased risk of coronary obstruction when compared with standard TAVI implantation. In particular, surgical valves that have the leaflets mounted on the outer surface of the posts (e.g. Trifecta) have an increased risk of obstruction (1).

Patient-prosthesis mismatch - again this is dependent upon the size and design of the original valve implanted. It is more frequently encountered when implanting into stented valves of smaller diameter (19/21mm). A number of strategies have been developed to mitigate this (valve fracture (2), supra-annular prosthesis design where appropriate (3)). A high residual gradient after successful TAVI valve insertion is associated with an increased incidence of adverse outcomes including re-hospitalisation, heart failure, and ongoing symptoms.

These are both possibilities with standard TAVI implantation, but are more likely following a valve-in-valve procedure. Other generic risks of any TAVI procedure (that equally apply to valve-in-valve TAVI) include (4,5):

Stroke (approximately 2%)

Myocardial infarction (2%)

Death (2-3%)

Annular Rupture - although here the risk is reduced due to the pre-existing valve sewing ring. (1%)

Emergency cardiac surgery (1%)

Paravalvular leak (2-3%)

Renal impairment (2%)

Requirement for a new permanent pacemaker - although here the risk is reduced due to the pre-existing valve sewing ring (10-20% depending upon prosthesis used)

Vascular injury - including need for vascular surgery (10%)

Major bleeding - due to a combination of the above. (10%)

Valve migration (<1%)

2. Anecdotal adverse events (known from experience)

As above. There are few adverse events that are not predictable nor reported in the literature.

3. Theoretical adverse events

There remains relatively little data on valve longevity up to 5 years in this specific population (6).

Large scale Valve-in-Valve registries have to date, reported results at one year, and there is a small volume of data from up to 5 years (5). Therefore there is relatively little in the way of longer term data (none beyond 5 years) to describe the outcomes of valve-in-valve procedures.

However, to date, there have no large scale safety concerns raised about the valve systems currently available on the market. Recent devices that have been withdrawn (Boston Lotus/Lotus edge and Direct Flow medical) were designs that were not well suited to valve-in-valve applications, and their withdrawl has had little effect on the procedure or technique.

References:

(1) Dvir et al. Coronary Obstruction following Transcatheter Aortic valve-in-valve implantation. Preprocedural evaluation, device selection, protection and treatment. Circulation: Cardiovascular Interventions 2015;8(1);e002079

(2) Saxon JT, Allen KB, Cohen DJ, Chhatriwalla AK.Bioprosthetic Valve Fracture During Valve-in-valve TAVR: Bench to Bedside.Interv Cardiol. 2018 Jan;13(1):20-26. doi: 10.15420/icr.2017:29:1.

(3) Simonato M, Azadani AN, Webb J, Leipsic J, Kornowski R, Vahanian A, Wood D, Piazza N, Kodali S, Ye J, Whisenant B, Gaia D, Aziz M, Pasala T, Mehilli J, Wijeysundera HC, Tchetche D, Moat N, Teles R, Petronio AS, Hildick-Smith D, Landes U, Windecker S, Arbel Y, Mendiz O, Makkar R, Tseng E, Dvir D.In vitro evaluation of implantation depth in valve-in-valve using different transcatheter heart valves. EuroIntervention. 2016 Sep 18;12(7):909-17

(4) Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D.et al., for the PARTNER 2 Investigators. Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients. NEJM 2016;374:1609-1620

(5) Michael J. Reardon, M.D., Nicolas M. Van Mieghem, M.D., Ph.D., Jeffrey J. Popma, M.D., Neal S. Kleiman, M.D., Lars Søndergaard, M.D., Mubashir Mumtaz, M.D., David H. Adams, M.D., G. Michael Deeb, M.D., Brijeshwar Maini, M.D., Hemal Gada, M.D., Stanley Chetcuti, M.D., Thomas Gleason, M.D., John Heiser, M.D., Rüdiger Lange, M.D., Ph.D., William Merhi, D.O., Jae K. Oh, M.D., Peter S. Olsen, M.D., Nicolo Piazza, M.D., Ph.D., Mathew Williams, M.D., Stephan Windecker, M.D., Ph.D., Steven J. Yakubov, M.D., Eberhard Grube, M.D., Ph.D., Raj Makkar, M.D., Joon S. Lee, M.D., John Conte, M.D., Eric Vang, Ph.D., M.P.H., Hang Nguyen, B.S., Yanping Chang, M.S., Andrew S. Mugglin, Ph.D., Patrick W.J.C. Serruys, M.D., Ph.D., and Arie P. Kappetein, M.D., Ph.D.et al., for the SURTAVI Investigator. Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients NEJM 2017; 376:1321-1331

(6) **Didier** R, Eltchaninoff H, Donzeau-Gouge P, Chevreul K, Fajadet J, Leprince P, Leguerrier A, Lièvre M, Prat A, Teiger E, Lefevre T, Tchetché D, Carrié D, Himbert D, Albat B, Cribier A, Sudre A, Blanchard D, Rioufol G, Collet F, Houel R, Dos Santos P, Meneveau N, Ghostine S, Manigold T, Guyon P, Cuisset T, Le Breton H, Delepine S, Favereau X, Souteyrand G, Ohlmann P, Doisy V, Lognoné T, Gommeaux A, Claudel JP, Bourlon F, Bertrand B, Iung B, Gilard M. Five-Year Clinical Outcome and Valve Durability After Transcatheter **Aortic** Valve Replacement in High-Risk Patients. Circulation. 2018 Dec 4;138(23):2597-2607

4.2. What are the key efficacy outcomes for this procedure?

Procedural -
Valve gradient
Absence of paravalvular leak
Absence of procedural complications
Safety outcomes (as detailed above and reportable to NICOR).

Longer term outcomes -

Valve gradient
Symptomatic improvement (taken generically as improvement in NYHA class - there remains no standardized form of data collection).

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

There are two main concerns regarding the efficacy of Valve in valve TAVI, both of which are detailed and referenced above:

1. residual gradient/patient prosthesis mismatch - this can be predicted to some extent pre-procedure, and a number of steps taken to mitigate the risk of this occurring. This has to be balanced in each individual patient to achieve the optimal outcome for that particular individual (for example a

higher gradient may be accepted if there is an increased risk of annular rupture or stroke).

2. Valve longevity - There remains a degree of uncertainty about the longevity of TAVI valves used in this circumstance. If the data collated in registries is typical of the cohorts treated, then the majority of patients are over the age of 80, and have already had at least one cardiac surgical procedure (by definition). When this question is addressed with patients, then they are not overly concerned - due mainly to their own perception of lifespan and the wish to avoid further surgery.
However, as the profile of patients considered for TAVI evolves, younger patients are being treated - and in this cohort valve longevity remains a largely unanswered question. Certainly, I am not aware of any published data beyond the small cohort of patients for whom 5 year outcomes are available (as referenced above).

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

Operators need to be familiar with TAVI valve implantation. There are no specific training requirements, but operators should be
There are no specific facilities required other than that required to perform a standard TAVI procedure, namely:

A cath lab with appropriate radiographic technology
Vascular/cardiothoracic surgical support available
Recovery/nursing staff familiar with the care of patients following large calibre arterial access, and cardiac monitoring (i.e. a CCU/CHDU area) for procedural recovery.

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

There is a large scale ongoing registry (STS/ACC VinV registry) based in the US, the results of which have been partly reported (1). There is also the longer term follow up of the Partner 2 VinV registry - due to report 5 year data in 2020-2021.

The SOURCE 3 registry is a post marketing registry of the Edwards S3 system, the results of which will be available in 2019, but only a small proportion of those patients were VinV (n=30, 1.6%).

(1) Tuzcu EM, Kapadia SR, Vemulapalli S, Carroll JD, Holmes DR Jr, Mack MJ, Thourani VH, Grover FL, Brennan JM, Suri RM, Dai D, Svensson LG. Transcatheter Aortic Valve Replacement of Failed Surgically Implanted Bioprostheses: The STS/ACC Registry. J Am Coll Cardiol. 2018 Jul 24;72(4):370-382
(2) Webb JG, Mack MJ, White JM, Dvir D, Blanke P, Herrmann HC, Leipsic J, Kodali SK, Makkar R, Miller DC, Pibarot P, Pichard A, Satler LF, Svensson L, Alu MC, Suri RM, Leon MB.Transcatheter Aortic Valve Implantation

Within Degenerated Aortic Surgical Bioprostheses: PARTNER 2 Valve-in-Valve Registry. J Am Coll Cardiol. 2017 May 9;69(18):2253-2262
(3) Wendler O, Schymik G, Treede H, Baumgartner H, Dumonteil N, Neumann FJ, Tarantini G, Zamorano JL, Vahanian A. SOURCE 3: 1-year outcomes post-transcatheter aortic valve implantation using the latest generation of the balloon-expandable transcatheter heart valve. Eur Heart J. 2017 Sep 21;38(36):2717-2726.

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?

Yes - but only related to the question of long term valve durability as is detailed and referenced above.

5 Audit Criteria

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

All TAVI centres already contribute to a comprehensive national audit coordinated by NICOR, and have done since TAVI begun in the UK. A variety of data is collected - pre, peri, and post procedural factors - and have been reported nationally. The latest summary of data from NICOR (for 2016) has recently been made available,

Additional factors that have been considered regionally to reflect quality include:
Procedural mortality/morbidity
Length of bed stay (elective)
Readmission rates
Ratio of Transfemoral:nonTransfemoral TAVI (although this does vary from unit:unit)
number of ICU bed days/proportion of patients requiring ICU admission

In our own unit, we monitor bed stay, post procedural transthoracic aortic gradient/presence of paravaluvular leak, and all the required fields the are inputable on the NICOR dataset (available nationally).

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:

Markers of technical procedural success are summarised above but include:
Absence/presence and severity of any paravalvular leak
Post procedural gradient
Femoral complications - including bleeding/requirement for transfusion.
Length of stay

There are no current standardised measures of symptomatic improvement that are collected by centres currently outside of clinical research studies. Taking the UK TAVI trial as an example, then data has been collected using the Minnesota living with heart failure questionnaire and the EQ-5D-5L quality of life questions - but neither are suitable for routine clinical practice. If such measures are being considered, then a UK consensus - with the key stakeholders comprising the various national cardiac societies (including BCIS and BCS) should be devised.

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:

These are detailed above.

6 Trajectory of the procedure

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

This procedure is already widespread in clinical practice across the UK.

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

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

Comments:
It is likely to be carried out in all TAVI centres, which currently numbers 45, in the UK. It is anticipated by the end of 2019 that all centres that offer cardiothoracic surgery will have begun TAVI implantation. All are likely to offer Valve in valve therapy as part of the programme as it has become a standard treatment offered.

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:

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?

This is an established and valuable technique used in the treatment of patients who present (often acutely) with degenerative aortic valve bioprosthesis. Whilst there is limited data on longevity, this will become available in the literature within the next 2 years. The procedure has been used for over 8 years now in routine clinical practice, and there are no signals of premature valve failure observable or reported to date.

My final comment is that the use of peripheral bypass to perform the procedure is extremely rare (we have never done) and I would suggest that this statement is removed from the description. I would estimate maybe 1-2 cases per year in the UK. The default position in many centers now for a transfemoral case is using conscious sedation and percutaneous closure, i.e. much less invasive rather than peripheral ECMO cannulation. In addition, trans-esophageal echocardiography is only used occasionally rather than being the usual practice. I would consider wording: *with imaging guidance using fluoroscopy and usually echocardiography (either trans-thoracic or transoesophageal).*

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.

☐ 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. **YES**

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 have a **personal pecuniary** interest? The main examples are as follows:

Consultancies or directorships attracting regular or occasional payments in cash or kind **NO**

Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice** **NO**

Shareholdings – any shareholding, or other beneficial interest, in shares 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 **NO**

Investments – any funds that include investments in the healthcare industry **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? **NO**

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

Fellowships endowed by the healthcare industry **NO**

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

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

Comments:

I have attended a number of conferences sponsored by Edwards Lifesciences in 2018, none of which could be considered beyond that reasonably required to attend the meetings (PCR London Valves 2018, BSMICS Dublin 2018). For the sake of completeness, I declare this here.

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)

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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

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