NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension (CTPH) (1301/1)**
Name of Specialist Advisor:	**Dr Christoph Wiedenroth**
Specialist Society:	**British Thoracic Society**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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:

Please correct "CTPH" into CTEPH

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 procedure is based on an interdisciplinary approach (thoracic surgery, interventional radiology, cardiology, pneumology, anaesthesiology, intensive care medicine).

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:
BPA interventions are performed in 5 patients per week in our hospital.

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:
There are several ongoing scientific projects, which will be published in the near future.

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:

Established in only a few CTEPH_expert centers.

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

Medical treatment with riociguat.

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:

BPA is only performed in a few CTEPH-expert centers all over the world.

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

Reperfusion edema, hemoptysis, bleeding, vascular injury, arterio-venous fistula, renal failure, allergic reactions, hyperthyreosis, persisting pulmonary hypertension, infection, arrhythmia, thrombosis, pulmonary embolism, stroke, death, radiation complications.

2. Anecdotal adverse events (known from experience)

Actually 184 interventions performed in our hospital:

Hemoptysis	7,6 %
Dissection (pulmonary artery)	3,3 %
Reperfusion edema	5 %
Retroperitoneal hematoma	0,5 %
Mortality in hospital	0 %
30-day-mortality	1,9 %

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

Reperfusion edema	6,5 %
Hemoptysis	
Mortality	1,9 – 3,4 %

Inami et al. JACC Cardiovasc Interv. 2013 Jul;6(7):725-36.

Kataoka et al. Circ Cardiovasc Interv. 2012 Dec;5(6):756-62.

4.2 What are the key efficacy outcomes for this procedure?

Improvement in exercise capacity (WHO-functional class, 6 minute walking distance)
Improvement in pulmonary hemodynamics (right-heart-catheter)
Improvement in right-heart function

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

There are no true long-term results.

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

A multidisciplinary interventional team is mandatory as well as a biplanar angiography system.

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

The ICA (International CTEPH association) runs a CTEPH registry including BPA interventions.

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.

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

A multidisciplinary CTEPH-expert team is mandatory.

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):

NT-pro-BNP test (parameter of right heart function)

Bodyplethysmography with blood-gas-analysis

Echocardiography

6-minute-walk distance

Spiroergometry

Quality of life questionnaire

CT and MR evaluation of right heart function

Formatiert: Englisch (USA)

Right-heart-catheter

Formatiert: Englisch (USA)

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

Using the same examinations written under 5.1.

Early complications like reperfusion edema or hemoptysis require imaging examinations like X-ray or CT. Afterbleeding requires ultrasound of the access area (neck or femoral vein).

6 Trajectory of the procedure

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

As CTEPH is a rare disease, and the number of CTEPH-experts is limited, the speed of diffusion will be slow.

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:

There should be only 1 or 2 centers.

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

☐ Major.

☐ Moderate.

☒ Minor.

Comments:

7 Other information

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

8 Data protection and conflicts of interest

8.1 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**
	☒	**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	☐	**YES**

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

accommodation, meals and travel to attend meetings and conferences	☒ 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:

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

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

Procedure Name:	**Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension (CTPH) (1301/1)**
Name of Specialist Advisor:	**Mr David P Jenkins**
Specialist Society:	**British Thoracic Society**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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

X☐X Yes.

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

1.1 Does the title used above describe the procedure adequately?

X☐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☐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:

No controversy, but the exact place of BPA in the treatment of CTEPH yet to be determined. Current guidelines still class as 'emerging therapy', and at present restricted to inoperable patients, although the latter definition necessarily subjective.

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:

I am in a related specialty, as a cardiothoracic surgeon that performs pulmonary endarterectomy.

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

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

Comments:

I lead the national CTEPH MDT that determines operability and advises on best treatment modality. Current guidelines suggest that all patients with CTEPH should be referred for pulmonary endarterectomy assessment before considering medical treatment or indeed BPA. We now have a small list of patients that may benefit from BPA.

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

X☐X 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:

I have extensive knowledge of CTEPH and all its treatments and have published widely but not specifically directly on BPA at clinical or lab level. I was part of the CTEPH task force at the last world symposium conference, and am an executive board member of the International CTEPH Association.

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.

X☐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?

None, only 3 treatments, pulmonary endarterectomy surgery remains first line treatment, vasodilator drug (Riociguat) for inoperable or residual CTEPH and this new treatment.

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

☐ Cannot give an estimate.

Comments:

First 3 cases performed in UK this month. Programmes started in Germany and France in the last 2 years. Internationally, only Japan has significant experience with 4-5 centres and ~ 500 patients treated.

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

PA rupture and airway bleeding. Reperfusion injury. Limited response and residual PH with right heart failure. Renal failure due to contrast.

2. Anecdotal adverse events (known from experience)

As above, early experience from Japan of 'reperfusion injury' more likely wire perforations.

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

As above

4.2 What are the key efficacy outcomes for this procedure?

Improvement in haemodynamics (PVR and PH), improvement in functional class and 6 min walk distance, improvement in quality of life, improved survival.

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

Some. Reported literature mainly from one country and some have questioned how the opening of relatively few pulmonary artery branches results in a haemodynamic improvement equivalent to that of pulmonary endarterectomy surgery. Initial experience from Europe is positive, but only one study (from Norway) published which demonstrates early learning curve experience.

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

Visits to experienced centres (Japan and Europe), proctor supervision of first few cases. Established cardiology interventional (wire skills from coronary artery interventions) training. Also institutional experience and knowledge of PH and CTEPH. Cardiothoracic surgical facilities, ICU and ECMO necessary to deal with full range of potential complications and ICU experience of CTEPH necessary.

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

Yes, International CTEPH Association registry of all CTEPH treatments commenced this year, currently open, but will not be reporting for some years.

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, apart from small series at recent European thoracic conference, main reports all listed in PUBMED.

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

Not in UK. There are concerns internationally, that patients are referred for BPA when they would benefit from the more established surgical procedure, and that all patients must be reviewed by an experienced CTEPH team including pulmonary

endarterectomy surgeon prior to considering BPA. Ref CTEPH guidelines Kim et al JACC 2013.

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):

In hospital survival, 1 year survival.
Change in PVR pre and post
Improvement in imaging (subjective)
Morbidity and complications
Change in WHO functional class
Change in 6 min walk distance or CPET result
Change in QoL, dedicated CAMPHOR score

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

Reperfusion injury
Need for CPAP/ventilation
Need for ECMO
Bleeding complications
Renal failure
Hospital LOS

6 Trajectory of the procedure

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

I suggest should be limited to one (or a few) centres until the benefit/risks better understood. CTEPH remains a rare disease, so the demand will not be large.

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☐X Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Should be confined to designated PH specialist centres with a PH specialist team including 24 hour availability on-call, interventional cardiology laboratory and cardiothoracic ICU experience including ECMO support facilities.

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

☐ Major.

☐ Moderate.

X☐X Minor.

Comments:

CTEPH is a rare disease, ref UK PH audit 2014

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?

NA

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.

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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.	**X** ☐	**YES**
Consultant for Bayer and Actelion in relation to educational work for CTEPH and adjudicator for clinical trials of PH drugs. Not directly related to BPA	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice.**	☐ **X**	**YES**
I perform cardiothoracic surgery and pulmonary endarterectomy on private patients.	☐	**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**
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:

See above. Consultant for Bayer and Actelion in relation to educational work for CTEPH and adjudicator for clinical trials of PH drugs. Not directly related to BPA. I perform cardiothoracic surgery and pulmonary endarterectomy on private patients.

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

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

Procedure Name:	**Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension (CTPH) (1301/1)**
Name of Specialist Advisor:	**Dr Ghada Mikhail**
Specialist Society:	**British Cardiovascular Intervention Society**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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

X Yes.

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

1.1 Does the title used above describe the procedure adequately?

X Yes.

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

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X Yes.

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

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

Comments:

The next 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:

I am an interventional cardiologist who has experience in balloon angioplasty in treating coronary artery disease. I also have a background interest in pulmonary hypertension and have conducted research on the subject and have been awarded a higher degree (MD, University of London) on the Pathophysiology of Pulmonary Hypertension. At Imperial College Healthcare NHS Trust we have an active Pulmonary Hypertension Specialist unit. We have formulated an MDT to discuss patients who have CTEPH and are planning to perform Balloon Pulmonary Angioplasty (BPA) on selected suitable patients.

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.

x Other (please comment)

Comments:

I have not conducted research in this particular area of BPA in CTEPH patients. However, I have a background knowledge and research interest in the area of pulmonary hypertension and was awarded a higher degree (MD, University of London) on the Pathophysiology of Pulmonary Hypertension and have published extensively on the subject.

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.

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?

The technique of balloon angioplasty is well established in treating coronary artery disease. The same technique will apply to treating selected patients with CTEPH who are deemed inoperable and unsuitable for pulmonary endarterectomy surgery.

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:

BPA for CTEPH has been pioneered in Japan and interest to undertake such procedures has been expressed worldwide. The procedure is new to the UK with programmes due to start in selected centres.

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

See point 3

2. Anecdotal adverse events (known from experience)

See point 3

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

BPA needs to be performed in a staged procedure over subsequent sessions in order to minimize lung injury

Potential adverse events include:

Reperfusion lung injury

Pulmonary artery dissection

Extravascular leak

Lung injury can range from minor (requiring oxygen therapy) to major (requiring intubation and ventilation and extracorporeal membrane oxygenation - ECMO)

4.2 What are the key efficacy outcomes for this procedure?

- **Symptomatic improvement**
- **WHO Functional class**
- **6 minute Walk Test**
- **Haemodynamic improvement**

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

There are no large clinical trials in the area of BPA in CTEPH. The use of BPA, however, is increasing worldwide with a number of recent reports from multiple centres. BPA is a means of treating patients with end stage CTEPH who have failed medical therapy and who are deemed inoperable, with pulmonary endarterectomy, because of multiple co-morbidities or inaccessible distal disease.

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

BPA should be performed by interventional cardiologist who have experience in balloon angioplasty in coronary arteries. In certain centres, interventional radiologist who perform intervention in the pulmonary arteries should also be part of the team performing such procedures.

Interventional operators should visit centres where the procedure is being performed. Proctorship from experienced operators, who regularly perform such procedures, is essential at the start of any programme

Specialist Pulmonary Hypertension centres must have a comprehensive MDT available with pulmonary hypertension specialists, interventional cardiologist, radiologist, anaesthetists, cardiothoracic surgeons and specialist pulmonary hypertension nurses. The procedures needs to be performed in a cardiac catheter laboratory where full resuscitation facilities are available and where there is cardiothoracic support available. Access to an ECMO machine should be available whether on site or where emergency pathways are in place for gaining access to ECMO.

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

There are no major trials currently, however, there are several reports in the literature from multiple centres worldwide on the use of BPA in CTEPH

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 main series reports are available on PUBMED

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

N/A

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):

- **Symptomatic improvement**
- **WHO Functional class**
- **6 minute Walk Test**
- **Haemodynamic improvement**
- **BNP levels**
- **Quality of life questionnaires**

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

Reperfusion lung injury

Pulmonary artery dissection

Extravascular leak

Need for Ventilation

Need for ECMO

Mortality

6 Trajectory of the procedure

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

The diffusion of this procedure is therefore likely to be slow as BPA for CTEPH can only be offered in Specialist Pulmonary Hypertension centres with cardiothoracic surgical support. The clinical outcomes and efficacy are still to be determined in clinical trials.

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:

BPA for CTEPH should only be performed in Pulmonary Hypertension Specialist units where a comprehensive MDT is available with pulmonary

hypertension specialists, interventional cardiologist, radiologist, anaesthetists, cardiothoracic surgeons and specialist pulmonary hypertension nurses.

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

☐ Major.

☐ Moderate.

X Minor.

Comments:

BPA for CTEPH is a novel technique which should be offered to patients with end stage pulmonary hypertension who have failed medical therapy and have been deemed inoperable and unsuitable for pulmonary endarterectomy surgery either because of multiple co-morbidities or inaccessible distal disease. There is also a residual group of patients who remain symptomatic despite pulmonary endarterectomy and who will require additional treatment with BPA

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.

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**
	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**
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:

As an interventional cardiologist with an interest in pulmonary hypertension, I will be part of a multidisciplinary team and will be performing this procedure at Imperial College Healthcare NHS Trust

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

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

Procedure Name:	**Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension (CTPH) (1301/1)**
Name of Specialist Advisor:	**Dr Joanna Pepke-Zaba**
Specialist Society:	**British Cardiovascular Intervention Society**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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 team of interventional cardiologists (or interventional cardiologist/interventional radiologist) supported by anaesthesiologist, cardiac technicians, scrub nurses and radiographers is needed to perform the procedure. The patient has to be carefully monitored for side effects (eg.: reperfusion lung injury) either on HDU or ITU for 24h after the procedure.

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:

I have visited and observed several centres performing BPA programs in Japan, Oslo and Bad Nauheim, Germany . I have presented the outcomes to PH physicians community who have supported the need to establish BPA service in UK . Papworth Hospital was chosen to start the program as can secure the highest safety for the patients at the time of learning experience with the procedure and its peri-procedural potential side effects. Papworth is sole provider of surgery with pulmonary endarterectomy (PEA) in UK , therefore the patients can be offered the full back up for potential complications related to the procedure including ECMO.

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:

For several months we have been preparing for the BPA procedures and selecting potential patient's at the time of weekly National PEA MDT at Papworth. Patients considered for the BPA are the patients who are not suitable for surgery with PEA.

Selected cases were further re-discussed with the world expert on BPA ,Dr Takeshi Ogo from Division of Pulmonary Circulation, Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Centre, Osaka, Japan when he visited Papworth Hospital on 29th August 2015.

Independently we closely collaborate with Prof Eckhard Mayer BPA team at Kerckhoff-Klinik in Bad Nauheim Germany. This group has well established, busy PEA and BPA services which allows for well balanced decision on patient's suitability for management either with PEA or BPA.

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:

I was one of the world's CTEPH experts (International Association for CTEPH) who visited BPA centres in Japan in October 2013 . The aim was to understand risks and benefits from the BPA procedure and establish its role in management of patient's with CTEPH. Since, the BPA services were started in several European countries and San Diego in USA in parallel to established PEA services

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:

This is new procedure in UK however it is performed in several Japanese centres, Oslo in Norway, for several years with encouraging short and limited long term results (published follow up results up to 4 years for two small n=20 series). Several European centers have started this procedure in the last 1-2 years.

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

This procedure is predominantly for patients with distal distribution of CTEPH , not suitable for the surgery with PEA .Those ones, are normally to be considered for the therapy with new licensed oral therapy –riociguat or other expensive PAH

modifying therapys according to agreed CRG PH treatment policy. Riociguat, costs in the region of £ 15000- 24000 per year and this is continued lifelong. The upfront costs per BPA are similar to other complex percutaneous procedures but unlike these treatments, multiple BPA sessions are often required to safely treat the various different scarred pulmonary artery segments to achieve haemodynamic and functional improvement. Despite this, the costs are similar to one year medical therapy with licensed treatment.

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 **but very few**

Comments:

In UK, first 3 procedures on 3 patients were performed on 2nd of October 2015 at Papworth Hospital.
Consultant interventional cardiologist Dr Stephen Hoole (Papworth) performed the procedures in assistance of consultant interventional cardiologist Dr Gerry Coghlan (Royal Free) in the presence of 2 proctors from Kerckhoff-Klinik , Bad Nauheim.
Those two consultants interventional cardiologists should now work together to gain experience. Next session of BPA is planned for 13th of November still in assistance of 2 proctors from Kerckhoff-Klinik , Bad Nauheim.

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

Lung reperfusion injury

Pulmonary artery perforation leading to haemorrhage

2. Anecdotal adverse events (known from experience)

Acute kidney injury (due to dye contrast nephrotoxicity)

Exposure to high radiation in patient's requiring repeated procedures

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

Reperfusion oedema can lead to critical conditions. It is still a relatively common complication after BPA, with a reported incidence of 53–60%.

One of the most critical complications in BPA is pulmonary artery perforation, which may lead to severe lung haemorrhage and death. Pulmonary perforation is recognized in 0–7% of cases.

Original papers:

- Kataoka M, Inami T, Hayashida K, et al. Percutaneous transluminal pulmonary angioplasty for the treatment of chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv 2012; 5:756–762.
- Mizoguchi H, Ogawa A, Munemasa M, et al. Refined balloon pulmonary angioplasty for inoperable patients with chronic thromboembolic pulmonary hypertension. Circ Cardiovasc Interv 2012; 5:748–755.
- Andreassen AK, Ragnarsson A, Gude E, et al. Balloon pulmonary angioplasty in patients with inoperable chronic thromboembolic pulmonary hypertension. Heart 2013; 99:1415–1420.

Review :

- Takeshi Ogo. Balloon pulmonary angioplasty for inoperable chronic thromboembolic pulmonary hypertension. Curr Opin Pulm Med 2015, 21:425–431

4.2 What are the key efficacy outcomes for this procedure?

Pulmonary haemodynamics (measured by Right Heart Catheterisation) and functional status (WHO classification, six minute walk distance improvement). Improvement in right heart haemodynmics is followed by improvement in functional status . This will allow to remove the need of lifelong therapy with complex and expensive PAH targeted therapies . There is no yet data on long term survival but small published series are showing good results. One series describes remodelling of right ventricle in response to the series of BPA procedures. It is known that improvement in right heart function is directly related to improved survival and functional status in CTEPH.

Ref:

- Fukui S, Ogo T, Morita Y, et al. Right ventricular reverse remodelling after balloon pulmonary angioplasty. Eur Respir J 2014; 43:1394–1402.
- Tsugu T, Murata M, Kawakami T, et al. Significance of echocardiographic assessment for right ventricular function after balloon pulmonary angioplasty in patients with chronic thromboembolic induced pulmonary hypertension. Am J Cardiol 2015; 115:256–261.

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

Current published data and evidence are from single centres experience only. There are slight differences between the centres criteria in acceptance of patient's suitable for the procedure. There are differences between the centres in imaging modalities used for the procedure. The peri- procedural mortality and morbidity varied between centres, patients type (disease distribution) and institutional learning curve .

Independently from those differences, published haemodynamic BPA effects are consistently showing improved haemodynamics followed by improved functional stats of patients.

There is no data from the registry or multicenter studies. There is currently ongoing prospective New International CTEPH Registry, were BPA cases are included along patients treated with PEA and medically with PAH targeted therapies.
Papworth is participating in the Registry and I am CI for UK and member of Scientific Committee on behalf of ICA.

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

The team:

- There is a need for the CTEPH/PEA/BPA team :
  CTEPH/PEA MDT (Papworth Hospital) including consultant PEA surgeon, specialist pulmonary vascular radiologists and respiratory / cardiology PH physicians – to determine patient suitability for PEA or BPA.
- Highly experience consultant interventional cardiologist/ radiologist to undertake BPA. At least 2 experienced interventional consultants will undertake each procedure.
- Consultant anaesthetists to provide support peri-BPA procedure
- Paramedical staff: cardiac technicians, scrub nurses and radiographers – undertake BPA
- Consultant respiratory/ cardiologist with PH experience to manage the patient care pre- and post BPA.
- Specialist BPA/CTEPH nurse – patient support and information

.
At the start of the program we proposed all procedures to be undertaken at Papworth Hospital. This centre has the most developed infrastructure and expertise of imaging and peri-operative/procedural CTEPH management. The interventional consultants from the other centre will have honorary contracts to allow them to gain experience before transferring their skills to the other centres . The Papworth interventional team already has an excellent safety and governance record delivering other complex percutaneous procedures including transcatheter aortic valve intervention and repair of cardiac paravalvular leaks. It is also a designated centre for extracorporal membrane oxygenation (ECMO), PEA and heart and lung transplantation. Together we expect this will result in a reduced peri-procedural morbidity and mortality rate which is paramount to patient safety.

The first 3 UK BPA cases performed on 2nd of October 2015 at Papworth had no peri-operative morbidity and/or mortality. Case 1 was discharged after 2 days and other 2 cases after 3 days of monitoring.

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

The prospective "New International CTEPH Registry " is collecting information from international centres managing CTEPH patients and performing BPA procedure. Papworth is participating to the Registry . I am CI for UK and member of Scientific Committee (as the executive board member for International Association of CTEPH).

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.

At recent annual ECS meeting 30 August -2nd September 2015 in London , there was scientific session where several posters on BPA were presented with experience from Japan predominantly. Additionally there was debate on BPA vs PEA presented by Dr Andreassen from Oslo for BPA vs Mr Jenkins (Papworth) for PEA on 31st August 2015.

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

According to current guidance endorsed by all scientific societies, all patients diagnosed with CTEPH should be considered for the surgery with PEA as the treatment of choice. However, in countries with underdeveloped PEA surgery service, the patients with surgical distribution of the disease are considered for BPA (eg Japan). Those patients therefore are not offered optimal therapy for their condition and are of higher risk for the peri-procedural (BPA) morbidity and mortality. Therefore we propose patient pathway to be starting at the National PEA MDT to considered the treatment which is well established and with known good long term outcomes. However only 60% of total CTEPH patients are operated and 18% are left with residual pulmonary hypertension requiring PAH targeted therapies and those should be considered for the BPA procedure.
As the BPA procedure has still high peri-procedural morbidity, mortality even in experienced centres, therefore should be performed only in the centre with the most developed infrastructure and expertise of managing CTEPH patients and in specific in management of peri-procedural complications. Papworth Hospital was chosen by the PH community as the first to gain the experience with BPA. The Papworth interventional team already has an excellent safety and governance record delivering other complex percutaneous procedures.
The interventional consultants from other UK PH centre(s) will have honorary contracts with Papworth Hospital to allow them to gain experience before transferring their skills to the other PH centre in UK (eg Dr Gerry Coghlan currently).

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):

Short term outcomes:

- **improved haemodynamics (reduced pulmonary vascular resistance)**
- **improved six minute walking distance**
- **improved WHO functional class.**
- **Improved QoL (measured by CAMPHOR)**

Long term outcomes:

- **Improved survival of patients**
- **Maintain good functional status free from expensive PAH targeted therapy and oxygen**

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

Per-procedural :

haemoptysis, reperfusion pulmonary oedema, need for ventilation and death (up to 10%). It is important to recognise that the complication and death rate seen with the procedure are associated with the centre's experience in managing severe CTEPH patients.

Long term:
No obvious adverse outcomes were described.

6 Trajectory of the procedure

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

It is difficult to predict . There is need to repeat the BPA procedure to achieve desired effect, therefore same patient's might need to return for the procedures. It is likely that in the future , there will be need to establish up to 2-3 BPA centre in UK to allow for maintaining high volume of the procedures per operator / centre to secure the best outcomes and safety of patients.

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

☐ Most or all district general hospitals.

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

☒ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Should be perform only in the highly specialised centres with good records of CTEPH patient management, well established percutanous interventional cardiac /vascular procedures and were safety backup with experienced in PH anaesthetists and ECMO surgeons/ intensivists are available

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

☐ Major.

☐ Moderate.

☒ Minor.

Comments:

This is minor impact for the NHS as CTEPH is a rare disease however this procedure should introduce improvement in patients outcomes and reduce overall costs of management for NHS by maintain good functional status of patients free from expensive PAH targeted therapy

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?

Despite literature being dominated by the Japanese experience, there are several BPA centres in Europe and US were BPA has been successfully practiced for several years (Oslo Group) and under two years e.g.: Kerckhoff-Klinik in Bad Nauheim, Medizinische Hochschule Hannover, Medical University of Vienna, Leuven University , University of San Diego. Experience from those centers is confirming improvement in patients hemodynamic with limited peri-procedural morbidity and mortality.

BPA is crossing the gap for unmet needs for the patients with CTEPH who are not suitable for the PEA surgery and at the same time is offering long term financial savings related to keeping patients free from expensive PAH targeted therapies (eg riociguat recently introduced to Commissioners PH policy).

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**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare	☐	**YES**

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

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	☐	**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:

1. Relevant financial activities outside the submitted work.: I have received educational, speaker fees and honoraria for consultations from Actelion, Bayer, GSK. My institution received educational and research grants from Actelion, Bayer, GSK

2. I have submitted the application to review BPA procedure by the NICE Interventional Procedures Committee.

15.10.15
Dr. Joanna Pepke-Zaba PhD FRCP
Consultant Chest Physician
Director of National Pulmonary Vascular Diseases Unit

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

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's 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

Procedure Name:	**Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension (CTPH) (1301/1)**
Name of Specialist Advisor:	**Dr Stephen Hoole**
Specialist Society:	**British Cardiovascular Intervention Society**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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 procedure should be carried out by appropriately trained interventional cardiologists or interventional radiologists, supported by physicians and anaesthetists familiar with CTEPH management.

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:

I performed the first BPA procedure in the UK.

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:

Patient selection for BPA should be within a MDT meeting involving PEA surgeons, pulmonary hypertension specialists, interventional cardiologists, radiologists and nurse specialists.

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:

I have undertaken research into patients with CTEPH but not specifically BPA.

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:

This procedure applies techniques familiar to coronary and peripheral intervention to a new location within the segmental and sub-segmental pulmonary arteries. There are data confirming safety and efficacy in reducing symptoms and improving pulmonary haemodynamics but not yet survival.

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

Surgical pulmonary endarterectomy

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:

World-wide there are fewer than 20 interventionists performing this procedure regularly.

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

Death

Cardiovascular collapse

Major pulmonary haemorrhage

Arrhythmia

Tamponade

2. Anecdotal adverse events (known from experience)

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

Reperfusion lung oedema and hypoxaemia

Pulmonary artery perforation

Haemoptysis

Contrast induced nephropathy

Right heart failure

Vascular access complications/ bleeding

Ogo T. *Curr Opin Pulm Med 2015; 21: 425-431*

4.2 What are the key efficacy outcomes for this procedure?

Improvement in WHO functional class status
Improved QoL
Improved CPEX
Improved 6 minute walk distance
Improved pulmonary haemodynamics: mPAP, PVR
Improved tissue perfusion (contrast blush) and increased rapidity of pulmonary venous phase during angiography

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

There are good data supporting evidence of improvement in all the outcomes outlined in 4.2. It often requires several BPA procedures to achieve these outcome goals. Staging the procedure reduces the risk of contrast induced nephropathy and reperfusion lung oedema.

Most of the haemodynamic benefit seems to occur after the ballooned artery has remodelled and healed, so the benefit may lag some weeks-months after the initial procedure. There are limited data to guide intraoperative efficacy at the time of the procedure. The haemodynamics often do not change immediately, but contrast blush into the lung parenchyma and speed of contrast passage into the pulmonary veins are anecdotally useful guides to the adequate restoration of flow following BPA.
We have no data on mortality benefit following BPA.

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

Training should be by proctorship from experienced BPA operators and visits to BPA centres to observe. Trainees in BPA should already have experience in vascular intervention.

Essential facility requirements:

1. Catheter laboratory experienced in interventional procedures
2. Availability of intensive and high dependency care
3. Anaesthetic support on site
4. Cardiothoracic surgery on site
5. ECMO available on site
6. Physicians experienced in the management of CTEPH to assist in MDT patient selection and perioperative care

Desirable facility requirements:

1. Established PEA programme for CTEPH

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

None that I am aware of.

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.

Most abstracts are of small case reports and small case series reporting unit outcomes and complications.

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

All BPA cases should be discussed in an MDT with an experience PEA surgeon and deemed inoperable on anatomical or clinical grounds. In my opinion, BPA treatment of CTEPH obstructive lesions (webs and slits) should be limited to inoperable cases where there is inaccessible, distal disease. In some institutions around the world,

BPA has been performed on proximal webs/ obstructions that are eminently treatable by PEA. PEA has confirmed data for symptomatic, haemodynamic and survival benefit and should be the preferred treatment choice until trial data suggest otherwise.

It is unclear where this service should be performed. In my opinion it should be ideally performed in a PEA centre with facilities and expertise to support these often challenging patients. V-A ECMO must be available on site as it would be necessary to salvage a patient with haemodynamic collapse (e.g. pulmonary haemorrhage) during a BPA case.

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):

WHO functional class
QoL questionnaires
6-minute walk
CPEX
Pulmonary haemodynamics: PVR and mPAP

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

Early
Death
Pulmonary reperfusion injury and oedema
Pulmonary perforation
Right heart failure and hypotension
Contrast induced nephropathy
Haematoma/ Bleeding from the access site

Late
Pulmonary reperfusion injury and oedema (up to 7 days post procedure)
Access site complications: fistulae
Radiation skin damage

6 Trajectory of the procedure

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

I think it will and should be concentrated in specialist units, with careful patient selection and commitment to further collaborative research into the potential BPA benefits.

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:

For the reasons outlined above with regard to the availability of PEA (for MDT case selection) and ECMO on site.

The techniques employed in BPA are relatively easily transferred at an interventional level, but the perioperative care of these complex patients will limit the role out to more centres, until we have more experience with the treatment.

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:

CTEPH candidates for BPA are carefully selected and therefore initially the volume of cases will be low. However, CTEPH is underdiagnosed and undertreated. Raised awareness and screening may increase the number of referrals through the CTEPH service, perhaps necessitating more rapid expansion of BPA, particularly if there are outcome data of benefit compared to medical therapy and equivalence to PEA. This may have implications on catheter laboratory services in the specialist centres, necessitating wider spread adoption.

The consumable cost for a BPA is small whereas the cost of medical management of CTEPH is large. It is possible that successful treatment with BPA will enable patients to be managed without expensive medical treatment. I'd be surprised if BPA weren't more cost effective.

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.

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

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare	☒	**YES**

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

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	☐	**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 have received speaker honoraria from Abbott Vascular, St Jude and AstraZeneca.

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

Conflicts of Interest for Specialist Advisers

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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).

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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

Procedure Name:	**Balloon Pulmonary Angioplasty for Chronic Thromboembolic Pulmonary Hypertension (CTPH) (1301/1)**
Name of Specialist Advisor:	**Dr Takeshi Ogo**
Specialist Society:	**British Thoracic Society**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

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:

We usually use “CTEPH” instead of “CTPH" as abbreviation of chronic thromboembolic pulmonary hypertension.

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:

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:

Balloon pulmonary angioplasty (BPA) has been done for pulmonary stenosis for children. BPA for CTEPH is a relatively new procedure for CTEPH. Efficacy and safety has been already published.

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

Currently, pulmonary endarterectomy is the golden standard therapy for CTEPH. Balloon pulmonary angioplasty and drug (Riociguat) are considered to be the treatment for inoperable CTEPH.

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:

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

Reperfusion oedema (5-10%), Pulmonary artery perforation (1-5%), Haemoptysis (5-10%), Death (1-5%)

2. Anecdotal adverse events (known from experience)

Reperfusion oedema, anaphylaxis shock for contrast medium

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

Severe reperfusion oedema (2-7%), Pulmonary artery perforation (0-7%), Peri-procedural mortality (0-10%)

Ogo T. Balloon pulmonary angioplasty for inoperable chronic thromboembolic pulmonary hypertension. Curr Opin Pulm Med 2015; 21(5):425-31

4.2 What are the key efficacy outcomes for this procedure?

Survival rate (No long term data), Symptom, exercise capacity, Haemodynamic improvement, right heart function

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

Long term survival, restenosis in long term

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

This operator should have some training for pulmonary angiography and vascular catheter intervention. Also, the operator should have some training for BPA in an experienced centre. BPA should be done in PH (CTEPH) centre in the area. The facilities should be the one which diagnose pulmonary hypertension patients regularly.

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

International CTEPH association started new CTEPH registry including some experienced BPA centres. There is a BPA registry in Japan.

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.

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

Indication of BPA to drug should be discussed. Also, pulmonary endarterectomy is still the golden standard therapy. We do BPA for inoperable CTEPH patients. However, we are not sure the effect and safety in operable CTEPH patients.

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):

Survival, QOL, symptom, exercise capacity, haemodynamics, right heart function

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

Death, Reperfusion edema, pulmonary artery perforation, haemoptysis

6 Trajectory of the procedure

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

When one PH centre master this procedure which need some learning period (6 month – 1 year), then it will diffuse to other PH centres rapidly

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

☐ Most or all district general hospitals.

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

■ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

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

☐ Major.

■ Moderate.

☐ Minor.

Comments:

7 Other information

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

8 Data protection and conflicts of interest

8.1 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).

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:

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

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.

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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).

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