

REQUEST FOR AUTHORISATION OF A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE COMMUNITY

For official use:

Date of receiving the request :	Date of request for additional information :	Grounds for non acceptance/ negative opinion : ^
Date of request for information to make it valid :		Give date :
Date of valid application :	Date of receipt of additional / amended information :	Authorisation/ positive opinion : ^
Date of start of procedure :		Give date:
Competent authority registration number :	Withdrawal of application : ^	
Ethics Committee registration number :	Give date :	

To be filled in by the applicant:

The questions in this form for the request for authorisation from the Competent Authority are also relevant for the opinion from an Ethics Committee (it represents module 1 of the form for applying to an ethics committee) and can be used as part of that application. Please indicate the relevant purpose in a box below.

REQUEST FOR AUTHORISATION TO THE COMPETENT AUTHORITY: ^

A. TRIAL IDENTIFICATION

A.1 Member State in which the submission is being made : UNITED KINGDOM
A.2 EudraCT number¹: 2007-001036-31 A.3 Full title of the trial: A 2-COHORT, MULTI-CENTRE, RANDOMIZED, DOUBLE BLIND (3RD PARTY OPEN), PLACEBO CONTROLLED 4-WAY CROSSOVER STUDY TO ASSESS THE EFFICACY OF SINGLE ORAL DOSES OF PF-00446687 ON ERECTILE FUNCTION IN MEN SUFFERING FROM ERECTILE DYSFUNCTION, USING 100 MG SILDENAFIL AS A POSITIVE CONTROL. A.4 Sponsor's protocol code number²: A8361011 Sponsor's protocol version²: Final Sponsor's protocol date²: 2007-04-11 A.5 Name or abbreviated title of the trial where available: n/a A.6 ISRCTN number³, if available : n/a

A.7 Is this a resubmission ? yes¹ no²

If Yes, indicate the resubmission letter⁴ : **First submission**

¹ Append the EudraCT number confirmation receipt

² Any translation of the protocol should be assigned the same date and version as those in the original document.

³ International Standard Randomised Controlled Trial Number. Sponsors may wish to use an International Standard Randomised Controlled Trial Number (ISRCTN) to identify their trial in addition to the EudraCT number; for instance if their trial is part of a multinational trial with sites outside the Community. They can obtain the number and guidance from the Current Controlled Trials website <http://www.controlled-trials.com/isrctn> to which there is a link from the EudraCT database website <http://www.eudract.emea.eu.int>. When available they should provide it in Section A.6 of the application form.

⁴ For a resubmission following previous withdrawal of an application or unfavourable opinion of an ethics committee, or previous withdrawal of an application or refusal of a request by the competent authority, enter a letter in the sequence, A for first resubmission, B for second, C for third et seq.

B. IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

B.1 Sponsor

B.1.1 Name of organisation : Pfizer Limited, Ramsgate Road, Sandwich, Kent. UK. CT13 9NJ

B.1.2 Name of the person to contact:

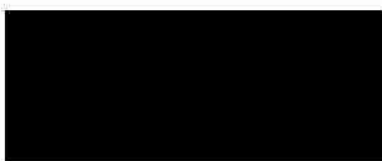


B.1.3 Address :
Ramsgate Road
Sandwich/Kent
CT13 9NJ
UNITED KINGDOM

B.1.4 Telephone number :

B.1.5 Fax number :

B.1.6 e-mail:



B.3 Status of the sponsor : B.3.1 commercial⁶ ^ B.3.2 non commercial[^]

B.2 Legal representative⁵ of the sponsor in the Community for the purpose of this trial (if different from the sponsor)

B.2.1 Name of organisation :

B.2.2 Name of the person to contact:

B.2.3 Address :

B.2.4 Telephone number :

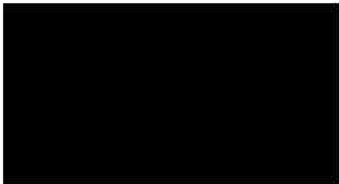
B.2.5 Fax number :

B.2.6 e-mail:

⁵ : In accordance with article 19 of Directive 2001/20/EC

⁶ : A commercial sponsor is a person or organisation that takes responsibility for a trial which at the time of the application is part of the development programme for a marketing authorisation of a medicinal product.

C. APPLICANT IDENTIFICATION, (please tick the appropriate box)

C.1 Request for the competent authority [^]	
C.1.1 - Sponsor	☐
C.1.2 - Legal representative of the sponsor	☐
C.1.3 - Person or organisation authorised by the sponsor to make the application.	☐
C.1.4 Complete the details of the applicant below even if they are provided elsewhere on the form:	
C.1.4.1 Organisation :	Pfizer Ltd. Ramsgate Road, Sandwich, Kent. CT13 9NJ. UK
C.1.4.2 Name of contact person :	
C.1.4.3 Address :	Ramsgate Road, Sandwich, Kent. CT13 9NJ UNITED KINGDOM
C.1.4.4 Telephone number :	
C.1.4.5 Fax number :	
C.1.4.6 e-mail:	
C.1.5 Request to receive an .xml copy of CTA data :	
C.1.5.1 Do you want an .xml file copy of the CTA form data saved on EudraCT ?	yes ☐ no ☐
C.1.5.1.1 If Yes provide the e-mail address(es) to which it should be sent (up to 5 addresses) :	
C.1.5.1.2 Do you want to receive this via password protected link(s) ⁷ ?	yes ☐ no ☐
If you answer No to question C.1.5.1.2 the .xml file will be transmitted by less secure e-mail link(s)	

⁷ This requires a EudraLink account. (See www.eudract.emea.eu.int) for details)

D. INFORMATION ON EACH IMP

Information on each 'bulk product' before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator and each placebo, if applicable. If the trial is performed with several products use extra pages and give each product a sequential number in D.1.1. If the product is a combination product information should be given for each active substance.

D.1 IMP IDENTIFICATION

Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial(assign numbers from 1-n):

D.1.1 This refers to the IMP number :

PR1

D.1.2 IMP being tested

^

D.1.3 IMP used as a comparator

^

for placebo go directly to D.7

D.2 STATUS OF THE IMP. If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2.

D.2.1 Has the IMP to be used in the trial a marketing authorisation ? yes ^ no ^

D.2.1.1 If yes to D.2.1, specify for the product to be used in the trial :

D.2.1.1.1 Trade name⁹

D.2.1.1.2 Name of the MA holder⁹

D.2.1.1.3 MA number (if MA granted by a Member State)⁹

D.2.1.1.4 Is the IMP modified in relation to its MA ? yes ^ no ^

D.2.1.1.4.1 If Yes, please specify

D.2.1.2 Which country granted the MA ?

D.2.1.2.1 Is this the Member State concerned with this application ? yes ^ no ^

D.2.1.2.2 Is this another Member State ? yes ^ no ^

D.2.2 Situations where an IMP to be used in the CT has a MA in the MS concerned , but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

D.2.2.1 In the protocol, is treatment defined only by active substance ?	yes ☐ no ☐
D.2.2.1.1 If Yes, give active substance in D.3.8 or D.3.9	
D.2.2.2 In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS ?	yes ☐ no ☐
D.2.2.2.1 If Yes, give active substance in D.3.8 or D.3.9	
D.2.2.3 The products to be administered as IMPs are defined as belonging to an ATC group ⁹ .	yes ☐ no ☐
D.2.2.3.1 If Yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4 Other :	yes ☐ no ☐
D.2.2.4.1 If Yes, please specify :	

D.2.3 IMPD submitted :

D.2.3.1 Full IMPD	yes ☐ no ☐
D.2.3.2 Simplified IMPD ¹⁰ .	yes ☐ no ☐
D.2.3.3 Summary of product characteristics (SmPC) only	yes ☐ no ☐

D.2.4 Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community ?

	yes ☐ no ☐
D.2.4.1 If Yes, specify which Member States : BELGIUM	

D.2.5 Has the IMP been designated in this indication as an orphan drug in the Community ?

yes ☐ no ☐
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D.2.5.1 If yes, give the orphan drug designation number¹¹:

D.2.6 Has the IMP been the subject of scientific advice related to this clinical trial ?

yes ⁹ no ⁹

D.2.6.1 If Yes to D.2.6 please indicate source of advice and provide a copy in the CTA request :

D.2.6.1.1 From the CHMP ¹²?

yes ⁹ no ⁹

D.2.6.1.2 From a MS competent authority ?

yes ⁹ no ⁹

⁹ Available from the Summary of Product Characteristics

¹⁰ Provide justification for using simplified dossier in the covering letter.

¹¹ According to the Community register on orphan medicinal products (Regulation (EC) n° 141/2000) :
<http://pharmacos.eudra.org/F2/register/orphreg.htm>

¹² Committee for Medicinal Products for Human Use of the European Medicines Agency.

D.3 DESCRIPTION OF THE IMP

D.3.1 Product name where applicable¹³ : PF-00446687

D.3.2 Product code where applicable¹⁴ : PF-00446687

D.3.3 ATC code, if officially registered¹⁵ :

D.3.4 Pharmaceutical form (use standard terms) : Powder For Oral Solution

D.3.5 Maximum duration of treatment of a subject according to the protocol :

35 days

D.3.6 Maximum dose allowed (specify : per day or total dose; units and route of administration) :

200 mg

Per day or total dose :

Per day

Units :

200 mg milligram(s)

Route of administration :

Oral Use

D.3.7 Route of administration (use standard terms): Oral Use

D.3.8 Name of each active substance (INN or proposed INN if available) :

D.3.9 Other available name for each active substance (CAS¹⁶, current sponsor code(s), other descriptive name, etc : provide all available) :

- CAS 662281-92-3

- Current sponsor code(s) PF-00446687

- Other Descriptive name

D.3.10 Strength (specify all strengths to be used) :

D.3.10.1 - concentration unit : mg milligram(s)

D.3.10.2 - concentration type ("exact number", "range", "more than" or "up to"). up to

D.3.10.3 - concentration number : 200

¹³ To be provided only where there is no tradename. This is the name routinely used by the sponsor to identify the IMP in the CT documentation (protocol, IB...)

¹⁴ To be provided only where there is no tradename. This is the code designated by the sponsor which represents the name routinely used by the sponsor to identify the product in the CT documentation. For example, a code may be used for combinations of drugs or drugs and devices..

¹⁵ Available from the Summary of Product Characteristics

¹⁶ Chemical Abstracts Service.

D.3.11 Type of IMP

Does the IMP contain an active substance :

D.3.11.1 - of chemical origin ? yes ^ no ^

D.3.11.2 - of biological / biotechnological origin?¹⁷ yes ²⁶ no ²⁶

Is this a:

D.3.11.3 - Cell therapy medicinal product?¹⁷ yes^x no^x

D.3.11.4 - Gene therapy medicinal product?¹⁷ yes ¹⁸ no ¹⁸

D.3.11.5 - Radiopharmaceutical medicinal product ? yes ^ no ^

D.3.11.6 - Immunological medicinal product (such as vaccine, allergen, immune serum)? yes [^] no [^]

D.3.11.7 - Plasma derived medical product?	yes ^	no ^
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D.3.11.8 - Other extractive medical product? yesⁿ noⁿ

D.3.11.9 - Herbal medicinal product?	yes ^N	no ^N
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D.3.11.10 - Homeopathic medicinal product? yes^{*} no^{*}

D.3.11.11 - Medicinal product containing genetically modified organisms?	yes [*]	no [*]
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•If yes to D.3.11.11

■D.3.11.11.1 Has the authorisation for contained use or release been granted?	yes [^] no [^]
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D.3.11.11.2 Is it pending ? yes ^ no ^

D.3.11.12 - Another type of medicinal product? yes [^] no [^]

.D.3.11.12.1 If yes, specify :

¹⁷ Complete also sections D.4, and where applicable sections D.5 and D.6

D.4. BIOLOGICAL / BIOTECHNOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS INCLUDING VACCINES

D.4.1 Type of product		
D.4.1.1 - Extractive	yes [^]	no [^]
D.4.1.2 - Recombinant	yes [^]	no [^]
D.4.1.3 - Vaccine	yes [^]	no [^]
D.4.1.4 - GMO	yes [^]	no [^]
D.4.1.5 - Plasma derived products	yes [^]	no [^]
D.4.1.6 - Others	yes [^]	no [^]
D.4.1.6.1 If others, specify :		

D.5 SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)

D.5.1 Origin of cells		
D.5.1.1 - Autologous	yes [^]	no [^]
D.5.1.2 - Allogeneic	yes [^]	no [^]
D.5.1.3 - Xenogeneic	yes [^]	no [^]
D.5.1.3.1 - If yes, specify species of origin :		

D.5.2 Type of cells

D.5.2.1 - Stem cells

yes [^] no [^]

D.5.2.2 - Differentiated cells

yes [^] no [^]

D.5.2.2.1 If yes, specify the type (e.g. keratinocytes, fibroblasts, chondrocytes,...) :

D.5.2.3 - Others :

yes [^] no [^]

D.5.2.3.1 If others, specify :

D.6. GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**D.6.1 Gene(s) of interest :****D.6.2 In vivo gene therapy:**[^]**D.6.3 Ex vivo gene therapy :**[^]**D.6.4 Type of gene transfer product**

D.6.4.1 - Nucleic acid (e.g. plasmid) :

yes [^] no [^]

If yes, specify

D.6.4.1.1 - Naked :

yes [^] no [^]

D.6.4.1.2 - Complexed :

yes [^] no [^]

D.6.4.2 - Viral vector :

yes [^] no [^]

D.6.4.2.1 If yes, specify the type : adenovirus, retrovirus, AAV, ...:

D.6.4.3 - Others :

yes [^] no [^]

D.6.4.3.1 If others, specify :

D.6.5 Genetically modified cells :yes[^] no[^]

If yes, specify origin of the cells :

D.6.5.1 - Autologous :

yes[^] no[^]

D.6.5.2 - Allogeneic :

yes[^] no[^]

D.6.5.3 - Xenogeneic :

yes[^] no[^]

D.6.5.3.1 - If yes, specify species of origin :

D.6.5.4 - Other type of cells (hematopoietic stem cells, ...): yes[^] no[^]

-If Yes specify :

D.6.6 Comments on novel aspects of gene therapy investigational product if any (free text) :

D.1 IMP IDENTIFICATION

Indicate which of the following is described below, then repeat as necessary for each of the numbered IMPs to be used in the trial(assign numbers from 1-n):

D.1.1 This refers to the IMP number : PR2

D.1.2 IMP being tested ^

D.1.3 IMP used as a comparator ^

for placebo go directly to D.7

D.2 STATUS OF THE IMP. If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2.

D.2.1 Has the IMP to be used in the trial a marketing authorisation ? yes ^ no ^

D.2.1.1 If yes to D.2.1, specify for the product to be used in the trial :

D.2.1.1.1 Trade name⁹ VIAGRA ® 100 mg film-coated tablets.

D.2.1.1.2 Name of the MA holder⁹ Pfizer Ltd, Ramsgate Road, Sandwich. UK. CT13 9NJ

D.2.1.1.3 MA number (if MA granted by a Member State)⁹ EU/1/98/077/009-012

D.2.1.1.4 Is the IMP modified in relation to its MA ? yes ^ no ^

D.2.1.1.4.1 If Yes, please specify Tablet is debossed only on one side (commercial supply tablets have debossing on both sides)

D.2.1.2 Which country granted the MA ? EUROPEAN UNION

D.2.1.2.1 Is this the Member State concerned with this application ? yes ^ no ^

D.2.1.2.2 Is this another Member State ? yes ^ no ^

D.2.2 Situations where an IMP to be used in the CT has a MA in the MS concerned , but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

D.2.2.1 In the protocol, is treatment defined only by active substance ?	yes [^] no [^]
D.2.2.1.1 If Yes, give active substance in D.3.8 or D.3.9	
D.2.2.2 In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS ?	yes [^] no [^]
D.2.2.2.1 If Yes, give active substance in D.3.8 or D.3.9	
D.2.2.3 The products to be administered as IMPs are defined as belonging to an ATC group ⁹ .	yes [^] no [^]
D.2.2.3.1 If Yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.3	
D.2.2.4 Other :	yes [^] no [^]
D.2.2.4.1 If Yes, please specify :	

D.2.3 IMPD submitted :

D.2.3.1 Full IMPD	yes [^] no [^]
D.2.3.2 Simplified IMPD ¹⁰ .	yes [^] no [^]
D.2.3.3 Summary of product characteristics (SmPC) only	yes [^] no [^]

D.2.4 Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community ?

yes [^] no [^]

D.2.4.1 If Yes, specify which Member States :
AUSTRIA

BELGIUM

CZECH REPUBLIC

DENMARK

ESTONIA
FINLAND
FRANCE
GERMANY
GREECE
HUNGARY
IRELAND
ITALY
NETHERLANDS
NORWAY
POLAND
PORTUGAL
SLOVAKIA
SPAIN
SWEDEN
UNITED KINGDOM

D.2.5 Has the IMP been designated in this indication as an orphan drug in the Community ?

yes ☐ no ☐

D.2.5.1 If yes, give the orphan drug designation number¹¹:

D.2.6 Has the IMP been the subject of scientific advice related to this clinical trial ?

yes ☐ no ☐

D.2.6.1 If Yes to D.2.6 please indicate source of advice and provide a copy in the CTA request :

D.2.6.1.1 From the CHMP ¹²?

yes ☐ no ☐

D.2.6.1.2 From a MS competent authority ?

yes ☐ no ☐

⁹ Available from the Summary of Product Characteristics

¹⁰ Provide justification for using simplified dossier in the covering letter.

¹¹ According to the Community register on orphan medicinal products (Regulation (EC) n° 141/2000) :
<http://pharmacos.eudra.org/F2/register/orphreg.htm>

¹² Committee for Medicinal Products for Human Use of the European Medicines Agency.

D.3 DESCRIPTION OF THE IMP

D.3.1 Product name where applicable¹³ :

D.3.2 Product code where applicable¹⁴ :

D.3.3 ATC code, if officially registered¹⁵ : G04B E03

D.3.4 Pharmaceutical form (use standard terms) : Tablet

D.3.5 Maximum duration of treatment of a subject according to the protocol :

35 days

D.3.6 Maximum dose allowed (specify : per day or total dose; units and route of administration) :

100 mg/day

Per day or total dose :

Per day

Units :

100 mg milligram(s)

Route of administration :

Oral Use

D.3.7 Route of administration (use standard terms): Oral Use

D.3.8 Name of each active substance (INN or proposed INN if available) :

SILDENAFIL CITRATE

D.3.9 Other available name for each active substance (CAS¹⁶, current sponsor code(s), other descriptive name, etc : provide all available) :

- CAS	171,599-83-0
- Current sponsor code(s)	UK-92,480
- Other Descriptive name	Viagra®

D.3.10 Strength (specify all strengths to be used) :

D.3.10.1 - concentration unit : mg milligram(s)

D.3.10.2 - concentration type ("exact number", "range", "more than" or "up to"). equal

D.3.10.3 - concentration number : 100

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¹³ To be provided only where there is no tradename. This is the name routinely used by the sponsor to identify the IMP in the CT documentation (protocol, IB...)

¹⁴ To be provided only where there is no tradename. This is the code designated by the sponsor which represents the name routinely used by the sponsor to identify the product in the CT documentation. For example, a code may be used for combinations of drugs or drugs and devices..

¹⁵ Available from the Summary of Product Characteristics

¹⁶ Chemical Abstracts Service.

D.3.11 Type of IMP

Does the IMP contain an active substance :

D.3.11.1 - of chemical origin ? yes ^ no ^

D.3.11.2 - of biological / biotechnological origin?¹⁷

yes²⁸ no²⁹

Is this a:

D.3.11.3 - Cell therapy medicinal product?¹⁷

yes [*]	no [*]
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D.3.11.4 - Gene therapy medicinal product?¹⁷

yes ☐ no ☒

D.3.11.5 - Radiopharmaceutical medicinal product ? yes ^ no ^

D.3.11.6 - Immunological medicinal product (such as vaccine, allergen, immune serum)?

D.3.11.7 - Plasma derived medical product? yes^{*} no^{*}

D.3.11.8 - Other extractive medical product? yesⁿ noⁿ

D.3.11.9 - Herbal medicinal product? yes ²⁸ no ²⁹

D.3.11.10 - Homeopathic medicinal product? yes ^ no ^

D.3.11.11 - Medicinal product containing genetically modified organisms? yes ^ no ^

- If yes to D.3.11.11

■D.3.11.11.1 Has the authorisation for contained use or release been granted? yes [^] no [^]

D.3.11.11.2 Is it pending ? yes ^ no ^

D.3.11.12 - Another type of medicinal product? yes [^] no [^]

.D.3.11.12.1 If yes, specify :

¹⁷ Complete also sections D.4, and where applicable sections D.5 and D.6

D.4. BIOLOGICAL / BIOTECHNOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS INCLUDING VACCINES

D.4.1 Type of product		
D.4.1.1 - Extractive	yes [^]	no [^]
D.4.1.2 - Recombinant	yes [^]	no [^]
D.4.1.3 - Vaccine	yes [^]	no [^]
D.4.1.4 - GMO	yes [^]	no [^]
D.4.1.5 - Plasma derived products	yes [^]	no [^]
D.4.1.6 - Others	yes [^]	no [^]
D.4.1.6.1 If others, specify :		

D.5 SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)

D.5.1 Origin of cells		
D.5.1.1 - Autologous	yes [^]	no [^]
D.5.1.2 - Allogeneic	yes [^]	no [^]
D.5.1.3 - Xenogeneic	yes [^]	no [^]
D.5.1.3.1 - If yes, specify species of origin :		

D.5.2 Type of cells

D.5.2.1 - Stem cells

yes [^] no [^]

D.5.2.2 - Differentiated cells

yes [^] no [^]

D.5.2.2.1 If yes, specify the type (e.g. keratinocytes, fibroblasts, chondrocytes,...) :

D.5.2.3 - Others :

yes [^] no [^]

D.5.2.3.1 If others, specify :

D.6. GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**D.6.1 Gene(s) of interest :****D.6.2 In vivo gene therapy:**[^]**D.6.3 Ex vivo gene therapy :**[^]**D.6.4 Type of gene transfer product**

D.6.4.1 - Nucleic acid (e.g. plasmid) :

yes [^] no [^]

If yes, specify

D.6.4.1.1 - Naked :

yes [^] no [^]

D.6.4.1.2 - Complexed :

yes [^] no [^]

D.6.4.2 - Viral vector :

yes [^] no [^]

D.6.4.2.1 If yes, specify the type : adenovirus, retrovirus, AAV, ...:

D.6.4.3 - Others :

yes [^] no [^]

D.6.4.3.1 If others, specify :

D.6.5 Genetically modified cells :yes[^] no[^]

If yes, specify origin of the cells :

D.6.5.1 - Autologous :

yes[^] no[^]

D.6.5.2 - Allogeneic :

yes[^] no[^]

D.6.5.3 - Xenogeneic :

yes[^] no[^]

D.6.5.3.1 - If yes, specify species of origin :

D.6.5.4 - Other type of cells (hematopoietic stem cells, ...): yes[^] no[^]

-If Yes specify :

D.6.6 Comments on novel aspects of gene therapy investigational product if any (free text) :

D.7 INFORMATION ON PLACEBO (if relevant repeat as necessary)

D.7.1 Is there a placebo:

yes ²⁵ no ²⁵

D.7.2 This refers to Placebo number (.....)

PL1

D.7.3 Pharmaceutical form :

Powder For Oral Solution

D.7.4 Route of administration :

Oral Use

D.7.5 Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1

PR1

D.7.5.1 Composition, apart from the active substance(s) :

D.7.5.2 - is it otherwise identical to the IMP?

yes ² no ²

D.7.5.2.1- if not, specify major ingredients :

denatonium benzoate

D.7.2 This refers to Placebo number (.....)

PL2

D.7.3 Pharmaceutical form :

Tablet

D.7.4 Route of administration :

Oral Use

D.7.5 Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1

PR2

D.7.5.1 Composition, apart from the active substance(s) :

D.7.5.2 - is it otherwise identical to the IMP?

yes ² no ²

D.7.5.2.1- if not, specify major ingredients :

D.8 SITE WHERE THE QUALIFIED PERSON CERTIFIES BATCH RELEASE¹⁸

*This section is dedicated to **finished** IMPs i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. If there is more than one site or more than one IMP is certified, use extra pages and give each IMP its number from Section D.1.1 or D.7.2. In the case of multiple sites indicate the product certified by each site.*

D.8.1 Do not fill in section 8.2 for an IMP that:

- Has an MA in the EU **and**
- Is sourced from the EU market **and**
- Is used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labelling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive)

If all these conditions are met tick ²⁶ and list the number(s) of each IMP including placebo from sections D.1.1 and D.7.2. to which this applies

¹⁸ In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medical Products in the European Union

D.8.2 Who is responsible in the Community for the certification of the finished IMP ? :

This site is responsible for certification of (list the number(s) of each IMP including placebo concerned from sections D.1.1 and D.7.2) :

PR2

PL2

Please tick the appropriate box:

D.8.2.1 - Manufacturer

☐

D.8.2.2 - Importer

☐

D.8.2.3 Name of the organisation :

Pfizer Ltd

D.8.2.3.1 Address :

Ramsgate Road

Sandwich/ Kent

CT13 9NJ

UNITED KINGDOM

D.8.2.4 - Give the manufacturing authorisation number : MA (IMP) 57

D.8.2.4.1 If no authorisation, give the reasons :

Where the product does not have a MA in the EU but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2 of Directive 2005/28/EC/(GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial at D.8.2 above

D.8.2 Who is responsible in the Community for the certification of the finished IMP ? :

This site is responsible for certification of (list the number(s) of each IMP including placebo concerned from sections D.1.1 and D.7.2) :

PR1

PL1

Please tick the appropriate box:

D.8.2.1 - Manufacturer

☐

D.8.2.2 - Importer

☐

D.8.2.3 Name of the organisation :

Pfizer Ltd

D.8.2.3.1 Address :

Ramsgate Road

Sandwich/ Kent

CT13 9NJ

UNITED KINGDOM

D.8.2.4 - Give the manufacturing authorisation number : MA (IMP) 57

D.8.2.4.1 If no authorisation, give the reasons :

Where the product does not have a MA in the EU but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2 of Directive 2005/28/EC/(GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial at D.8.2 above

E. GENERAL INFORMATION ON THE TRIAL

The section should be used to provide information about the aims, scope and design of the trial. When the protocol includes a sub-study in the MS concerned section E.2.3 should be completed providing information about the sub-study. To identify it check the sub-study in the 'Objective of the trial' question below.

E.1 Medical condition or disease under investigation

E.1.1 Specify the medical condition(s) to be investigated¹⁹ (free text) :

Male erectile dysfunction (MED).

E.1.2 MedDRA version, level, term and classification code²⁰ (repeat as necessary) :

Version	Level	Code	Term
9.1	LLT	10052003	Erectile dysfunction NOS

E.1.3 Is any of the conditions to be studied a rare disease²¹ ? yes ^ no ^

E.2 Objective of the trial

E.2.1 Main objective :

To confirm the efficacy of single oral doses of PF-00446687 200 mg in improving penile erectile activity, utilizing the penile plethysmography (Rigiscan® Plus) technique, in males suffering from erectile dysfunction.

E.2.2 Secondary objectives :

To establish efficacy of lower doses of PF-00446687 in improving penile erectile activity and if possible, determine the dose response, in this population.

To assess subjective assessment of sexual arousal and desire by means of questionnaire following single doses of PF-00446687.

To determine the safety and toleration of PF-00446687 in this population.

To assess PK after single doses of PF-00446687 and sildenafil in this population.

To assess Agouti Related Protein (AgRP) levels in this population.

E.2.3 Is there a sub-study ? yes ^ no ^

E.2.3.1 If Yes, give the full title, date and version of each sub-study and their related objectives :

¹⁹ In the case of healthy volunteer trial, the intended indication for the product under development should be provided.

²⁰ Applicants are encouraged to provide the MedDRA lower level term if applicable and classification code. These can be accessed from the EMEA EudraCT website (<http://www.emea.eu.int>)

²¹ Points to consider on the calculation and reporting of the prevalence of a condition for Orphan drug designation : COM/436/01 (www.emea.eu.int/hums/human/comp/orphaapp.htm)

E.3 Principal inclusion criteria (list the most important)

1. Male subjects aged 18-65 years.
2. Subjects who have given written informed consent to participate in the study.
3. Subjects must be in a heterosexual stable relationship for at least the last 6 months.
4. Subjects with erectile dysfunction of at least six months duration prior to entering the study. Erectile dysfunction is defined as “the inability to attain and/or maintain penile erection sufficient for satisfactory performance”. [protocol ref 1]
5. Subjects with moderate to severe (6-16) erectile dysfunction as classified on the International Index of Erectile Function (IIEF).
6. Subjects who, in the opinion of the investigator, are known responders to PDE5i's, such as subjects with a current or recent (within 6 months) history of successful PDE5i use.
7. Subjects who are willing and able to comply with scheduled visits, treatment plan, laboratory tests and other trial procedures.

E.4 Principal exclusion criteria (list the most important)

1. Subjects who are either known non-responders to, or unlikely to respond to treatment with either MC4 agonists or PDE5i's. This includes subjects who are diabetic, subjects with significant neurological disease, spinal cord injury, multiple sclerosis, or previous pelvic surgery including radical and nerve sparing prostatectomy.
2. Subjects with any clinically significant abnormality, following review of pre-study laboratory data and after a full physical examination.
3. Subjects with a history of significant cardiac disease, particularly moderate or severe cardiac failure, unstable angina or recent myocardial infarction, stroke or life-threatening arrhythmia within the previous 6 months.
4. Subjects with a history of syncope or cardiac conduction abnormality (including paroxysmal brady or tachyarrhythmias).
5. Subjects who suffer from hypo- or hypertension (treated as well as untreated) or have a resting supine blood pressure below 90/50 mm Hg or above 170/110 or who show a postural drop in either systolic blood pressure of >20 mm Hg or diastolic blood pressure of >10 mm Hg at screening.
6. Subjects who are currently receiving vasoactive medication, such as (but not limited to) α -blockers, β -blockers, calcium antagonists.
7. Subjects who are receiving drugs known to inhibit CYP3A4, such as ketoconazole (systemic), erythromycin, cimetidine, clarithromycin, fluvoxamine, itraconazole (systemic), voriconazole, protease inhibitors.
8. Subjects with any clinically significant haematological, renal or hepatic abnormality.
9. Subjects with major psychiatric disorders and those who have received treatment for any major psychiatric disorder (eg, psychosis or hospitalization due to major depression) within the past 12 months.
10. Subjects who have received any experimental (ie, non-approved) drug within the past four months (prior to the first dosing day of the study).
11. Subjects who drink more than 21 units of alcohol per week. (1 unit = 285 mL of beer or 25 mL of spirits or 125 mL of wine).
12. Subjects with a history of controlled substance abuse within the past 2 years.
13. Subjects who, in the opinion of the principal investigator, have any medical or psychological condition or social circumstances which would impair their ability to participate reliably in the study, or who may increase the risk to themselves or others by participating.

14. Subjects who, in the opinion of the investigator, are not likely to complete the study for whatever reason.
 15. Subjects with a history of hypersensitivity to study drug and its excipients or known allergy to sildenafil and/or MC agonists.
 16. Subjects with other forms of sexual dysfunction (eg, retrograde ejaculation, an ejaculation, painful ejaculation, premature ejaculation, hypoactive sexual desire and inhibited or absent orgasm).
 17. Subjects with Peyrone's disease.
 18. Subjects with evidence or history of seizure disorder, clinically significant haematological, renal, hepatic, psychiatric, neurologic or allergic disease (including drug allergies, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).
 19. History of febrile illness within 5 days prior to the first dose.
 20. Subjects with any condition possibly affecting drug absorption (eg, gastrectomy).
 21. Blood donation of approximately 1 pint (500 mL) within 56 days prior to dosing and subjects intending to donate during the study.
 22. Subjects with a 12-lead ECG demonstrating QTc >450 msec at screening.
- Criteria specific to Sildenafil:
23. Subjects who are prescribed and/or taking medication which is contraindicated or cautioned with concomitant intake of PDE5 inhibitors, such as nitrates or nitric oxide donors in any form (oral, sublingual, buccal, inhalational or aerosols), cimetidine, CYP3A4 inhibitors, such as erythromycin, ketoconazole and protease inhibitors.
 24. Subjects with retinitis pigmentosa.
 25. Subjects who have loss of vision in one eye because of non-arteritic anterior ischaemic optic neuropathy (NAION), regardless of whether this episode was in connection or not with previous PDE5i exposure.
 26. Subjects with congestive cardiac failure or coronary artery disease causing unstable angina, recent history of myocardial infarction or stroke.

E.5 Primary end point(s) :

Total duration of erections > 60% rigidity at the base of the penis and area under the rigidity response curve (AUC) of erectile activity for the duration of the post dose time sequences.

Total duration of erections > 60% rigidity at the base of the penis and AUC for the duration of (VSS-1 + VSS-2).

Total duration of erections > 60% rigidity at the base of the penis and AUC for the duration of (Neutral-1 + Neutral-2).

Duration of erections > 60% rigidity at the base of the penis and AUC at defined time sequences.

Time to onset of first erection of > 60% rigidity and a minimum of 5 minutes duration

Assessment of sexual interest and ,mental arousal .

Diary of sexual events

Exploring the dose an/or response relationship of PF-00446687.

E.6 Scope of the trial – Tick all boxes where applicable

- E.6.1 - Diagnosis ☐
- E.6.2 - Prophylaxis ☐
- E.6.3 - Therapy ☐
- E.6.4 - Safety ☐
- E.6.5 - Efficacy ☐
- E.6.6 - Pharmacokinetic ☐
- E.6.7 - Pharmacodynamic ☐
- E.6.8 - Bioequivalence ☐
- E.6.9 - Dose Response ☐
- E.6.10 - Pharmacogenetic ☐
- E.6.11 - Pharmacogenomic ☐
- E.6.12 - Pharmacoeconomic ☐
- E.6.13 - Others ☐

E.6.13.1 If others, specify :

E.7 Trial type²² and phase

- E.7.1 Human pharmacology (Phase I) ☐ yes ☐ no ☐
- Is it:
- E.7.1.1 First administration to humans ☐ yes ☐ no ☐
- E.7.1.2 Bioequivalence study ☐ yes ☐ no ☐
- E.7.1.3 Other ☐ yes ☐ no ☐
- E.7.1.3.1 If Other, please specify :
- E.7.2 Therapeutic exploratory (Phase II) ☐ yes ☐ no ☐
- E.7.3 Therapeutic confirmatory (Phase III) ☐ yes ☐ no ☐
- E.7.4 Therapeutic use (Phase IV) ☐ yes ☐ no ☐

E.8 Design of the trial

E.8.1 Controlled : ☐ yes ☐ no ☐

• If yes, specify :

E.8.1.2 Open :	yes [^]	no [^]	
E.8.1.1 Randomised :	yes [^]	no [^]	
E.8.1.3 Single blind :	yes [^]	no [^]	E.8.1.4 Double blind : yes [^] no [^]
E.8.1.5 Parallel group :	yes [^]	no [^]	E.8.1.6 Cross over : yes [^] no [^]
E.8.1.7 Other :	yes [^]	no [^]	
E.8.1.7.1 If yes to other, specify : 3rd party open			
E.8.2 • If Controlled specify the comparator :			
E.8.2.1 - Other medicinal product(s)	yes [^]	no [^]	
E.8.2.2 - Placebo	yes [^]	no [^]	
E.8.2.3 - Other	yes [^]	no [^]	
E.8.2.3.1 If yes to other specify :			
E.8.3 Single site in the Member State concerned (see also section G) :	yes [^]	no [^]	
E.8.4 Multiple sites in the Member State concerned (see also section G) :	yes [^]	no [^]	
E.8.4.1 Number of sites anticipated in the Member State concerned :	2		
E.8.5 Multiple Member States :	yes [^]	no [^]	
E.8.5.1 Number of sites anticipated in the Community :	3		
E.8.6 Does this trial involve countries outside the EU ?	yes [^]	no [^]	
E.8.7 Does this trial have a data monitoring committee ?	yes [^]	no [^]	

²² The descriptions of the trial types provided are those recommended in preference to Phases. See page 5 of Community guideline CPMP/ICH/291/95. The development of a new indication after initial approval of a medicine should be considered as a new development plan.

E.8.8 Definition of the end of trial and justification, in the case where it is not the last visit of the last subject undergoing the trial :²³

End of Trial in a Member State of the European Union is defined as the time at which it is deemed that sufficient subjects have been recruited and completed the trial as stated in the regulatory application (ie, Clinical Trial Application (CTA)) and ethics application in the Member State.

End of Trial in all participating countries is defined as Last Subject Last Visit.

E.8.9 Initial estimate of the duration of the trial ²⁴ (years, months and days):

E.8.9.1 - in the MS concerned	0	years	9	months	0	days
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E.8.9.2 - in all countries concerned by the trial	0	years	9	months	0	days
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²³ If not provided in the protocol

²⁴ From the 1st inclusion until the last visit of the last subject

F. POPULATION OF TRIAL SUBJECTS

F.1 Age Span		
F.1.1 Less than 18 years	yes [^]	no [^]
If yes, specify:		
F.1.1.1 In Utero	yes [^]	no [^]
F.1.1.2 Preterm Newborn Infants (up to gestational age <= 37 weeks)	yes [^]	no [^]
F.1.1.3 Newborn (0-27 days)	yes [^]	no [^]
F.1.1.4 Infant and toddler (28 days - 23 months)	yes [^]	no [^]
F.1.1.5 Children (2-11 years)	yes [^]	no [^]
F.1.1.6 Adolescent (12-17 years)	yes [^]	no [^]
F.1.2 Adult (18-65 years)	yes [^]	no [^]
F.1.3 Elderly (> 65 years)	yes [^]	no [^]
F.2 Gender		
F.2.1 Female	yes [^]	no [^]
F.2.3 Male	yes [^]	no [^]

F.3 Group of trial subjects		
F.3.1 Healthy volunteers	yes [^]	no [^]
F.3.2 Patients	yes [^]	no [^]
F.3.3 Specific vulnerable populations	yes [^]	no [^]
F.3.3.1 - women of child bearing potential	yes [^]	no [^]
F.3.3.2 - women of childbearing potential using contraception	yes [^]	no [^]
F.3.3.3 - pregnant women	yes [^]	no [^]
F.3.3.4 - nursing women	yes [^]	no [^]
F.3.3.5 - emergency situation	yes [^]	no [^]
F.3.3.6 - subjects incapable of giving consent personally	yes [^]	no [^]
F.3.3.6.1 If yes, specify :		
F.3.3.7 - others :	yes [^]	no [^]

F.3.3.7.1 If yes, specify :

F.4 Planned number of subjects to be included :

F.4.1 - in the Member State :32

F.4.2 For a multinational trial:

F.4.2.1 - in the Community :48

F.4.2.2 - in the whole clinical trial : 48

F.5 Plans for treatment or care after a subject has ended his/her participation in the trial²⁵ If it is different from the expected normal treatment of that condition, please specify (free text) :

²⁵ If not already provided in the protocol

G. CLINICAL TRIAL SITES/INVESTIGATORS IN THE MEMBER STATE CONCERNED BY THIS REQUEST

G.1. Coordinating investigator (*for multicentre trial*) and principal investigator (*for single centre trial*)

G.1.1 and G.1.2 and G.1.3

Name :

G.1.4 Qualification

(MD.....)

G.1.5 Professional address:

G.2. Principal investigators *(for multicentre trial; where necessary, use additional forms)*

G.2.1 and G.2.2 and G.2.3

Name :



G.2.4 Qualification
(MD.....)

MB BCh BAO MRCP MD FRCP

G.2.5 Professional address :

The Royal Victoria Hospital

Grosvenor Road,

Belfast,

BT12 6BA

UNITED KINGDOM

G.2. Principal investigators *(for multicentre trial; where necessary, use additional forms)*

G.2.1 and G.2.2 and G.2.3

Name :



G.2.4 Qualification
(MD.....)

MBChB

G.2.5 Professional address :

Covance Clinical Research Unit Ltd

Springfield House Hyde Street

Leeds

LS2 9LH

UNITED KINGDOM

G.2. Principal investigators *(for multicentre trial; where necessary, use additional forms)*

G.2.1 and G.2.2 and G.2.3

Name :



G.2.4 Qualification
(MD.....)

BSc (Hons), MBChB

G.2.5 Professional address :

Covance Clinical Research Unit Ltd

Springfield House Hyde Street

Leeds

LS2 9LH

UNITED KINGDOM

G.2. Principal investigators *(for multicentre trial; where necessary, use additional forms)*

G.2.1 and G.2.2 and G.2.3

Name :



G.2.4 Qualification
(MD.....)

MA, MChir, FRCS (Urol), FEBU

G.2.5 Professional address :

Consultant Urologist

St. James Hospital

Beckett Street

Leeds

LS9 7TF

UNITED KINGDOM

G.3. Central technical facilities to be used in the conduct of the trial. Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised (repeat as needed for multiple organisations)

G.3.1 Organisation Department: York Bioanalytical solutions

Organisation Name: York

G.3.2 Name of contact person :

G.3.3 Address : Cedar House, Northminster Business Park, Northfield Lane

Upper Poppleton, York

UNITED KINGDOM

G.3.4 Telephone number :

G.3.5 Duties subcontracted : Other Duties subcontracted

AgRP

G.3. Central technical facilities to be used in the conduct of the trial. Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised (repeat as needed for multiple organisations)

G.3.1 Organisation Department: Covance Bioanalytical Services LLC

Organisation Name: Covance

G.3.2 Name of contact person :

G.3.3 Address : 8211 SciCor Drive, Suite B

Indianapolis, Indiana

46214

UNITED STATES

G.3.4 Telephone number :

G.3.5 Duties subcontracted : Clinical Chemistry

Primary/ surrogate endpoint test

G.3. Central technical facilities to be used in the conduct of the trial. Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised (repeat as needed for multiple organisations)

G.3.1 Organisation Department: Advion Bioservices Inc

Organisation Name: Advion Bioservices Inc

G.3.2 Name of contact person :

G.3.3 Address :

19, Brown Road

Ithaca, NY

NY 14850

UNITED STATES

G.3.4 Telephone number :

G.3.5 Duties subcontracted :

Clinical Chemistry

Primary/ surrogate endpoint test

G.4. Organisations to whom the sponsor has transferred trial related duties and functions (repeat as needed for multiple organisations)

G.4.1 Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party ?

yes ^ no ^

Repeat as necessary for multiple organisations :

G.4.1.1 Organisation Department:

Organisation Name:

G.4.1.2 Name of contact person :

G.4.1.3 Address :

G.4.1.4 Telephone number :

Duties/functions subcontracted :

G.4.1.5 All tasks of the sponsor yes ^ no ^

G.4.1.6 Monitoring yes ^ no ^

G.4.1.7 Regulatory yes ^ no ^

G.4.1.8 Investigator Recruitment yes ^ no ^

G.4.1.9 IVRS²⁶ - treatment randomisation yes ^ no ^

G.4.1.10 Data Management yes ^ no ^

G.4.1.11 E-data capture yes ^ no ^

G.4.1.12 SUSAR reporting yes ^ no ^

G.4.1.13 Quality assurance auditing yes ^ no ^

G.4.1.14 Statistical analysis yes ^ no ^

G.4.1.15 Medical writing yes ^ no ^

G.4.1.16 Other duties subcontracted yes ^ no ^

G.4.1.16.1 If Yes to Other please specify :

²⁶ Interactive Voice Response System : commonly used for randomisation of treatment and controlling the shipment of stock of product.

H. COMPETENT AUTHORITY / ETHICS COMMITTEE IN THE MEMBER STATE CONCERNED BY THIS REQUEST

H.1 Type of application

If this application is addressed to the Competent Authority, please tick the Ethics Committee box and give information on the Ethics committee concerned. If this application is addressed to the Ethics Committee, please tick the Competent Authority box and give information on the Competent Authority concerned.

H.1.1 Competent Authority [^]

H.1.2 Ethics Committee [^]

Information on Competent Authorities / Ethics Committees

H.2.1 Name : Sth East REC
Address : Kent and Medway Health
Preston Hall, Aylesford, Kent
ME20 7NJ
UNITED KINGDOM

H.2.2 Date of submission : 2007-04-13

H.3 Authorisation/opinion : [^] H.3.1 to be requested [^] H.3.2 pending [^] H.3.3 given

If given, specify: H.3.3.1 Date of authorisation / opinion:
[^] H.3.3.2 authorisation accepted / opinion favourable:
[^] H.3.3.3 not accepted / not favourable.

If not acceptable / not favourable, give :

H.3.3.3.1 - the reasons

H.3.3.3.2 - the eventual anticipated date of resubmission :

I. SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

I.1 I hereby confirm that / confirm on behalf of the sponsor (delete which is not applicable) that

- the above information given on this request is correct
- the trial will be conducted according to the protocol, national regulation and the principles of good clinical practice
- It is reasonable for the proposed clinical trial to be undertaken.
- I will submit reports of suspected unexpected serious adverse reactions and safety reports according to applicable guidance.
- I will submit a summary of the final study report to the competent authority and the ethics committee concerned within a maximum 1 year deadline after the end of the study in all countries.

I.3 APPLICANT of the request for the competent authority(as stated in section C1) :

I.3.1 Date : 17th April 2007

I.3.2 Signature :

I.3.3 Print name :

²⁷ On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.