EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

IMPLEMENTATION OF THE 'ADVANCED THERAPIES' REGULATION
Regulation (EC) No 1394/2007

PUBLIC CONSULTATION PAPER

DRAFT AMENDMENTS TO THE CLINICAL TRIAL APPLICATION FORM AS REGARDS ADANCED THERAPY MEDICINAL PRODUCTS

Version: 22 July 2008

Deadline for Public Consultation: 15 October 2008

This document does not represent an official position of the European Commission. It is a tool to explore the views of interested parties on a preliminary proposal. The suggestions contained in this document do not prejudge the form and content of any future proposal by the European Commission.

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1 About the Consultation

1.1 What is the purpose of this consultation?

Regulation (EC) No 1394/2007 on advanced therapy medicinal products[1] ("the Regulation") lays down specific rules concerning the authorisation, supervision and pharmacovigilance of advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue engineering). This Regulation will apply from 30 December 2008.

The European Commission has published on 13 December 2007 an implementation plan, outlining its priorities for the implementation of the Regulation[2]. The implementation plan has been developed and agreed with the European Medicines Agency (EMEA).

Annex 1 to the *'Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial*[3] defines the standard template for the Clinical Trial Application (CTA) form. It is necessary to amend this form in order to incorporate the changes entailed by the Regulation. This public consultation document includes the draft amendments. Changes compared to the current version of the CTA form are highlighted in 'tracked changes'.

1.2 Who is consulted?

Comments on this document are invited from all stakeholders dealing with advanced therapy medicinal products. Stakeholders who are not established within the European Union are equally invited to comment. Comments from Small and Medium-sized Enterprises (SMEs) involved in the sector are especially welcomed.

1.3 How can I contribute?

Contributions should be sent by e-mail to entr-pharmaceuticals@ec.europa.eu, **before 15 October 2008**. An acknowledgement of receipt will be issued for each contribution received, within five working days except in August.

1.4 What will happen next?

All contributions will be carefully analysed. Any future proposal amending the CTA form as regards advanced therapy medicinal products will build on this consultation.

1.5 Any questions?

Please contact the European Commission:
entr-pharmaceuticals@ec.europa.eu (tel.: +32 2 299 56 99)

[1] OJ L324, 10.12.2007, p. 121.

[2] http://ec.europa.eu/enterprise/pharmaceuticals/advtherapies/index.htm

[3] http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol10_en.htm

Annex 1: Clinical trial Application Form

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 information to make it valid :	Date of request for addition al information :	Grounds for non acceptance/ negative opinion : o Give date :
Date of valid application : Date of start of procedure:	Date of receipt of additional / amended information :	Authorisation/ positive opinion : o Give date :
Competent authority registration number: Ethics Committee registration number :		Withdrawal of application o 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: o
REQUEST FOR OPINION OF THE ETHICS COMMITTEE: o

A TRIAL IDENTIFICATION

A.1 Member State in which the submission is being made :
A.2 EudraCT number[4]
A.3 Full title of the trial :
A.3.1 Title of the trial for lay people, in easily understood language:
A.3.2 Name or abbreviated title of the trial when used
A.4 Sponsor's protocol code number, version, and date [5]**:**
A.5 ISRCTN number[6]**, if available**
A.6 Additional international study identifiers (e.g. WHO, clinicaltrials.gov, US NCT Number [7]**)**
A.7 Is this a resubmission? yes o **no** o **If yes, indicate the resubmission letter** [8]
A.8 Is the trial part of a Paediatric Investigation Plan yes o **no** o
A.9 EMEA Decision number of Paediatric Investigation Plan

[4] Append the EudraCT number confirmation receipt.
[5] Any translation of the protocol should be assigned the same date and version as those in the original document.
[6] International Standard Randomised Controlled Trial Number. Sponsors may wish to use an International Standardised Random 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://eudract.emea.europa.eu/. When available they should provide it in Section A.6 of the application form.
[7] US National Clinical Trial (NCT) Numbers required on the FDA clinical trial application form.
[8] 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 :
B.1.2	Name of the person to contact:
B.1.3	Address :
B.1.4	Telephone number :
B.1.5	Fax number :
B.1.6	E-mail:

B.2	**LEGAL REPRESENTATIVE [9] 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:

B.3	**STATUS OF THE SPONSOR:**	
B.3.1	Commercial	o
B.3.2	Non commercial	o

B.4	**Source(s) of Monetary or Material Support for the clinical trial:**
B.4.1	Name of organisation :
B.4.2	Country:

B.5	**Contact point [10] designated by the sponsor for further information on the trial**
B.5.1	Name of organisation :
B.5.2	Contact point (e.g. “Clinical Trial Information Desk”):
B.5.3	Address :
B.5.4	Telephone number :
B.5.5	Fax number :
B.5.6	E-mail: (use a functional e-mail address rather than a personal one)

[9] In accordance with Article 19 of Directive 2001/20/EC.

[10] The contact point should give functional information rather than details of one “person”, in order to avoid the need for update and maintenance of these contact details.

C APPLICANT IDENTIFICATION, (please tick the appropriate box)

C.1	**REQUEST FOR THE COMPETENT AUTHORITY**	o
C.1.1	Sponsor	o
C.1.2	Legal representative of the sponsor	o
C.1.3	Person or organisation authorised by the sponso r to make the application	o
C.1.4	Complete the details of the applicant below even if they are provided elsewhere on the form:	
C.1.4.1	Organisation :	
C.1.4.2	Name of contact person :	
C.1.4.3	Address :	
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 a .xml file copy of the CTA form data saved on EudraCT?	o yes o 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) [11]?	o yes o 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)		

C.2	**REQUEST FOR THE ETHICS COMMITTEE**	o
C.2.1	Sponsor	o
C.2.2	Legal representative of the sponsor	o
C.2.3	Person or organisation authorised by the sp onsor to make the application.	o
C.2.4	Investigator in charge of the application if applicable [12]:	
•	Co-ordinating investigator (for multicentre trial)	o
•	Principal investigator (for single centre trial).	o
C.2.5	Complete the details of the applica nt below even if they are provided elsewhere on the form:	
C.2.5.1	Organisation :	
C.2.5.2	Name :	
C.2.5.3	Address :	
C.2.5.4	Telephone number :	
C.2.5.5	Fax number :	
C.2.5.6	E-mail :	

[11] This requires a EudraLink account. (See www.EudraCT.europa.eu for details)
[12] According to national legislation.

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 . ***For placebo go directly to D7****. If the trial is performed with several products use extra pages and give each product a sequential number in D1.1 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:	(..)
D.1.2	IMP being tested	o
D.1.3	IMP used as a comparator	o

D.2 STATUS OF THE IMP.		
D.2.1	Has this IMP to be used in the trial a marketing authorisation?:	yes o no o
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.2.1.1	If yes to D.2.1, specify for the product to be used in the trial:	
D.2.1.1.1	Trade name[13]:	
D.2.1.1.2	Name of the MA holder:	
D.2.1.1.3	MA number (if MA granted by an EEA Member State):	
D.2.1.1.4	Is the IMP modified in relation to its MA?	yes o no o
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 o no o

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 o no o
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 o no o
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 [6]	yes o no o
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 o no o
D.2.2.4.1	If yes, please specify :	

D.2.3	IMPD submitted:	
D.2.3.1	Full IMPD	yes o no o
D.2.3.2	Simplified IMPD[14]	yes o no o
D.2.3.3	Summary of product characteristics (SmPC) only	yes o no o

[13] Available from the Summary of Product Characteristics (SmPC).

[14] Provide justification for using simplified dossier in the covering letter (see Section 4.1.6.2.1 and table 1).

D.2.4	Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?	yes o no o
D.2.4.1	If yes specify which Member States:	
D.2.5	Has the IMP been designated in this indication as an orphan drug in the Community?	yes o no o
D.2.5.1	If yes, give the orphan drug designation number [15] : ( )	

D.2.6	Has the IMP been the subject of scientific advice related to this clinical trial?	yes o no o
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 [16]?	yes o no o
D.2.6.1.2	From a MS competent authority?	yes o no o

D.3	**DESCRIPTION OF THE IMP**	
D.3.1	Product name where applicable [17] :	
D.3.2	Product code where applicable [18] :	
D.3.3	ATC code, if officially registered [19]:	
D.3.4	Pharmaceutical form (use standard terms) :	
D.3.4.1	Is this a specific paediatric formulation?	yes no
D.3.5	Maximum duration of treatment of a subject according to the protocol :	
D.3.6	Maximum dose allowed (specify : per day or total dose; units and route of administration,):	
D.3.6.1	First dose for first-in-human clinical trial (specify; per day or total dose; units and route of administration):	
D.3.6.2	Maximum dose allowed (specify; per day or total dose; units and route of administration):	
D.3.7	Route of administration (use standard terms):	
D.3.8	Name of each active substance (INN or proposed INN if available):	
D.3.9	Other available name f or each active substance (CAS [20], current sponsor code(s), other descriptive name, etc ; provide all available) :	
D.3.10	Strength (specify all strengths to be used) :	
D.3.10.1	Concentration unit:	
D.3.10.2	Concentration type (“exact number”, “range", "more than” or “up to”) :	
D.3.10.3	Concentration (number).	

[15] According to the Community register on orphan medicinal products (Regulation (EC) n° 141/2000) : http://ec.europa.eu/enterprise/pharmaceuticals/register/index.htm

[16] Committee for Medicinal Products for Human Use of the European Medicines Agency

[17] To be provided only when there is no trade name. This is the name routinely used by a sponsor to identify the IM P in the CT documentation (protocol, IB…).

[18] To be provided only when there is no trade name. This is a 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 c ode may be used for combinations of drugs or drugs and devices.

[19] Available from the Summary of Product Characteristics (SmPC).

[20] Chemical Abstracts Service.

D.3.11 Type of IMP

Does the IMP contain an active substance:

D.3.11.1 Of chemical origin? yes o no o

D.3.11.2 Of biological / biotechnological origin (other than Advanced Therapy IMP (ATIMP) ?[21] yes o no o

Is this a :

~~yes o no o~~

D.3.11.3 Advanced Therapy IMP (ATIMP)? yes o no o

D.3.11.3.1 Somatic cell therapy medicinal product[22]? yes o no o

D.3.11.3.2 Gene therapy medicinal product [23]? yes o no o

D.3.11.3.3 Tissue Engineered Product [24]? yes o no o

D.3.11.3.4 Combined ATIMP involving a medical device[25]? yes o no o

~~Is this a :~~

~~D.3.11.3~~D.3.11.4 Product that includes a device [22], other than a combined ATIMP ? yes o no o

~~Cell therapy medicinal product [17] ? yes o no o~~

~~D.3.11.3Gene therapy medicinal product [17]? yes o no o~~

D.3.11.5 Radiopharmaceutical medicinal product? yes o no o

D.3.11.6 Immunological medicinal product (such as vaccine, allergen, immune serum)? yes o no o

D.3.11.7 Plasma derived medicinal product? yes o no o

D.3.11.8 Other extractive medicinal product? yes o no o

D.3.11.9 Recombinant medicinal product? yes o no o

~~D.3.11.9~~D.3.11.10 Herbal medicinal product? yes o no o

~~D.3.11.10~~D.3.11.11 Homeopathic medicinal product? yes o no o

~~D.3.11.11~~D.3.11.12 Medicinal product containing genetically modified organisms? yes o no o

If yes to D.3.11.11:

~~D.3.11.11.1~~D.3.11.12.1 Has the authorisation for contained use or release been granted? ~~yes~~ o no o

~~D.3.11.11.2~~D.3.11.12.2 Is it pending? yes o no o

~~D.3.11.12~~D.3.11.13 Is it an IMP to be used in a first-in-human clinical trial? yes o no o

~~D.3.11.12.1~~D.3.11.13.1 If yes, are there risk factors identified, according to the guidance FIH? [26] yes o no o

~~D.3.11.13~~D.3.11.14 Another type of medicinal product? yes o no o

~~D.3.11.13.1~~D.3.11.14.1 If yes, specify :

D.3.12 Mode of action *(free text[27])*

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

[21] ~~Complete also sections D.4,and where applicable sections D.5,and D.6.~~

[22] Complete also section D.4 Cell therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.

[23] Complete also section D.5 Gene Therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.

[24] Complete also section D.6 - Tissue Engineered Product as defined in Article 2(1)(b) of Regulation 1394/2007/EC.

[25] Complete also section D.7

[26] Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007 19 July 2007

[27] The mode of action should briefly describe the chemical, biochemical, immunological or biological means the IMP uses to effect its pharmaceutical action.

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

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~~**D.5**~~**D.4 SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)**

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~~D.5.1~~D.4.1 Origin of cells

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~~D.5.1.1~~D.4.1.1 Autologous yes o no o

~~D.5.1.2~~D.4.1.2 Allogeneic yes o no o

~~D.5.1.3~~D.4.1.3 Xenogeneic yes o no o

~~D.5.1.3.1~~D.4.1.3.1 If yes, specify species of origin :

~~D.5.2~~D.4.2 Type of cells

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~~D.5.2.1~~D.4.2.1 Stem cells yes o no o

~~D.5.2.2~~D.4.2.2 Differentiated cells yes o no o

~~D.5.2.2.1~~D.4.2.2.1 If yes, specify the type (e.g. keratinocytes, fibroblasts, chondrocytes,…) :

~~D.5.2.3~~D.4.2.3 Others : yes o no o

~~D.5.2.3.1~~D.4.2.3.1 If others, specify :

~~D.6~~D.5 **GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS**

~~D.6.1~~D.5.1 **Gene(s) of interest :**

~~D.6.2~~D.5.2 In vivo gene therapy: yes o no o

~~D.6.3~~D.5.3 Ex vivo gene therapy: yes o no o

~~D.6.4~~D.5.4 Type of gene transfer product

~~D.6.4.1~~D.5.4.1 Nucleic acid (e.g. plasmid) : yes o no o

If yes, specify if:

~~D.6.4.1.1~~D.5.4.1.1 Naked: yes o no o

~~D.6.4.1.2~~D.5.4.1.2 Complexed yes o no o

~~D.6.4.2~~D.5.4.2 Viral vector: yes o no o

~~D.6.4.2.1~~D.5.4.2.1 If yes, specify the type: adenovirus, retrovirus, AAV, …:

~~D.6.4.3~~D.5.4.3 Others : yes o no o

~~D.6.4.3.1~~D.5.4.3.1 If others, specify :

~~D.6.5~~D.5.5 Genetically modified cells **:** yes o no o

If yes, specify - origin of the cells :

~~D.6.5.1~~D.5.5.1 Autologous : yes o no o

~~D.6.5.2~~D.5.5.2 Allogeneic : yes o no o

~~D.6.5.3~~D.5.5.3 Xenogeneic : yes o no o

~~D.6.5.3.1~~D.5.5.3.1 If yes, specify species of origin :

~~D.6.5.4~~D.5.5.4 Other type of cells (hematopoietic stem cells, …) : yes o no o If yes specify:

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

D.6 TISSUE ENGINEERED PRODUCT

The indication which determines that this is a Tissue Engineered Product as opposed to a Cell Therapy product is given in section E.1.1.

D.6.1 Origin of cells

D.6.1.1 Autologous yes o no o

D.6.1.2 Allogeneic yes o no o

D.6.1.3 Xenogeneic yes o no o

D.6.1.3.1 If yes, specify species of origin :

D.6.2 Type of cells

D.6.2.1 Stem cells yes o no o

D.6.2.2 Differentiated cells yes o no o

D.6.2.2.1 If yes, specify the type (e.g. keratinocytes, fibroblasts, chondrocytes,…) :

D.6.2.3 Others : yes o no o

D.6.2.3.1 If others, specify :

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~~D~~.7 PRODUCTS CONTAINING DEVICES (I.E. MEDICAL DEVICES, SCAFFOLDS ETC.)

D.7.1 Give a brief description of the device:
D.7.2 What is the name of the device ?
D.7.3 Is the device implantable? yes o no o
D.7.4 Does this product contain:
D.7.4.1 A medical device? yes o no o
D.7.4.1.1 Does this medical device have a CE mark? yes o no o
D.7.4.1.1.1 The notified body is:
D.7.4.2 Bio-materials? yes o no o
D.7.4.3 Scaffolds? yes o no o
D.7.4.4 Matrices? yes o no o
D.7.4.5 Other? yes o no o
D.7.4.6 If other, specify : yes o no o

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~~D.7~~D.8 INFORMATION ON PLACEBO (if relevant; repeat as necessary)

~~D.7.1~~D.8.1 Is a there a placebo: yes o no o
~~D.7.2~~D.8.2 This refers to placebo number: (..)
~~D.7.3~~D.8.3 Pharmaceutical form :
~~D.7.4~~D.8.4 Route of administration :
~~D.7.5~~D.8.5 Which IMP is it a placebo for? Specify IMP Number(s) from D1.1: (..)
~~D.7.5.1~~D.8.5.1 Composition, apart from t he active substance(s):
~~D.7.5.2~~D.8.5.2 Is it otherwise identical to the IMP? yes o no o
~~D.7.5.2.1~~D.8.5.2.1 If not, specify major ingredients :

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~~D.8~~D.9

*This section is dedicated to **finished** IMPs, i.e. medicinal products randomis ed, 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 produ ct certified by each site.*

~~D.8.1~~D.9.1 Do not fill in section D.8.2 for an IMP that:

*Has a MA in the EU **and***
*Is sourced from the EU market **and***
*Is used in the trial without modification(e.g. 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 o and list the number(s) of each IMP including placebo from sections D.1.1 and D.7.2 to which this applies: (..);

~~D.8.2~~D.9.2 **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 from sections D.1.1 and D.7.2): (..);

please tick the appropriate box :

~~D.8.2.1~~D.9.2.1 Manufacturer o
~~D.8.2.2~~D.9.2.2 Importer o

~~D.8.2.3~~D.9.2.3 Name of the organisation:
~~D.8.2.3.1~~D.9.2.3.1 Address :
~~D.8.2.4~~D.9.2.4 Give the manufacturing authorisation number :
~~D.8.2.4.1~~D.9.2.4.1 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.*

[28] In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medicinal Products in the European Union

E GENERAL INFORMATION ON THE TRIAL

This 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 box 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 investigated [29] (free text) :
E.1.1.1	Medical condition in easily understood language
E.1.1.2	Therapeutic area
E.1.2	MedDRA version, level, term and classification code [30](repeat as necessary) :
E.1.3	Is any of the conditions being studied a rare disease [31]? yes o no o

E.2	**OBJECTIVE OF THE TRIAL**
E.2.1	Main objective:
E.2.2	Secondary objectives:
E.2.3	Is there a sub-study? yes o no o
E.2.3.1	If yes give the full title, date and version of each sub -study and their related objectives:

E.3	**PRINCIPAL INCLUSION CRITERIA** ***(list the most important)***

E.4	**PRINCIPAL EXCLUSION CRITERIA** ***(list the most important)***

E.5	**END POINT(S) :**
E.5.1	Primary End Point (repeat as necessary) [32]
E.5.1.1	Timepoint(s) of evaluation of this endpoint
E.5.2	Secondary End Point (repeat as necessary)
E.5.2.1	Timepoint(s) of evaluation of this endpoint

[29] In the case of healthy volunteer trials, the intended indication for the product under development should be provided.
[30] 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://eudract.emea.europa.eu/).
[31] Points to consider on the calculation and reporting of the prevalence of a conditi on for Orphan drug designation : COM/436/01 (http://www.emea.europa.eu/htms/human/orphans/intro.htm).
[32] The protocol will usually identify a single primary end point but there may be a co-primary end point in some cases and/or a number of secondary end points.

E.6	**SCOPE OF THE TRIAL –** Tick all boxes where applicable	
E.6.1	Diagnosis	o
E.6.2	Prophylaxis	o
E.6.3	Therapy	o
E.6.4	Safety	o
E.6.5	Efficacy	o
E.6.6	Pharmacokinetic	o
E.6.7	Pharmacodynamic	o
E.6.8	Bioequivalence	o
E.6.9	Dose Response	o
E.6.10	Pharmacogenetic	o
E.6.11	Pharmacogenomic	o
E.6.12	Pharmacoeconomic	o
E.6.13	Others	o
E.6.13.1	If others, specify:	

E.7	**TRIAL TYPE[33] AND PHASE**	
E.7.1	Human pharmacology (Phase I) Is it:	o
E.7.1.1	First administration to humans	o
E.7.1.2	Bioequivalence study	o
E.7.1.3	Other :	o
E.7.1.3.1	If other, please specify	
E.7.2	Therapeutic exploratory (Phase II)	o
E.7.3	Therapeutic confirmatory (Phase III)	o
E.7.4	Therapeutic use (Phase IV)	o

[33] 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 indicatio n after initial approval of a medicine should be considered as a new development plan.

E.8	**DESIGN OF THE TRIAL**				
E.8.1	Controlled				yes o no o
	If yes, specify:				
E.8.1.1	Randomised				yes o no o
E.8.1.2	Open :				yes o no o
E.8.1.3	Single blind :				yes o no o
E.8.1.4	Double blind:				yes o no o
E.8.1.5	Parallel group:				yes o no o
E.8.1.6	Cross over :				yes o no o
E.8.1.7	Other :				yes o no o
E.8.1.7.1	If yes to other specify:				
E.8.2	If controlled, specify the comparator:				
E.8.2.1	Other medicinal product(s)				yes o no o
E.8.2.2	Placebo				yes o no o
E.8.2.3	Other				yes o no o
E.8.2.3.1	If yes to other, specify :				
E.8.2.4	Number of arms in the trial				
E.8.3	Single site in the Member State concerned (see also section G) **:**				yes o no o
E.8.4	Multiple sites in the Member State concerned(see also section G) **:**				yes o no o
E.8.4.1	Number of sites anticipated in Member State concerned ( )				
E.8.5	Multiple Member States **:**				yes o no o
E.8.5.1	Number of sites anticipated in the EEA ( )				
E.8.6	Does this trial involve sites outside the EEA?				yes o no o
E.8.6.1	Is the trial being conducted completely outside o f the EEA?				yes o no o
E.8.6.2	If yes, specify the regions in which trial sites are planned: (repeat as necessary)				
E.8.7	Does this trial have an independent data monitoring committee?				yes o no o
E.8.8	Definition of the end of trial, and justification in the case wh ere it is not the last visit of the last subject undergoing the trial **:**[34]				
E.8.9	Initial estimate of the duration of the trial [35](years ,months and days):				
E.8.9.1	In the MS concerned	years	months	days	
E.8.9.2	In all countries concerned by the trial	years	months	days	
E.8.10	Proposed date of start of recruitment				
E.8.10.1	In the Member State concerned				
E.8.10.2	In any country				

[34] If not provided in the protocol.
[35] From the first 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 o no o
	If yes specify the estimated number of subjects planned in each age span for the whole trial:		
		Approx. no. of patients [36]	
F.1.1.1	In Utero	( )	yes o no o
F.1.1.2	Preterm Newborn Infants (up to gestational age < 37 weeks)	( )	yes o no o
F.1.1.3	Newborns (0-27 days)	( )	yes o no o
F.1.1.4	Infants and toddlers (28 days - 23 months)	( )	yes o no o
F.1.1.5	Children (2-11 years)	( )	yes o no o
F.1.1.6	Adolescent (12-17 years)	( )	yes o no o
F.1.2	Adult (18-64 years)	**( )**	yes o no o
F.1.3	Elderly (>= 65 years)	**( )**	yes o no o

F.2	GENDER	
F.2.1	Female	o
F.2.2	Male	o

F.3	GROUP OF TRIAL SUBJECTS	
F.3.1	Healthy volunteers	yes o no o
F.3.2	Patients	yes o no o
F.3.3	Specific vulnerable populations	yes o no o
F.3.3.1	Women of child bearing potent ial not using contraception	yes o no o
F.3.3.2	Women of child bearing potential using contraception	yes o no o
F.3.3.3	Pregnant women	yes o no o
F.3.3.4	Nursing women	yes o no o
F.3.3.5	Emergency situation	yes o no o
F.3.3.6	Subjects incapable of giving consent personally	yes o no o
F.3.3.6.1	If yes, specify :	
F.3.3.7	Others :	yes o no o
F.3.3.7.1	If yes, specify	

F.4	PLANNED NUMBER OF SUBJECTS TO BE INCLUDED :	
F.4.1	In the Member State	( )
F.4.2	For a multinational trial **:**	
F.4.2.1	In the Community	( )
F.4.2.2	In the whole clinical tr ial	( )

F.5	PLANS FOR TREATMENT OR CARE AFTER A SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL [37]**. If it is different from the expected normal treatment of that condition, please specify** (free text):

[36] These numbers will be initial estimates. Applicants will not be required to update this information nor do they constitute an authorisation or restriction on the inclusion of these numbers of patients in the trial. The numbers of subjects whose inclusion is authorised are those set out in the authorised version of th e protocol, or subsequent authorised amendments.
[37] If not already provided in the protocol.

G CLINICAL TRIAL SITES/INVESTIGATORS IN THE M EMBER STATE CONCERNED BY THIS REQUEST

G.1 CO-ORDINATING INVESTIGATOR (*for multicentre trial*) and principal investigator (*for single centre trial*)
G.1.1 Given name
G.1.2 Middle name, if applicable
G.1.3 Family name
G.1.4 Qualification (MD…….)
G.1.5 Professional address:
G.1.6 E-mail address
G.1.7 Telephone number

G.2 PRINCIPAL INVESTIGATORS *(for multicentre trial ; where necessary, use additional forms)*
G.2.1 Given name
G.2.2 Middle name, if applicable
G.2.3 Family name
G.2.4 Qualification (MD…….)
G.2.5 Professional address
G.2.6 E-mail
G.2.7 Telephone

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:
G.3.2 Name of contact person :
G.3.3 Address :
G.3.4 Telephone number :
G.3.5 Duties subcontracted :

G.4 NETWORKS TO BE INVOLVED IN THE TRIAL **(e.g. Paediatric Networks involved in the trial)**
G.4.1 Organisation:
G.4.2 Name of contact person :
G.4.3 Address :
G.4.4 Telephone number :
G.4.5 Activities carried out by the network :

G.5	**ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS** (repeat as needed for multiple organisations)	
G.5.1	**Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or th ird party?**	yes o no o
Repeat as necessary for multiple organisations:		
G.5.1.1	Organisation :	
G.5.1.2	Name of contact person :	
G.5.1.3	Address :	
G.5.1.4	Telephone number :	
G.5.1.5	All tasks of the sponsor	yes o no o
G.5.1.6	Monitoring	yes o no o
G.5.1.7	Regulatory (e.g. preparation o f applications to CA and ethics committee)	yes o no o
G.5.1.8	Investigator recruitment	yes o no o
G.5.1.9	IVRS[38] – treatment randomisation	yes o no o
G.5.1.10	Data management	yes o no o
G.5.1.11	E-data capture	yes o no o
G.5.1.12	SUSAR reporting	yes o no o
G.5.1.13	Quality assurance auditing	yes o no o
G.5.1.14	Statistical analysis	yes o no o
G.5.1.15	Medical writing	yes o no o
G.5.1.16	Other duties subcontracted	yes o no o
G.5.1.16.1	If yes to other please specify:	

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

H COMPETENT AUTHORITY / ETHICS COMMITTEE IN TH E 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 the information on the Competent Authority concerned.	
H.1.1 Competent authority	o
H.1.2 Ethics Committee	o

H.2 INFORMATION ON COMPETENT AUTHORITY/ETHICS COMMITTEE
H.2.1 Name and address :
H.2.2 Date of submission :

H.3 AUTHORISATION/OPINION :	
H.3.1 To be requested	o
H.3.2 Pending	o
H.3.3 Given	o
If 'Given', specify:	
H.3.3.1 Date of authorisation / opinion:	
H.3.3.2 Authorisation accepted / opinion favourable	o
H.3.3.3 Not accepted / not favourable	o
If not accepted / 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 as soon as possible to the competent authority and the ethics committee concerned the date of inclusion of the first subject in the concerned Member State; • 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.2	**APPLICANT OF THE REQUEST FOR THE COMPETENT AU THORITY** (as stated in section C.1) :
I.2.1	Date :
I.2.2	Signature[39] :
I.2.3	Print name:

I.3	**APPLICANT OF THE REQUEST FOR THE ETHICS COMMITTEE** (as stated in section C.2) :
I.3.1	Date :
I.3.2	Signature [40]:
I.3.3	Print name:

[39] On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.
[40] On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.