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**

*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:** **Yes ●**
**REQUEST FOR OPINION OF THE ETHICS COMMITTEE:** **No ●**

## A. TRIAL IDENTIFICATION

| | | |
|---|---|---|
| A.1 | Member State in which the submission is being made: | **Sweden - MPA** |
| A.2 | EudraCT number: | **2020-000233-41** |
| A.3 | Full title of the trial: | |
| | **English** | **Labour induction in an outpatient setting - a multicenter randomized controlled trial. OPTION - OutPatienT InductiON** |
| A.3.1 | Title of the trial for lay people, in easily understood, i.e. non-technical, language: | |
| | **English** | **Labour induction in an outpatient setting - a multicenter randomized controlled trial. OPTION - OutPatienT InductiON** |
| A.3.2 | Name or abbreviated title of the trial where available: | |
| | **English** | **OPTION - OutPatienT InductiON** |
| A.4 | Sponsor's protocol code number, version and date[1]: | |
| A.4.1 | Sponsor's protocol code number: | **OPTION** |
| A.4.2 | Sponsor's protocol version: | **1.0** |
| A.4.3 | Sponsor's protocol date: | **2020-03-17** |
| A.5 | Additional international study identifiers (e.g. WHO, ISRCTN[2] , US NCT Number[3]) if available | |
| A.5.1 | ISRCTN number: | |
| A.5.2 | US NCT number: | |
| A.5.3 | WHO Universal Trial Number (UTN): | |
| A.5.4 | Other Identifier: | |
| A.6 | Is this a resubmission? | **No ●** |
| | If 'Yes', indicate the resubmission letter[4]: | **First Submission** |
| A.7 | Is the trial part of an agreed Paediatric Investigation Plan? | **No ●** |
| A.8 | EMA Decision number of Paediatric Investigation Plan: | |

## B. IDENTIFICATION OF THE SPONSOR RESPONSIBLE FOR THE REQUEST

| B.1 | SPONSOR | |
|---|---|---|
| B.1.1 | Name of organisation: | **Sahlgrenska University Hospital** |
| B.1.2 | Name of the person to contact: | |
| B.1.2.1 | Given name | **Verena** |
| B.1.2.2 | Middle name | |
| B.1.2.3 | Family name | **Sengpiel** |
| B.1.3 | Address: | |
| B.1.3.1 | Street address | **Diagnosvägen 15** |
| B.1.3.2 | Town/city | **Gothenburg** |
| B.1.3.3 | Post code | **41650** |
| B.1.3.4 | Country | **Sweden** |
| B.1.4 | Telephone number: | **0046 31 3429242** |
| B.1.5 | Fax number: | |
| B.1.6 | E-mail: | **verena.sengpiel@obgyn.gu.se** |

| B.2 | **LEGAL REPRESENTATIVE[5] 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 person to contact: |
| B.2.2.1 | Given name |
| B.2.2.2 | Middle name |
| B.2.2.3 | Family name |
| B.2.3 | Address: |
| B.2.3.1 | Street address |
| B.2.3.2 | Town/city |
| B.2.3.3 | Post code |
| B.2.3.4 | Country |
| 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: | **No •** |
| B.3.2 | Non commercial: | **Yes •** |

| B.4 | Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary): | |
|---|---|---|
| B.4.1 | Name of organisation: | **ALF-agreement funding (nr. S75710)** |
| B.4.2 | Country: | **Sweden** |

| B.4 | Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary): | |
|---|---|---|
| B.4.1 | Name of organisation: | **Project Grant from Dept of obstetrics and gynecology, Sahlgrenska Academy, University of Gothenburg** |
| B.4.2 | Country: | **Sweden** |

| B.5 | Contact point[6] designated by the sponsor for further information on the trial | |
|---|---|---|
| B.5.1 | Name of organisation: | **Sahlgrenska University Hospital** |
| B.5.2 | Functional name of contact point (e.g. "Clinical Trial Information Desk"): | **OPTION study** |
| B.5.3 | Address: | |
| B.5.3.1 | Street address | **Diagnosvägen 15** |
| B.5.3.2 | Town/city | **Gothenburg** |
| B.5.3.3 | Post code | **41650** |
| B.5.3.4 | Country | **Sweden** |

| | | |
|---|---|---|
| B.5.4 | Telephone number: | **0046 031 3436286** |
| B.5.5 | Fax number: | |
| B.5.6 | E-mail: (use a functional e-mail address rather than a personal one) | **OPTION@vgregion.se** |

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

| C.1 | REQUEST FOR THE COMPETENT AUTHORITY | |
|---|---|---|
| C.1.1 | Sponsor | **Yes •** |
| 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 | Name of Organisation: | **Sahlgrenska University Hospital** |
| C.1.4.2 | Name of contact person: | |
| C.1.4.2.1 | Given name | **Verena** |
| C.1.4.2.2 | Middle name | |
| C.1.4.2.3 | Family name | **Sengpiel** |
| C.1.4.3 | Address: | |
| C.1.4.3.1 | Street address | **Diagnosvägen 15** |
| C.1.4.3.2 | Town/city | **Gothenburg** |
| C.1.4.3.3 | Post code | **41650** |
| C.1.4.3.4 | Country | **Sweden** |
| C.1.4.4 | Telephone number: | **0046 31 3429242** |
| C.1.4.5 | Fax number: | |
| C.1.4.6 | E-mail: | **verena.sengpiel@obgyn.gu.se** |
| C.1.5 | Request to receive a copy of CTA data as XML: | |
| C.1.5.1 | Do you want a copy of the CTA form data saved on EudraCT as an XML file? | **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]? | **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)

## 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 D.8****. 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 | **Yes •** |
| D.1.3 | IMP used as a comparator | **No •** |

| **D.2** | **STATUS OF THE IMP** | |
|---|---|---|
| D.2.1 | Has the IMP to be used in the trial a marketing authorisation? | **Yes •** |
| **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', specify the product to be used in the clinical trial: | |
| D.2.1.1.1 | Trade name | |
| D.2.1.1.1.1 | EV Product Code (where applicable) | |
| D.2.1.1.2 | Name of the Marketing Authorisation Holder: | |
| D.2.1.1.3 | Marketing Authorisation number (if Marketing Authorisation granted by a Member State): | |
| D.2.1.1.4 | Is the IMP modified in relation to its Marketing Authorisation? | **No •** |
| D.2.1.1.4.1 | If 'Yes', please specify: | |
| D.2.1.2 | The country that granted the Marketing Authorisation | **Sweden** |
| D.2.1.2.1 | Is this the Member State concerned with this application? | **Yes •** |

| | | |
|---|---|---|
| D.2.2 | Situations where an IMP to be used in the CT has a Marketing Authorisation in the Member State concerned, but the protocol allows that any brand of the IMP with a Marketing Authorisation in that Member State 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 •** |
| 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? | **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] | **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: | **No •** |
| D.2.2.4.1 | If 'Yes', please specify: | |

| | | |
|---|---|---|
| D.2.3 | IMPD submitted: | |
| D.2.3.1 | Full IMPD: | **No •** |
| D.2.3.2 | Simplified IMPD: | **No •** |
| D.2.3.3 | Summary of product characteristics (SmPC) only: | **Yes •** |
| D.2.4 | Has the use of the IMP been previously authorised in a | **Yes •** |

| | | |
|---|---|---|
| | clinical trial conducted by the sponsor in the Community? | |
| D.2.4.1 | If 'Yes' specify which Member States: | **Sweden** |
| D.2.5 | Has the IMP been designated in this indication as an orphan drug in the Community? | **No •** |
| D.2.5.1 | If 'Yes', give the orphan drug designation number[10]**:** | |

| | | |
|---|---|---|
| D.2.6 | Has the IMP been the subject of scientific advice related to this clinical trial? | **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 | CHMP[11]? | **No •** |
| D.2.6.1.2 | National Competent Authority? | **No •** |

| **D.3** | **DESCRIPTION OF THE IMP** | |
|---|---|---|
| D.3.1 | Product name where applicable[12]: | |
| D.3.2 | Product code where applicable[13]: | |
| D.3.3 | ATC codes, if officially registered[14]: | **G02AD06** |
| D.3.4 | Pharmaceutical form (use standard terms): | **Tablet** |
| D.3.4.1 | Is this a specific paediatric formulation? | **No •** |
| D.3.5 | Maximum duration of treatment of a subject according to the protocol: **Up to 8 doses of 25microgram misoprostol tablets taken orally no closer than 2 hours apart/24 hours, for a maximum of 2 days. On day 3 of induction (if relevant), all women return to clinical routine at sites. Intake can be paused during the night.** | |
| D.3.6 | Dose allowed: | |
| D.3.6.1 | For first trial only: | |
| | Specify per day or total | **Total •** |
| | Specify total dose (number and unit): | |
| | Route of administration (relevant to the first dose): | |
| D.3.6.2 | For all trials | |
| | Specify per day or total | **Total •** |
| | Specify total dose (number and unit): | **400 µg microgram(s)** |
| | Route of administration (relevant to the maximum dose): | **Oral use** |
| D.3.7 | Routes of administration (use standard terms): | **Oral use** |

| | | |
|---|---|---|
| D.3.8 | Name of each active substance (INN or proposed INN if available): **Angusta** | |
| D.3.9 | Other available name for each active substance ( provide all available): | |
| D.3.9.1 | CAS[15] number | |
| D.3.9.2 | Current sponsor code | |
| D.3.9.3 | Other descriptive name **MISOPROSTOL** | |
| D.3.9.4 | EV Substance code | **SUB08998MIG** |
| D.3.9.5 | Full Molecular formula | |
| D.3.9.6 | Chemical/biological description of the Active Substance | |
| D.3.10 | Strength (specify all strengths to be used): | |
| D.3.10.1 | Concentration unit: | **µg microgram(s)** |
| D.3.10.2 | Concentration type ("exact number", "range", "more than" or "up to"): | **equal** |
| D.3.10.3 | Concentration (number). | **25** |

| | | |
|---|---|---|
| D.3.11 | Type of IMP | |
| Does the IMP contain an active substance: | | |
| D.3.11.1 | Of chemical origin? | **Yes •** |
| D.3.11.2 | Of biological / biotechnological origin (other than Advanced Therapy IMP (ATIMP)? | **No •** |

Is this a:

| | | |
|---|---|---|
| D.3.11.3 | Advanced Therapy IMP (ATIMP)? | **No** • |
| D.3.11.3.1 | Somatic cell therapy medicinal product[16]? | **No** • |
| D.3.11.3.2 | Gene therapy medicinal product[17]? | **No** • |
| D.3.11.3.3 | Tissue Engineered Product[18]? | **No** • |
| D.3.11.3.4 | Combination ATIMP (i.e. one involving a medical device[19])? | **No** • |
| D.3.11.3.5 | Has the Committee on Advanced Therapies issued a classification for this product? | **No** • |
| D.3.11.3.5.1 | If 'Yes' please provide that classification and its reference number: | |
| D.3.11.4 | Combination product that includes a device, but does not involve an Advanced Therapy? | **No** • |
| D.3.11.5 | Radiopharmaceutical medicinal product? | **No** • |
| D.3.11.6 | Immunological medicinal product (such as vaccine, allergen, immune serum)? | **No** • |
| D.3.11.7 | Plasma derived medicinal product? | **No** • |
| D.3.11.8 | Extractive medicinal product? | **No** • |
| D.3.11.9 | Recombinant medicinal product? | **No** • |
| D.3.11.10 | Medicinal product containing genetically modified organisms? | **No** • |
| D.3.11.10.1 | Has the authorisation for contained use or release been granted? | **No** • |
| D.3.11.10.2 | Is it pending? | **No** • |
| D.3.11.11 | Herbal medicinal product? | **No** • |
| D.3.11.12 | Homeopathic medicinal product? | **No** • |
| D.3.11.13 | Another type of medicinal product? | **No** • |
| D.3.11.13.1 | If 'another type of medicinal product' specify the type of medicinal product: | |
| D.3.12 | Mode of action (*free text*[20])<br>**Misoprostol is a synthetic analogue of prostaglandin E1, a naturally occurring uterine contracting agent. F and E series prostaglandins increase collagen activity in rabbit uterus cervical fibroblasts in vitro and cause cervical maturation and uterine contractions in vivo. These are considered to be the mechanism of action relevant to the clinical efficacy.** | |
| D.3.13 | Is it an IMP to be used in a first-in-human clinical trial? | **No** • |
| D.3.13.1 | If 'Yes', are there risk factors identified, according to the guidance FIH?[21] | |

| **D.4** | **SOMATIC CELL THERAPY INVESTIGATIONAL MEDICINAL PRODUCT (NO GENETIC MODIFICATION)** | |
|---|---|---|
| D.4.1 | Origin of cells | |
| D.4.1.1 | Autologous | **No** • |
| D.4.1.2 | Allogeneic | **No** • |
| D.4.1.3 | Xenogeneic | **No** • |
| D.4.1.3.1 | If 'Yes', specify the species of origin: | |
| D.4.2 | Type of cells | |
| D.4.2.1 | Stem cells | **No** • |
| D.4.2.2 | Differentiated cells | **No** • |
| D.4.2.2.1 | If 'Yes', specify the type (e.g. keratinocytes, fibroblasts, chondrocytes…): | |
| D.4.2.3 | Others: | **No** • |
| D.4.2.3.1 | If others, specify: | |

| **D.5** | **GENE THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS** | |
|---|---|---|
| D.5.1 | Gene(s) of interest: | |
| D.5.2 | In vivo gene therapy: | **No** • |
| D.5.3 | Ex vivo gene therapy: | **No** • |

| | | |
|---|---|---|
| D.5.4 | Type of gene transfer product | |
| D.5.4.1 | Nucleic acid (e.g. plasmid): | **No •** |
| | If 'Yes', specify if: | |
| D.5.4.1.1 | Naked: | **No •** |
| D.5.4.1.2 | Complexed | **No •** |
| D.5.4.2 | Viral vector: | **No •** |
| D.5.4.2.1 | If 'Yes', specify the type: adenovirus, retrovirus, AAV, …: | |
| D.5.4.3 | Others | **No •** |
| D.5.4.3.1 | If others, specify: | |
| D.5.5 | Genetically modified somatic cells: | **No •** |
| If 'Yes', specify the origin of the cells: | | |
| D.5.5.1 | Autologous: | **No •** |
| D.5.5.2 | Allogeneic: | **No •** |
| D.5.5.3 | Xenogeneic: | **No •** |
| D.5.5.3.1 | If 'Yes', specify the species of origin: | |
| D.5.5.4 | Specify type of cells (hematopoietic stem cells…): | |

| **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 | **No •** |
| D.6.1.2 | Allogeneic | **No •** |
| D.6.1.3 | Xenogeneic | **No •** |
| D.6.1.3.1 | If 'Yes', specify the species of origin: | |
| D.6.2 | Type of cells | |
| D.6.2.1 | Stem cells | **No •** |
| D.6.2.2 | Differentiated cells | **No •** |
| D.6.2.2.1 | If 'Yes', specify the type of cells(e.g. keratinocytes, fibroblasts, chondrocytes, …): | |
| D.6.2.3 | Others: | **No •** |
| D.6.2.3.1 | If others, specify: | |

| **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? | **No •** |
| D.7.4 | Does this product contain: | |
| D.7.4.1 | A medical device? | **No •** |
| D.7.4.1.1 | Does this medical device have a CE mark? | **No •** |
| D.7.4.1.1.1 | The notified body is: | |
| D.7.4.2 | Bio-materials? | **No •** |
| D.7.4.3 | Scaffolds? | **No •** |
| D.7.4.4 | Matrices? | **No •** |
| D.7.4.5 | Other? | **No •** |
| D.7.4.5.1 | If other, specify: | |

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

| | | |
|---|---|---|
| D.8.1 | Is there a placebo: | **No ●** |

| | | |
|---|---|---|
| D.8.2 | This refers to placebo number: | |
| D.8.3 | Pharmaceutical form: | |
| D.8.4 | Route of administration: | |
| D.8.5 | Which IMP is it a placebo for? Specify IMP Number(s) from D.1.1 | |
| D.8.5.1 | Composition, apart from the active substance(s): | |
| D.8.5.2 | Is it otherwise identical to the IMP? | **Yes ? No ? Not Answered ?** |
| D.8.5.2.1 | If not, specify major ingredients: | |

## D.9 SITE(S) WHERE THE QUALIFIED PERSON CERTIFIES BATCH RELEASE[22]

*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.8.2 In the case of multiple sites indicate the product certified by each site*

| | |
|---|---|
| D.9.1 | Do not fill in section D.9.2 for an IMP that:<br>*Has a MA in the EU **and***<br>*Is sourced from the EU market **and***<br>*Is used in the trial without modification( e.g. not overencapsulated) **and***<br>*The packaging and labelling is carried out for local use only as per article 9.2. of the Directive 2005/28/EC (GCP Directive)*<br>If all these conditions are met tick ● and list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2 to which this applies<br>**PR1** |

| | | |
|---|---|---|
| **D.9.2** | **Who is responsible in the Community for the certification of the finished IMPs?**<br>This site is responsible for certification of (list the number(s) of each IMP including placebo from sections D.1.1 and D.8.2):<br>please tick the appropriate box: | |
| D.9.2.1 | Manufacturer | **?** |
| D.9.2.2 | Importer | **?** |
| D.9.2.3 | Name of the organisation: | |
| D.9.2.4 | Address: | |
| D.9.2.4.1 | Street Address | |
| D.9.2.4.2 | Town/City | |
| D.9.2.4.3 | Post Code | |
| D.9.2.4.4 | Country | |
| D.9.2.5 | Give the manufacturing authorisation number: | |
| D.9.2.5.1 | 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.9.2 above.*

## 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[23] (free text): | |
| | **English** | **Induction of labour** |
| | **Swedish** | **Igångsättning av förlossning** |
| E.1.1.1 | Medical condition in easily understood language | |
| | **English** | **Induction of labour** |
| E.1.1.2 | Therapeutic area | |
| | **Diseases [C] - Female diseases of the urinary and reproductive systems and pregancy complications [C13]** | |
| E.1.2 | MedDRA version, system organ class, level, term and classification code[24]: | |
| | Version System Organ Class Classification Code Term Level | |
| E.1.3 | Is any of the conditions being studied a rare disease[25]? | **No •** |

| **E.2** | **OBJECTIVE OF THE TRIAL** | |
|---|---|---|
| E.2.1 | Main objective: | |
| | **English** | **1. To establish if induction in an outpatient setting is as safe for the child (composite outcome for mortality and severe morbidity) as induction in a hospital setting, including low-risk women only.**<br>**2. To investigate efficacy of outpatient induction by comparing proportions of women with vaginal delivery in the whole study population as well as in the group of women induced with either balloon or prostaglandin.** |
| E.2.2 | Secondary objectives: | |
| | **English** | **1. To investigate if other pregnancy and delivery-related outcomes differ btwn women induced in an outpatient vs hospital setting including safety, e.g. mother admitted to ICU, post-partum bleeding >1000ml, proportion of women delivered vaginally within 24 or 48 hrs from induction start as well as for the children, e.g. variables part of the primary safety composite outcome will be studied individually in exploratory analyses**<br>**2. To increase the understanding of women with low-risk induction experiences of induction in an outpatient and a hospital setting by comparison of general self-efficacy (GSE), health-related quality of life (EQ-VAS, EQ-5D), pain catastrophizing (PCS), sense of coherence (SOC), anxiety and depression (HAD) before randomization and 3 mon post-delivery. Childbirth experiences (CEQ), induction experiences, EPDS and breastfeeding levels (BSES) will be compared btwn groups 3 mon post-delivery. Qualitative interviews with 20-25 women will be done 3-6 mon post-delivery** |
| | **Swedish** | **3. To increase the understanding of partners to women with low-risk induction experiences of induction in an outpatient and a hospital setting by comparison of GSE, health-related quality of life (EQ-VAS, EQ-5D), PCS, SOC, anxiety and depression (HAD) before randomization as well as 3 mon post-delivery. Childbirth experience (FTFQ), induction experiences, and EPDS will be compared btwn groups 3 mon post-delivery. Also qualitative interviews with 20-25 partners will be performed 3-6 mon post-delivery. Partners to participating women at** |

**Sahlgrenska university hospital will be asked to answer a qualitative questionnaire 3-6 mon post-delivery**
**4. To increase the understanding of the healthcare staff's experiences of outpatient versus inpatient induction of low-risk pregnancies by qualitative interviews**
**5. To study if induction in an outpatient setting is more cost-effective compared to a hospital setting**
**6. To compare future pregnancy outcome in the outpatient and inpatient group**

E.2.3 Is there a sub-study? **Yes •**

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

**English**

**The following four substudies are planned as tentative publications. No full titles with date and version are yet available. The general main objectives to be evaluated are indicated below for the specified populations.**

**Substudy 1: Outpatient induction with oral misoprostol.**
**- Population: Only those who receive oral misoprostol for induction.**

**Substudy 2: Outpatient induction with a balloon catheter.**
**- Population: Only those who receive balloon catheter for induction.**

**Substudy 3: Womens and partners experience of outpatient induction of labour with oral misoprostol.**
**- Population: Only women and partners of women who receive oral misoprostol.**

**Substudy 4: Womens and partners experience of outpatient induction of labour with balloon catheter.**
**- Population: Only women and partners of women who receive oral misoprostol.**

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

**English**

**Based on medical history:**
**• women 18-45 years old**
**• able to communicate with the hospital**
**• uncomplicated live singleton pregnancy**
**• pregnancy week >=37+0 to 41+6 according to crown rump length (CRL) or biparietal diameter (BPD<55 mm) at first or second trimester ultrasound**
**• engaged and stable cephalic presentation**

**Based on clinical examination before start of induction including Leopolds maneuvers, digital cervical exam, abdominal ultrasound, temperature, blood pressure and cardiotocography (CTG) scan:**
**• engaged and stable cephalic presentation with**
**• Bishop score <6 (<5 in parous women)**
**• CTG classified as normal according to the antepartal Swedish Society of obstetrics and gynecology (Svensk Förening för Obstetrik och Gynekologi, SFOG) criteria (www.ctgutbildning.se)**

**Based on observation the first 45 min after start of induction:**
**• in case of induction with balloon method: CTG classified as normal according to the antepartal Swedish Society of Obstetrics and Gynecology (Svensk Förening för Obstetrik och Gynekologi, SFOG) criteria (www.ctgutbildning.se)**

| E.4 | PRINCIPAL EXCLUSION CRITERIA *(list the most important)* | |
|---|---|---|
| | **English** | **Based on medical history:**<br>**● previous uterine surgery with uterine scar, e.g. caesarean section or myomectomy**<br>**● pregestational or medically treated gestational diabetes (insulin or metformin)**<br>**● dietary treated gestational diabetes with large for gestational age foetus**<br>**● preeclampsia or instable hypertensive disease**<br>**● multiple pregnancy**<br>**● intrauterine foetal death (IUFD) in current or previous pregnancy**<br>**● known foetal malformations or other foetal condition affecting the delivery or immediate care of the newborn**<br>**● congenital uterine malformation which may affect safety**<br>**● other condition requiring inpatient care, e.g. delivery within 60 min from arriving at the hospital in previous pregnancy**<br>**● not able to reach the hospital in a reasonable time, at the discretion of the investigator with a maximum of 60 min as a benchmark**<br><br>**Based on clinical examination before start of induction including Leopold's manoeuvres, digital cervical exam, abdominal ultrasound, temperature, blood pressure and cardiotocography (CTG) scan:**<br>**● Small for gestational age (SGA/IUGR/FGA)**<br>**Screened for as follows depending on the indication for induction:**<br>**1.□late term >=41+0 to 41+6 weeks:**<br>**abdominal ultrasound will be performed and mean abdominal diameter (MAD) needs to be >= 110 mm**<br>**In case MAD < 110 mm, the foetal weight will be estimated to exclude SGA foetus defined as <2 standard deviation according to Marsal et al.**<br>**2.□dietary treated gestational diabetes or stable hypertension:**<br>**foetal weight estimated by abdominal ultrasound within the last two weeks before induction and showing no SGA defined as <2 standard deviation according to Marsal et al**<br>**3.□prolonged latent phase, maternal age, mild intrahepatic cholestasis, pelvic girdle pain, PROM, psychosocial:**<br>**Normal fundal height measurement according to the Swedish reference curves is needed**<br>**In case of not-normal fundal height measurement: foetal weight estimation must be performed and showing no SGA defined as <2 standard deviation according to Marsal et al**<br>**4.□Other indications: at the discretion of the investigator**<br>**● oligohydramniosis: deepest vertical pocket <20 mm or amniotic fluid index <50 mm**<br>**● polyhydramniosis if head not engaged or amniotic fluid index >300 mm**<br>**● maternal pyrexia >= 38 degrees Celsius**<br>**● known low-lying placenta (less than 20 mm from internal os measured by vaginal ultrasound in week 36)**<br>**● high head (>=4/5 palpable abdominally)**<br>**Regarding premature rupture of membranes (PROM):**<br>**● exclusion criteria for balloon method**<br>**● exclusion criteria for prostaglandin method if:**<br>**o□PROM >30 hours**<br>**o□Known colonisation with group B streptococci or previous pregnancy complication linked to group B streptococcus**<br><br>**Based on observation the first 45 min after start of induction:**<br>**● any adverse events within the first 45 min after start of induction, e.g. heavy bleeding, pain, PROM in case PROM was not indication for induction of labour**<br>**● start of contractions** |

| E.5 | END POINT(S): | |
|---|---|---|
| E.5.1 | Primary End Point (repeat as necessary)[26] | |
| | **English** | **1. Safety defined as a composite outcome of severe perinatal morbidity or mortality**<br><br>**2. Efficacy defined as proportion of women with vaginal delivery** |
| E.5.1.1 | Timepoint(s) of evaluation of this end point | |
| | **English** | **1. For the safety primary endpoint, neonatal mortality is defined between day 0-27 and thus the time point is day 27 after delivery.**<br><br>**2. For the efficacy primary endpoint, the time point is upon delivery.** |
| E.5.2 | Secondary End Point (repeat as necessary) | |
| | **English** | **1. Pregnancy and delivery-related outcomes (including safety, e.g. mother admitted to the intensive care unit, post-partum bleeding >1000 ml, proportion of women delivered vaginally within 24 or 48 hours from start of induction as well as for the children, e.g. the different variables being part of the primary safety composite outcome will be studied individually in form of exploratory analyses). These secondary end points are descriptive and obtained via registry data.**<br><br>**2. Woman and partner's experience of self-efficacy, health-related quality of life, pain catastrophizing, anxiety and depression; women and partners' experience of childhood experiences and levels of breastfeeding; women and partners' experience as per qualitative interviews**<br><br>**3. Understanding of healthcare staff's experience of outpatient vs inpatient induction of low-risk pregnancies**<br><br>**4. Cost-effectiveness**<br><br>**5. Future pregnancy outcome** |
| E.5.2.1 | Timepoint(s) of evaluation of this end point | |
| | **English** | **1. Up to 42 days after delivery. These secondary end points are descriptive and obtained via registry data.**<br><br>**2. 3-6 months after delivery compared to at randomization (questionnaires will be send out three months after delivery, interviews will take place 3-6 months after delivery)**<br><br>**3. At the earliest 6 months after introduction of outpatient induction**<br><br>**4. Completion of follow-up**<br><br>**5. 10 years after completion of recruitment** |

| E.6 | SCOPE OF THE TRIAL – Tick all boxes where applicable | |
|---|---|---|
| E.6.1 | Diagnosis | **No •** |
| E.6.2 | Prophylaxis | **No •** |
| E.6.3 | Therapy | **No •** |
| E.6.4 | Safety | **Yes •** |
| E.6.5 | Efficacy | **Yes •** |
| E.6.6 | Pharmacokinetic | **No •** |
| E.6.7 | Pharmacodynamic | **No •** |

| | | |
|---|---|---|
| E.6.8 | Bioequivalence | **No •** |
| E.6.9 | Dose Response | **No •** |
| E.6.10 | Pharmacogenetic | **No •** |
| E.6.11 | Pharmacogenomic | **No •** |
| E.6.12 | Pharmacoeconomic | **No •** |
| E.6.13 | Others | **Yes •** |
| E.6.13.1 | If others, specify: | |
| | **English** | **The aim of this study is not to test the safety/efficacy of the medication (or medical device) itself, but of taking the medication (or use of medical device) as an inpatient or at home.** |

| **E.7** | **TRIAL TYPE AND PHASE[27]** | |
|---|---|---|
| E.7.1 | Human pharmacology (Phase I) | **No •** |
| Is it: | | |
| E.7.1.1 | First administration to humans | **No •** |
| E.7.1.2 | Bioequivalence study | **No •** |
| E.7.1.3 | Other: | **No •** |
| E.7.1.3.1 | If other, please specify: | |
| E.7.2 | Therapeutic exploratory (Phase II) | **No •** |
| E.7.3 | Therapeutic confirmatory (Phase III) | **No •** |
| E.7.4 | Therapeutic use(Phase IV) | **Yes •** |

| **E.8** | **DESIGN OF THE TRIAL** | |
|---|---|---|
| E.8.1 | Controlled | **Yes •** |
| | If 'Yes', specify: | |
| E.8.1.1 | Randomised: | **Yes •** |
| E.8.1.2 | Open: | **Yes •** |
| E.8.1.3 | Single blind: | **No •** |
| E.8.1.4 | Double blind: | **No •** |
| E.8.1.5 | Parallel group: | **Yes •** |
| E.8.1.6 | Cross over: | **No •** |
| E.8.1.7 | Other: | **No •** |
| E.8.1.7.1 | If other specify: | |
| E.8.2 | If controlled, specify the comparator: | |
| E.8.2.1 | Other medicinal product(s) | **No •** |
| E.8.2.2 | Placebo | **No •** |
| E.8.2.3 | Other | **Yes •** |
| E.8.2.3.1 | If 'Yes' to other, specify : | |
| | **Swedish** | **The medication has 2 arms and the balloon catheter has 2 arms** |
| | **English** | **We aim to test the setting and monitoring of induction - not the drug or balloon catheter itself** |
| E.8.2.4 | Number of treatment arms in the trial | **4** |
| E.8.3 | Single site in the Member State concerned (see also section G): | **No •** |
| E.8.4 | Multiple sites in the Member State concerned(see also section G): | **Yes •** |
| E.8.4.1 | Number of sites anticipated in Member State concerned | **30** |
| E.8.5 | Multiple Member States: | **No •** |
| E.8.5.1 | Number of sites anticipated in the EEA: | |
| E.8.6 | Trial involving sites outside the EEA: | |
| E.8.6.1 | Trial being conducted both within and outside the EEA: | **No •** |
| E.8.6.2 | Trial being conducted completely outside of the EEA: | **No •** |
| E.8.6.3 | If E.8.6.1 or E.8.6.2 are Yes, specify the regions in which trial sites are planned: | |
| E.8.6.4 | If E.8.6.1 or E.8.6.2 are Yes, specify the number of sites anticipated outside of the EEA: | |
| E.8.7 | Trial having an independent data monitoring committee: | **Yes •** |
| E.8.8 | Definition of the end of trial: If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition: | |
| | **English** | **10 years after LVLS. However, the last intervention will be in** |

| | | |
|---|---|---|
| | | **connection with the last subject's last admission for delivery, but all patients will be followed for 10 years after delivery using registry data.** |
| E.8.9 | Initial estimate of the duration of the trial[28] (years, months and days) | |
| E.8.9.1 | In the Member State concerned | **14 years 6 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 | **2020-07-01** |
| E.8.10.2 | In any country | |

## F. POPULATION OF TRIAL SUBJECTS

| F.1 | AGE RANGE | | |
|---|---|---|---|
| F.1.1 | Are the trial subjects under 18? | | **Yes •** |
| | If 'Yes', specify the estimated number of subjects planned in each age range for the whole trial: | | **8891** |
| | | Approx. No. of patients[29] | |
| F.1.1.1 | In utero | (**8891**) | **Yes •** |
| F.1.1.2 | Preterm newborn infants (up to gestational age < 37 weeks) | () | **No •** |
| F.1.1.3 | Newborns (0-27 days) | () | **No •** |
| F.1.1.4 | Infants and toddlers (28 days - 23 months) | () | **No •** |
| F.1.1.5 | Children (2-11 years) | () | **No •** |
| F.1.1.6 | Adolescents (12-17 years) | () | **No •** |
| F.1.2 | Adults (18-64 years) | (**8891**) | **Yes •** |
| F.1.3 | Elderly (>= 65 years) | () | **No •** |

| F.2 | GENDER | |
|---|---|---|
| F.2.1 | Female | **Yes •** |
| F.2.2 | Male | **Yes •** |

| F.3 | GROUP OF TRIAL SUBJECTS | |
|---|---|---|
| F.3.1 | Healthy volunteers | **No •** |
| F.3.2 | Patients | **No •** |
| F.3.3 | Specific vulnerable populations | **Yes •** |
| F.3.3.1 | Women of child bearing potential not using contraception | **No •** |
| F.3.3.2 | Women of child bearing potential using contraception | **No •** |
| F.3.3.3 | Pregnant women | **Yes •** |
| F.3.3.4 | Nursing women | **No •** |
| F.3.3.5 | Emergency situation | **No •** |
| F.3.3.6 | Subjects incapable of giving consent personally | **Yes •** |
| F.3.3.6.1 | If 'Yes', specify: | |
| | **English** | **All women must provide consent, which also includes consent to collect data on their child regarding the scientific questions posed in this study. Thus the pregnant women provide consent on behalf of their child in utero and upon delivery.** |
| F.3.3.7 | Others: | **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 | **17782** |
| F.4.2 | For a multinational trial**:** | |
| F.4.2.1 | In the EEA | |
| F.4.2.2 | In the whole clinical trial | |

| F.5 | PLANS FOR TREATMENT OR CARE AFTER THE SUBJECT HAS ENDED HIS/HER PARTICIPATION IN THE TRIAL. **please specify** (free text): | |
|---|---|---|
| | **English** | **None.** |

## G. CLINICAL TRIAL SITES/INVESTIGATORS IN THE MEMBER 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: | **Verena** |
| G.1.2 | Middle name, if applicable: | |
| G.1.3 | Family name: | **Sengpiel** |
| G.1.4 | Qualification (MD…….) | **MD, Docent** |
| G.1.5 | Professional address: | |
| G.1.5 | Institution name | **Sahlgrenska University Hospital** |
| G.1.5 | Institution department | **Obstetrics** |
| G.1.5.1 | Street address | **Diagnosvägen 15** |
| G.1.5.2 | Town/city | **Gothenburg** |
| G.1.5.3 | Post code | **41650** |
| G.1.5.4 | Country | **Sweden** |
| G.1.6 | Telephone number: | **0046 31 3429242** |
| G.1.7 | Fax number: | |
| G.1.8 | E-mail: | **verena.sengpiel@obgyn.gu.se** |

| 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.2.5 | Institution name |
| G.2.5 | Institution department |
| G.2.5.1 | Street address |
| G.2.5.2 | Town/city |
| G.2.5.3 | Post code |
| G.2.5.4 | Country |
| G.2.6 | Telephone number: |
| G.2.7 | Fax number: |
| G.2.8 | E-mail: |

| G.3 | CENTRAL TECHNICAL FACILITIES TO BE USED IN THE CONDUCT OF THE TRIAL<br><br>**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 | Name of organisation: | |
| G.3.2 | Department | |
| G.3.3 | Name of contact person: | |
| G.3.3.1 | Given name | |
| G.3.3.2 | Middle name | |
| G.3.3.3 | Family name | |
| G.3.4 | Address: | |
| G.3.4.1 | Street address | |
| G.3.4.2 | Town/city | |
| G.3.4.3 | Post code | |
| G.3.4.4 | Country | |
| G.3.5 | Telephone number: | |
| G.3.6 | Fax number: | |
| G.3.7 | E-mail: | |
| G.3.8 | Enter the details of any duties subcontracted to this central technical facility in this trial | |
| G.3.8.1 | Routine clinical pathology testing | **Yes** ? **No** ? **Not Answered** ? |

| | | |
|---|---|---|
| G.3.8.2 | Clinical chemistry | **Yes ? No ? Not Answered ?** |
| G.3.8.3 | Clinical haematology | **Yes ? No ? Not Answered ?** |
| G.3.8.4 | Clinical microbiology | **Yes ? No ? Not Answered ?** |
| G.3.8.5 | Histopathology | **Yes ? No ? Not Answered ?** |
| G.3.8.6 | Serology/ endocrinology | **Yes ? No ? Not Answered ?** |
| G.3.8.7 | Analytical chemistry | **Yes ? No ? Not Answered ?** |
| G.3.8.8 | ECG analysis/ review | **Yes ? No ? Not Answered ?** |
| G.3.8.9 | Medical image analysis/ review - X-ray, MRI, ultrasound, etc. | **Yes ? No ? Not Answered ?** |
| G.3.8.10 | Primary/ surrogate endpoint test | **Yes ? No ? Not Answered ?** |
| G.3.8.11 | Other Duties subcontracted? | **Yes ? No ? Not Answered ?** |
| G.3.8.11.1 | If 'Yes', specify the other duties | |

| **G.4** | **NETWORKS TO BE INVOLVED IN THE TRIAL (e.g. Paediatric Networks involved in the trial)** | |
|---|---|---|
| G.4.1 | Name of organisation: | **Swedish Network for Clinical Studies in Obstetrics and Gynecology (SNAKS)** |
| G.4.2 | Name of contact person: | |
| G.4.2.1 | Given name | **Verena** |
| G.4.2.2 | Middle name | |
| G.4.2.3 | Family name | **Sengpiel** |
| G.4.3 | Address: | |
| G.4.3.1 | Street address | **Diagnosvägen 15** |
| G.4.3.2 | Town/city | **Gothenburg** |
| G.4.3.3 | Post code | **41650** |
| G.4.3.4 | Country | **Sweden** |
| G.4.4 | Telephone number: | **0046 31 3429242** |
| G.4.5 | Fax number: | |
| G.4.6 | E-mail: | **verena.sengpiel@obgyn.gu.se** |
| G.4.7 | Activities carried out by the network: | |

**SNAKS aims to:**
**a) conduct high quality studies and engage as many of the country's OB / Gyn clinics as possible**
**b) utilize the quality records and receive more evidence-based care**
**c) strengthen Swedish OB / Gyn's academic position.**

**SNAKS has a steering group that works to strengthen collaboration between clinics in research. The steering group is happy to receive proposals for studies and then has a continued dialogue with proposers to assess whether the study is suitable as a national study where SNAKS can facilitate contacts between clinics.**

| **G.5** | **ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS** | |
|---|---|---|
| G.5.1 | **Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?** | **Yes •** |

Repeat as necessary for multiple organisations:

| | | |
|---|---|---|
| G.5.1.1 | Organisation name: | **Medical Products Agency** |
| G.5.1.2 | Organisation department | |
| G.5.1.3 | Name of contact person : | |
| G.5.1.3.1 | Given name | **NA** |
| G.5.1.3.2 | Middle name | |
| G.5.1.3.3 | Family name | **NA** |
| G.5.1.4 | Address: | |
| G.5.1.4.1 | Street address | **Box 26** |
| G.5.1.4.2 | Town/city | **Uppsala** |
| G.5.1.4.3 | Post code | **751 03** |
| G.5.1.4.4 | Country | **Sweden** |

| | | |
|---|---|---|
| G.5.1.5 | Telephone number: | |
| G.5.1.6 | Fax number: | |
| G.5.1.7 | E-mail: | **registrator@lakemedelsverket.se** |
| G.5.1.8 | All tasks of the sponsor | **No •** |
| G.5.1.9 | Monitoring | **No •** |
| G.5.1.10 | Regulatory (e.g. preparation of applications to CA and ethics committee) | **No •** |
| G.5.1.11 | Investigator recruitment | **No •** |
| G.5.1.12 | IVRS[30] – treatment randomisation | **No •** |
| G.5.1.13 | Data management | **No •** |
| G.5.1.14 | E-data capture | **No •** |
| G.5.1.15 | SUSAR reporting | **Yes •** |
| G.5.1.16 | Quality assurance auditing | **No •** |
| G.5.1.17 | Statistical analysis | **No •** |
| G.5.1.18 | Medical writing | **No •** |
| G.5.1.19 | Other duties subcontracted? | **No •** |
| G.5.1.19.1 | If 'Yes' to other, please specify: | |

| | | |
|---|---|---|
| **G.5** | **ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS** | |
| G.5.1 | **Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?** | **Yes •** |

Repeat as necessary for multiple organisations:

| | | |
|---|---|---|
| G.5.1.1 | Organisation name: | **Gothia Forum** |
| G.5.1.2 | Organisation department | |
| G.5.1.3 | Name of contact person : | |
| G.5.1.3.1 | Given name | **Cecilia** |
| G.5.1.3.2 | Middle name | |
| G.5.1.3.3 | Family name | **Johansson** |
| G.5.1.4 | Address: | |
| G.5.1.4.1 | Street address | **Guldhedsgatan 10C** |
| G.5.1.4.2 | Town/city | **Göteborg** |
| G.5.1.4.3 | Post code | **41345** |
| G.5.1.4.4 | Country | **Sweden** |
| G.5.1.5 | Telephone number: | **0046 076 349080** |
| G.5.1.6 | Fax number: | |
| G.5.1.7 | E-mail: | **cecilia.johansson@vgregion.se** |
| G.5.1.8 | All tasks of the sponsor | **No •** |
| G.5.1.9 | Monitoring | **No •** |
| G.5.1.10 | Regulatory (e.g. preparation of applications to CA and ethics committee) | **Yes •** |
| G.5.1.11 | Investigator recruitment | **No •** |
| G.5.1.12 | IVRS[30] – treatment randomisation | **No •** |
| G.5.1.13 | Data management | **No •** |
| G.5.1.14 | E-data capture | **No •** |
| G.5.1.15 | SUSAR reporting | **No •** |
| G.5.1.16 | Quality assurance auditing | **No •** |
| G.5.1.17 | Statistical analysis | **No •** |
| G.5.1.18 | Medical writing | **No •** |
| G.5.1.19 | Other duties subcontracted? | **No •** |
| G.5.1.19.1 | If 'Yes' to other, please specify: | |

| | | |
|---|---|---|
| **G.5** | **ORGANISATIONS TO WHOM THE SPONSOR HAS TRANSFERRED TRIAL RELATED DUTIES AND FUNCTIONS** | |
| G.5.1 | **Has the sponsor transferred any major or all the sponsor's trial related duties and functions to another organisation or third party?** | **Yes •** |

Repeat as necessary for multiple organisations:

| | | |
|---|---|---|
| G.5.1.1 | Organisation name: | **Statistiska konsultgruppen** |
| G.5.1.2 | Organisation department | |

| | | | |
|---|---|---|---|
| G.5.1.3 | Name of contact person : | | |
| G.5.1.3.1 | Given name | **Nils-Gunnar** | |
| G.5.1.3.2 | Middle name | | |
| G.5.1.3.3 | Family name | **Pehrsson** | |
| G.5.1.4 | Address: | | |
| G.5.1.4.1 | Street address | **Thorild Wulffsgatan 1** | |
| G.5.1.4.2 | Town/city | **Gothenburg** | |
| G.5.1.4.3 | Post code | **41319** | |
| G.5.1.4.4 | Country | **Sweden** | |
| G.5.1.5 | Telephone number: | **0046 070 9633613** | |
| G.5.1.6 | Fax number: | | |
| G.5.1.7 | E-mail: | **info@stat-grp.se** | |
| G.5.1.8 | All tasks of the sponsor | | **No •** |
| G.5.1.9 | Monitoring | | **No •** |
| G.5.1.10 | Regulatory (e.g. preparation of applications to CA and ethics committee) | | **No •** |
| G.5.1.11 | Investigator recruitment | | **No •** |
| G.5.1.12 | IVRS[30] – treatment randomisation | | **No •** |
| G.5.1.13 | Data management | | **No •** |
| G.5.1.14 | E-data capture | | **No •** |
| G.5.1.15 | SUSAR reporting | | **No •** |
| G.5.1.16 | Quality assurance auditing | | **No •** |
| G.5.1.17 | Statistical analysis | | **Yes •** |
| G.5.1.18 | Medical writing | | **No •** |
| G.5.1.19 | Other duties subcontracted? | | **No •** |
| G.5.1.19.1 | If 'Yes' to other, please specify: | | |

## 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 the information on the Competent Authority concerned. | | |
| H.1.1 | Competent Authority | **No ●** |
| H.1.2 | Ethics Committee | **Yes ●** |

| **H.2** | **INFORMATION ON ETHICS COMMITTEE** | |
|---|---|---|
| H.2.1 | Name: | **Swedish Ethical Review Authority** |
| H.2.2 | Address | |
| H.2.2.1 | Street address | **Box 2110** |
| H.2.2.2 | Town/city | **Uppsala** |
| H.2.2.3 | Post code | **75002** |
| H.2.2.4 | Country | **Sweden** |
| H.2.3 | Date of submission: | |

| **H.3** | **OPINION** | |
|---|---|---|
| H.3.1 | To be requested | **Yes ●** |
| H.3.2 | Pending | **No ●** |
| H.3.3 | Given | **No ●** |
| | If 'Given', specify: | |
| H.3.3.1 | Date of opinion: | |
| H.3.3.2 | Opinion favourable | **No ●** |
| H.3.3.3 | Opinion not favourable | **No ●** |
| | If 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:<br>• the information provided is complete;<br>• the attached documents contain an accurate account of the information available;<br>• the clinical trial will be conducted in accordance with the protocol; and<br>• the clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation. |

| **I.2** | **APPLICANT OF THE REQUEST FOR THE COMPETENT AUTHORITY** (as stated in section C.1): |
|---|---|
| I.2.1 | Date: |
| I.2.2 | Signature[31]: |
| 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[32]: |
| I.3.3 | Print name: |

## ENDNOTES

[1] Any translation of the protocol should be assigned the same date and version as those in the original document.
[2] 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.ema.europa.eu. When available they should provide it in Section A.6 of the application form.
[3] US National Clinical Trial (NCT) Numbers required on the FDA clinical trial 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.
[5] In accordance with Article 19 of Directive 2001/20/EC.
[6] 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.
[7] This requires a EudraLink account. (See https://eudract.ema.europa.eu/document.html for details)
[8] According to national legislation.
[9] Available from the Summary of Product Characteristics (SmPC)
[10] According to the Community register on orphan medicinal products (Regulation (EC) n° 141/2000): http://ec.europa.eu/enterprise/pharmaceuticals/register/index.htm
[11] Committee for Medicinal Products for Human Use of the European Medicines Agency
[12] To be provided only when there is No trade name. This is the name routinely used by a sponsor to identify the IMP in the CT documentation (protocol, IB…).
[13] 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 code may be used for combinations of drugs or drugs and devices.
[14] Available from the Summary of Product Characteristics (SmPC).
[15] Chemical Abstracts Service.
[16] Complete also section D.4 Cell therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.
[17] Complete also section D.5 Gene Therapy as defined in Annex 1 part IV of Directive 2001/83/EC as amended.
[18] Complete also section D.6 - Tissue Engineered Product as defined in Article 2(1)(b) of Regulation1394/2007/EC.
[19] Complete also section D.7
[20] The mode of action should briefly describe the chemical, biochemical, immunological or biological means the IMP uses to effect its pharmaceutical action.
[21] 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
[22] In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medical Products in the European Union.
[23] In the case of healthy volunteer trials, the intended indication for the product under development should be provided.
[24] 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.ema.europa.eu/).
[25] Points to consider on the calculation and reporting of the prevalence of a condition for Orphan drug designation: COM/436/01 (http://www.ema.europa.eu/htms/human/orphans/intro.htm).
[26] 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.
[27] 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.
[28] From the first inclusion until the last visit of the last subject.
[29] 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 the protocol, or subsequent authorised amendments.
[30] Interactive Voice Response System: commonly used for randomisation of treatment and controlling the shipment of stock of product.
[31] On an application to the Competent Authority only, the applicant to the Competent Authority needs to sign.

[32] On an application to the Ethics Committee only, the applicant to the Ethics Committee needs to sign.