

**CB-1606**

## Individualised replacement therapy for haemophilia patients

### Introduction

The aim of the KCE Trials programme is to ensure that high quality research information is produced on the effectiveness, costs and broader impact of health technology in the most efficient way for those who use, manage, provide care in or develop policy for the Belgian healthcare system.

An overview of the selection procedure can be found in the document "Information for candidate sponsors and guidance note for expression of interest" (v1.1), associated with this commissioning brief and available on our website.

### Research question

Is individualised replacement therapy more (cost)effective than standard replacement therapy in patients with haemophilia?

- 1. Intervention:** individualised, pharmacokinetic guided replacement therapy with factor VIII / factor IX
- 2. Patient group:** patients with severe haemophilia needing replacement therapy
- 3. Setting:** hospital.
- 4. Control:** standard dose replacement therapy with factor VIII / factor IX
- 5. Study design:** Preferably a multicentre, randomised controlled trial, to be defined by the applicant, with or without an internal pilot to test the ability to recruit and randomise patients. If a pilot is included, the criteria to continue or not from pilot to full trial should be specified.
- 6. Important outcomes:** To be defined by the applicant. Outcomes should be patient-centred, measured at appropriate time-points and validated. A health economic analysis should be included. The study could include a search for predictive markers of treatment response if of relevance for the health economic evaluation.
- 7. Minimum duration of follow-up:** one year

Proposals should be complementary with the ongoing trial in The Netherlands (see link below, contains protocol summary in English) and other available ongoing research.

<http://www.zonmw.nl/nl/projecten/project-detail/opti-clot-peri-operative-pharmacokinetic-guided-dosing-of-clotting-factor-in-hemophilia/samenvatting/>

#### **Decision problem to be addressed by this research:**

Severe haemophilia is a rare coagulation disorder characterised by spontaneous and repeated bleeding episodes mainly in the joints and muscles. The prevalence of haemophilia is 1/12,000 in the general population. There is increasing evidence that haemophilia replacement therapy should be individualised and personalised considering the specific bleeding phenotype of each patient, their lifestyle, musculoskeletal status and the pharmacokinetic behaviour of exogenous factor VIII and factor IX in the blood circulation after intravenous administration. The high cost of haemophilia in Belgium is principally due to replacement therapy with clotting factors. Rationalisation of the cost of haemophilia care is an important challenge for the community.

# KCE TRIALS PROGRAMME

## Notes to Applicants

To ensure the highest quality research, the appropriate guidelines and regulations must be followed and KCE recommendations for applicants are provided.

**Methodology:** for many of the research questions posed by the KCE Trials programme, a randomised controlled trial is the most appropriate method of providing an answer. Suggestions for how a randomised controlled trial could be designed and constructed most efficiently are encouraged.

**Quality, ethical and legal:** applicants are asked to follow the Declaration of Helsinki and ICH-GCP guidelines and all applicable legislation such as Belgian Law of 7 May 2004 concerning experiments on the human person, when planning their trial. Note that trials involving medicinal products must comply with "The Medicines for Human Use (Clinical Trials) Regulations 2004" and be submitted to the Federal Agency for Medicines and Health Products (FAMHP). The [FAMHP website](#) contains the latest information about Clinical Trial regulations.

Inspections by FAMHP to document conformity with GCP requirements and local legislation can take place at any time during the progress of KCE funded studies.

In line with the government's transparency agenda, any contract resulting from this tender may be published in its entirety and made available to the general public.

## Clinical Trials Toolkit

General information on the conduct of clinical trials can be found in the [Clinical Trials Toolkit](#). This NIHR resource is designed to help researchers navigate through the complex landscape of setting up and managing clinical trials. Please note that the website is developed for the UK, therefore local regulations and references may not apply in Belgium.

## Research networks

The KCE Trials programme expects, where appropriate, that applicants will work with relevant existing research networks.

## Making an application

If you wish to submit an Expression of Interest (EOI) on this topic, complete the associated application form available on our website, and submit it (as a PDF) via email to [trials@kce.fgov.be](mailto:trials@kce.fgov.be) by **August 8<sup>th</sup> before 13.00 hours**. Applications received after 13.00 hours on the due date will not be considered.

Applications will be considered by the KCE Trials Board at its meeting during the week of September 5<sup>th</sup> 2016.

Please read the document "Information for candidate sponsors and guidance note for expression of interest", associated with this commissioning brief and available on our website.

**IMPORTANT:** For shortlisted EOI, investigators will be given six weeks to submit a full research proposal.