NHS
National Patient Safety Agency

National Research Ethics Service

NOTICE OF SUBSTANTIAL AMENDMENT

For use in the case of all research other than clinical trials of investigational medicinal products (CTIMPs). For substantial amendments to CTIMPs, please use the EU-approved notice of amendment form (Annex 2 to ENTR/CT1) at http://eudract.emea.eu.int/document.html#guidance.

To be completed in typescript by the Chief Investigator in language comprehensible to a lay person and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC"). In the case of multi-site studies, there is no need to send copies to other RECs unless specifically required by the main REC.

Further guidance is available at http://www.nres.npsa.nhs.uk/applicants/review/after/amendments.htm.

Details of Chief Investigator:

Name:	Dr John D Grainger
Address:	Consultant Paediatric Haematologist Royal Manchester Children's Hospital Oxford Road Manchester M13 9WL
Telephone:	0161 7018418
Email:	John.grainger@cmft.nhs.uk
Fax:	0161 7018410

Full title of study:	**United Kingdom Paediatric Chronic ITP Registry**
Name of main REC:	NHS Northern and Yorkshire Multi-Centre Research Ethics Committee
REC reference number:	**06/MRE03/9**
Date study commenced:	01 JAN 2007
Protocol reference *(if applicable)*, current version and date:	Version 1 10/03/2006
Amendment number and date:	Amendment 1 07/11/2009

Type of amendment (indicate all that apply in bold)

(a) Amendment to information previously given on the NRES Application Form

Yes

If yes, please refer to relevant sections of the REC application in the "summary of changes" below.

(b) Amendment to the protocol

Yes

If yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

Yes

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Is this a modified version of an amendment previously notified to the REC and given an unfavourable opinion?

No

Summary of changes

Briefly summarise the main changes proposed in this amendment using language comprehensible to a lay person. Explain the purpose of the changes and their significance for the study. In the case of a modified amendment, highlight the modifications that have been made.

If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

Title: UK childhood ITP Registry
The previous inclusion of "chronic" in the title was causing some confusion amongst local clinicians. By dropping the term we wish to emphasise that we are interested in recruiting patients at initial presentation.

Key Collaborators:
Dr Sarah Ball has now retired
Dr Nichola Cooper has been added

Addition to CI's team: Mrs Anne Littley, Research Nurse

Protocol changes:

i. **Patient identification**

In the original application (A20 below) the timing of original participant and recruitment was quite loose which has led to initial data been entered at variable time points. We propose to tighten this up so that initial identification of patients is performed ideally within 2 weeks of presentation and initial data entry is performed at 6 weeks.

ii. **Exclusion criteria**

Patients with a previous episode of ITP will no longer be excluded as recent evidence suggests that new episodes behave independent to prior episodes. If a patient has been previously on the registry then data will be linked to the previous episode.

A20. How will potential participants in the study be (i) identified, (ii) approached and (iii) recruited?

In this system local paediatricians will alert the chief investigator of potential participants (patients) to facilitate recruitment and informed consent by the chief investigator's team. Consent forms and information sheets will be mailed to the local doctors or downloaded from the study server. The local clinician will then discuss the contents with the participants and their parents. Participants will have opportunity to ask any additional questions to members of the working party by telephone. Written consent will then be taken locally and stored in the patient's notes locally. A unique patient number will then be allocated to the patient. The local doctor will return a form to the data manager for the study stating that consent has been obtained. Thus data released to the chief investigator will be anonymised.

iii. **Additional data collection**- Kids ITP Tool (KIT) an ITP-specific health related quality of life outcome measure.

We have recently completed work on producing a validating an ITP-specific health related quality of life outcome measure. The Kids ITP Tool (KIT) is a 26 question questionnaire with a version for children and a separate "proxy" version for parent/ guardian to complete on behalf of their child. Completion of the questionnaire takes 5-10 minutes per individual. Our work and that of others has highlighted the importance of such measures to assess disease outcome. Following on from this work we now wish to utilise this tool in the registry. To participate families will be asked to provide an email address so that secure login details can be provided to them.

The questionnaire will then be completed on line by the child and parent/guardian on a secure website accessed via www.uk-itp.org . Access to the questionnaire on the website will be via their unique patient number which will be generated at the time of consent and made available to the families by email. Additional information about ITP written for families which has previously been developed by the CI for the ITP Support Association will also be accessible to families on this website.

Families will be able to access the questionnaires either from home or from a computer whilst in hospital or attending out-patient clinics. For those families without email access the login details can be posted out upon request.

Child and parent/guardian will be requested to complete the online questionnaire at the same time points as the clinician is requested to enter disease updates i.e. at time of consent (within 2 weeks of presentation), 6 weeks, 6 months, 1 year and then yearly only if disease remains persistent (less than 10% of cases persist greater than 12 months). A paper copy of the questionnaires is supplied with this application the only difference on the online version is that questions will be read aloud to aid the understanding of younger children who may have difficulty reading the questions.

Changes to the protocol (attached) and to the PIS (attached) have been made to include

this additional data collection. The consent remains unchanged as consent specific to the questionnaires is implied by the actual completion of the questionnaire.

iv. **Side studies**- a separate ethics application is being made to collect blood samples to develop new laboratory tools based on blood clotting ability and genetic factors that may help identify patients of higher and lower bleeding risks. Over the last 24 months we have run a pilot study to asses the ability of a new laboratory coagulation test, on blood of patients with a low platelet count, to detect variations in patients ability to produce thrombin (the end result of a blood clot). This new test may provide a marker of which patients may be at higher risk of bleeding and whom therefore require prompt treatment whilst also identifying patients at lower risk of bleeding in whom treatment may be safely withheld. This new test has shown promising results but needs to be tested on a larger cohort of children. In addition other groups have identified genetic markers that might predict disease duration and predict response to certain treatments. We are therefore making separate ethics request to collect blood samples from children who are having routine blood tests taken. Rather than replicate data collection for this separate study we wish to link the data from the registry to the patients on this separate study. Already in the registry we are consenting for patients to be approached regarding other studies. When the families consent for the new study we will consent for allowing data from the registry to be linked. As both studies are run by the same CI we do not foresee any Ethical objection to this linking of data.

Any other relevant information

Applicants may indicate any specific ethical issues relating to the amendment, on which the opinion of the REC is sought.

List of enclosed documents

Document	*Version*	*Date*
Protocol	2	07/11/2009
PIS	2	07/11/2009

Declaration

- I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.

- I consider that it would be reasonable for the proposed amendment to be implemented.

Signature of Chief Investigator: 

Print name: Dr John D Grainger

Date of submission: 27/11/2009