APPLICANT'S CHECKLIST

All studies except clinical trials of investigational medicinal products

REC Ref:	06/MRE/03/09
Short Title of Study:	United Kingdom Paediatric Chronic ITP Registry version 1.0
CI Name:	Dr John D Grainger
Sponsor:	Central Manchester and Manchester Children's University Hospitals NHS Trust

Please complete this checklist and send it with your application

- Send ONE copy of each document (except where stated)
- ALL accompanying documents must bear version numbers and dates (except where stated)
- When collating please do NOT staple documents as they will need to be photocopied.

Document	Enclosed?	Date	Version	Office use
Covering letter on headed paper	○ Yes ○ No			
NHS REC Application Form, Parts A&B	Mandatory			
NHS REC Application Form, Part C (SSA)	○ Yes ○ No			
Research protocol (6 copies) or project proposal	Mandatory			
Summary C.V. for Chief Investigator (CI)	Mandatory			
Summary C.V. for supervisor (student research)	○ Yes ○ No			
Research participant information sheet (PIS)	○ Yes ○ No			
Research participant consent form	○ Yes ○ No			
Letters of invitation to participants	○ Yes ○ No			
GP/Consultant information sheets or letters	○ Yes ○ No			
Statement of indemnity arrangements	○ Yes ○ No			
Letter from sponsor	○ Yes ○ No			
Letter from statistician	○ Yes ○ No			
Letter from funder	○ Yes ○ No			
Referees' or other scientific critique report	○ Yes ○ No			
Summary, synopsis or diagram (flowchart) of protocol in non–technical language	○ Yes ○ No			
Interview schedules or topic guides for participants	○ Yes ○ No			
Validated questionnaire	○ Yes ○ No			
Non–validated questionnaire	○ Yes ○ No			
Copies of advertisement material for research participants, e.g. posters, newspaper adverts, website. For video or audio cassettes, please also provide the printed script.	○ Yes ○ No			

WELCOME TO THE NHS RESEARCH ETHICS COMMITTEE APPLICATION FORM

This page is important. An application form specific to your project will be created from the answers you give.

1. Select one research category from the list below:

- ○ Clinical trials of investigational medicinal products (including phase 1 drug development)
- ○ Clinical investigations of medical devices
- ◉ Research administering questionnaires for quantitative analysis
- ○ Research involving qualitative methods only
- ○ Research limited to taking and working with new samples
- ○ Non–interventional research

If your work does not fit any of these categories, select the option below:

- ○ Other research

1a. Please answer the following questions:

a) Does your study involve the use of any radiation?	○ Yes	◉ No
b) Will you be taking new samples?	○ Yes	◉ No
c) Will you be using existing samples?	○ Yes	◉ No

2. Is your research confined to one site?

○ Yes ◉ No

3. Does your research involve work with prisoners?

○ Yes ◉ No

4. Does your research involve adults unable to consent for themselves through physical or mental incapacity?

○ Yes ◉ No

5. Is your work an educational project?

○ Yes ◉ No

6. Is your project an audit or service evaluation?

○ Yes ◉ No

NHS Research Ethics Committee NHS
Application form for research administering questionnaires for quantitative analysis

This form should be completed by the Chief Investigator, after reading the guidance notes. See glossary for clarification of different terms in the application form.

Short title and version number: (maximum 70 characters – this will be inserted as header on all forms)
United Kingdom Paediatric Chronic ITP Registry version 1.0

Name of NHS Research Ethics Committee to which application for ethical review is being made:
Northern and Yorkshire MREC

Project reference number from above REC: 06/MRE/03/09
Submission date: 10/03/2006

PART A: Introduction

A1. Title of the research

Full title: United Kingdom Paediatric Chronic ITP Registry

Key words: Thrombocytopenia
Paediatric
ITP
PARC

A2. Chief Investigator

Title:	Dr
Forename/Initials:	John D
Surname:	Grainger
Post:	Consultant Paediatric Haematologist
Qualifications:	MRCP(Paediatrics) MRCPath
Organisation:	Royal Manchester Children's Hospital
Address:	Pendlebury Manchester
Post Code:	M27 4HA
E–mail:	john.grainger@cmmc.nhs.uk
Telephone:	01619222245
Fax:	06169222545

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application

A3. Proposed study dates and duration

Start date: 01/04/2006
End date: 01/04/2026
Duration: Months: 0 ; Years: 20

A4. Primary purpose of the research: *(Tick as appropriate)*

- ☐ Commercial product development and/or licensing
- ☐ Publicly funded trial or scientific investigation
- ☐ Educational qualification
- ☑ Establishing a database/data storage facility
- ☐ Other

A6. Does this research require site–specific assessment (SSA) of each research site? (Advice can be found in the guidance notes on this topic.)

○ Yes ◉ No

If No, please justify:
The research consists of simple data collection from patient medical records with no direct patient intervention. Each new centre and patient will be allocated a unique reference number so that there is no need to store patient identifying details on the regisrty. The research thus is unlikely to cause harm or emotional distress to the paticipants. The data templates sent to the childs physician requests information which would be collected as a routine in patients presenting with immune thrombocytopenic purpura (ITP).

In the UK the vast majority of children with ITP are managed at local hospitals and only those patients with severe problems tend to be referred to specialist centres. This research project has been designed to increase the likelihood of recruiting patients from the local units. Restriction to specialist centres will give a false impression of the severity of this condition.

Local paediatricians will alert the chief investigator to potential participants (patients) so that recruitment and informed consent can be taken by the chief investigator's team. Consent forms and information sheets will be mailed to the local doctors or downloaded from the secure study server. The local clinician will be available to discuss the contents with the participants and their parents. In addition 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 research group will be anonymised.

If Yes, Part C of the form will need to be completed for each research site and submitted for SSA to the relevant Local Research Ethics Committee. Do not submit Part Cs for other sites until the application has been booked for review and validated by the main Research Ethics Committee.

Management approval to proceed with the research will be required from the RDDepartment for each NHS care organisation in which research procedures are undertaken. This applies whether or not the research is exempt from SSA.

PART A: Section 1

A7. What is the principal research question/objective? *(Must be in language comprehensible to a lay person.)*

The objective of the registry is to establish a prospective registry of children with immune thrombocytopenic purpura (ITP) in the UK . The prime aim is to relate the long term consequences of a low platelet count on the frequency and severity of bleeding symptoms and requirement for treatment. Adults are not included in this application as there is already a registry established for adults in the UK.

Data collected from the UK registry will be contributed to an international registry (PARC, Paediatric and Adult intercontinental Registry on Chronic ITP). The international registry is already collecting data from 21 countries. Consent for sharing of patient's information from the registry is not compulsary to participate in the UK registry although is strongly encouraged.

Immune thrombocytopenic purpura (ITP) is a blood condition characterised by a low platelet count. The platelet count drops because antibodies produced by the patient coat the platelets which are then recognised as abnormal and are removed from the circulation by the normal body scavenging systems. We do not understand why people suddenly start producing antibodies against their own platelets (i.e. the cause of the disorder is not known). Individuals with a very low platelet count are at a higher risk of severe and sometimes life−threatening bleeds. In ITP the risk and severity of bleeding is generally less than predicted by the severity of the low platelet count. In particular, children with very low platelet counts due to ITP rarely have serious bleeding.

The majority of children and some adults may recover from ITP spontaneously and without treatment (within days, weeks or months). However, individuals who have a persistently low platelet count after six months from initial diagnosis are defined as having chronic ITP. These people may be at a higher risk of bleeds, particularly if the count remains very low, and may require more aggressive treatment such as surgical removal of the spleen (splenectomy).

ITP is an uncommon disorder in children and previous research has focused on the platelet count alone, assuming that this is a good surrogate marker for bleeding risk; there is disagreement about the optimal management of these patients resulting in very variable guidelines for management in different countries.

A8. What are the secondary research questions/objectives? *(If applicable, must be in language comprehensible to a lay person.)*

To determine the long−term effects of immune thrombocytopenic purpura (ITP).

To document the frequency of serious bleeds and the outcome following such bleeds.

To document therapies administered to raise platelet count and document response to therapy.

To identify information that may be used in future to identify individuals with ITP who are at higher risk of life−threatening bleeding, and require early treatment.

To identify information that may be used in future to identify individuals with ITP who are at a low risk of life−threatening bleeding in whom interventional treatment can be safely avoided.

To identify other individuals whom can teach us more about the outcome of ITP and would be eligible for enrolment in other ethically approved studies.

To stimulate scientific research into the development and outcome of ITP

A9. What is the scientific justification for the research? What is the background? Why is this an area of importance?*(Must be in language comprehensible to a lay person.)*

Although immune thrombocytopenic purpura (ITP) has been observed and treated for many years, we know surprisingly little about its causes (i.e. why some people make antibodies against their own body tissues). ITP in childhood occurs at an incidence of 1:25,000 children, about the same as acute leukaemia. In two national surveys, only about 400 new cases per year were recorded in the UK. Management of these children was not generally in line with guidelines available in the

literature at that time (Bolton−Maggs PHB and Moon I, Lancet 1997: 350; 620−623 'Assessment of UK practice for management of acute childhood ITP against published guidelines').

The national audit have given a snapshot of the incidence and severity of new children with ITP however the longer term outcome, such as persistent low platelet counts, bleeding and requirement for treatment has not been studied. Children with ongoing ITP (chronic ITP) are at a higher risk of severe bleeding problems than children with acute ITP. However the majority of children with chronic ITP still do not have serious bleeding and it is not always possible to identify those few individuals at higher risk of life−threatening bleeding based on the platelet count alone. The longterm follow−up of children from initial presentation and into chronic ITP allows analyis of features and treatment in the early part of the disease which might predict recovery or severity of disease.

All treatments are associated with side effects, some of which (such as high dose steroids) may be worse than the disease. In addition, while treatments can effectively raise the platelet count, these drugs do not treat the underlying cause of the low platelet count, which may then fall when the therapy is stopped. The preferred treatment of individuals with a persistently low platelet count who fail to respond spontaneously or to medical treatment may be surgical removal of the spleen (splenectomy). Splenectomy caries a risk of mortality and morbidity from the surgical procedure itself and from a life−long higher risk of certain infections which the spleen would normally protect against. As there is insufficient evidence concerning whom to treat, when to treat and how to treat, experts have disagreed; North American physicians are more aggressive in recommendations for therapy (George JN, Woolf SH, Raskob GE, et al.: Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology . Blood 1996; 88(1): 3−40), while European physicians are more comfortable not treating the majority of children with therapy to raise the count(BCSH: Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003; 120(4): 574−96).

Disease registries allow us to build up a more complete picture of the disorder including its natural history and complications. This is particularly helpful for rare disorders where it is very difficult for single centres to accumulate sufficient patients to have a clear idea of optimal management. It may be possible to separate patients into distinct subgroups which may help guide future treatment decisions.

A10. Give a full summary of the purpose, design and methodology of the planned research, including a brief explanation of the theoretical framework that informs it. It should be clear exactly what will happen to the research participant, how many times and in what order. Describe any involvement of research participants, patient groups or communities in the design of the research.

This section must be completed in language comprehensible to the lay person. It must also be self−standing as it will be replicated in any applications for site−specific assessment on Part C. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.

Patients up to the age of 16 years with newly diagnosed ITP will be invited to participate in the registry (a separate application is being made for adults). After giving informed consent anonymised data will be collected according to a standard proforma. This gathers information about initial symptoms, frequency and severity of bleeds, investigations performed and treatment required.

At six months after initial presentation further information will be collected by means of a second proforma, focusing on symptoms, investigations and need for treatment. At six months the majority of children will have remitted spontaneously of ITP and will no longer be followed in the study. The registry will continue to follow up only those individuals with persisting ITP (about 20%, chronic ITP). Data will then be collected every twelve months until there is either resolution of the disease or the study closes.

Patients with intracranial haemorrhage or other life−threatening bleeds form a special subgroup in whom additional information will be collected. Intracranial haemorrhage occurs very rarely; there are about 2 cases in the UK per year ('Closing the audit loop – outcome of the second national audit of the management of acute ITP – a change in practice' – Bolton−Maggs PHB and Moon I. Plenary presentation at the RCPCH meeting, April 15th, 2002, York, published abstract no 3847 in Blood 2001; 98 (11) 58b).

Although treatment is usually not required at presentation patients do occasionally need therapy to raise their platelet counts prior to surgery or dental procedures. We will identify those patients requiring such therapy to investigate the success of therapy to raise the platelet count and the degree of bleeding observed. Splenectomy is the current treatment of choice for the small subgroup of children with chronic ITP who have persistent severe bleeding problems. We will collect information on the outcome following splenectomy.

A13. Give details of any non–clinical research–related intervention(s) or procedure(s). *(These include interviews, non–clinical observations and use of questionnaires.)*

Additional Intervention	Average number per patient	Average time taken (mins/hours/days)	Details of additional intervention or procedure, who will undertake it, and what training they have received.

A14. Will individual or group interviews/questionnaires discuss any topics or issues that might be sensitive, embarassing or upsetting, or is it possible that criminal or other disclosures requiring action could take place during the study (e.g. during interviews/group discussions, or use of screening tests for drugs)?

○ Yes ◉ No

The Information Sheet should make it clear under what circumstances action may be taken

A18. What is the potential for benefit to research participants?

There is no immediate benefit to individuals other than the knowledge that this research may help us understand their disorder better, and may lead to changes in therapy, e.g. identify a group of adults who need no therapy. In a recent survey of patient views, the inability to give a cause for the disorder, and the side effects of steroids were major points of worry ('Management strategies in immune thrombocytopenic purpura (ITP) – more than medication – What do the patients think?' S Watson, PHB Bolton–Maggs. Blood 2000; 96: 438a).

Information gathered from the registry may identify patients whom are likely to benefit or not from therapy to raise the platelet count. Information gathered should lead to updated UK guidelines for the treatment and management of children with ITP.

A20. How will potential participants in the study be (i) identified, (ii) approached and (iii) recruited?
Give details for cases and controls separately if appropriate:

i) Patients with ITP are normally referred direct to their local hospital where they will be seen usually by paediatricians and sometimes by haematologists. The UK national audit identified aproximately 400 such cases per year.

ii) We have obtained permission from the Royal College of Paediatrics and Child Health to use their mailing list of consultant paediatricians (as was done for the two national audit projects in 1995 and 2000). Consultant haematologists will be informed by a notice in the mailing from the British Society of Haematology. We will mail haematologists and paediatricians at local and regional centres to inform them about the study and encourage their participation. The study will be publicised at haematology and paediatric meetings and in general college and society mailings. Reminders will be sent out every six months ('have you seen a case?'). Patients with ITP will be identified and approached by local consultants.

iii) "Postal consent" (as outlined in A6) will be sent form the research group with the opportunity for participant or clinician to contact one of the working party for more information.

A21. Where research participants will be recruited via advertisement, give specific details.

☑ Not Applicable

If applicable, enclose a copy of the advertisement/radio script/website/video for television (with a version number and date).

A22. What are the principal inclusion criteria? *(Please justify)*

– Children from the age of 2 months and young people up to the age of 16 years with newly or recently diagnosed ITP. Children younger than 2 months are excluded to reduce the likelihood of a congenital thrombocytopenia or cytopenia of other cause. Patients over the age of 16 will be recruited as part of a seperate adult registry.

A23. What are the principal exclusion criteria? *(Please justify)*

Previously diagnosed ITP (the prospective study is designed to collect only newly diagnosed cases)

Low platelet count not due to ITP – there are many other causes of a low platelet count; ITP is a diagnosis of exclusion. Therefore some patients who are intially included may be subsequently diagnosed with an alternative cause.

A24. Will the participants be from any of the following groups? *(Tick as appropriate)*

- [x] Children under 16
- [ ] Adults with learning disabilities
- [ ] Adults who are unconscious or very severely ill
- [ ] Adults who have a terminal illness
- [ ] Adults in emergency situations
- [ ] Adults with mental illness (particularly if detained under Mental Health Legislation)
- [ ] Adults with dementia
- [ ] Prisoners
- [ ] Young Offenders
- [ ] Adults in Scotland who are unable to consent for themselves
- [ ] Healthy Volunteers
- [ ] Those who could be considered to have a particularly dependent relationship with the investigator, e.g. those in care homes, medical students
- [ ] Other vulnerable groups

Justify their inclusion.

ITP can affect any individual at any age in the presence or absence of other disability. Childhood ITP behaves differently to adult ITP, the management is controversial and is one focus of the study. Data about adults over 16 years will be collected by the adult registry (new application in progress)

A29. What arrangements have been made for participants who might not adequately understand verbal explanations or written information given in English, or who have special communication needs? *(e.g. translation, use of interpreters etc.)*

Where English is not the participant's first language then recruitment will only take place following discussion through an interpreter.

A33. Will individual research participants receive any payments for taking part in this research?

○ Yes ◉ No

A34. Will individual research participants receive *reimbursement of expenses* or any other *incentives or benefits* for taking part in this research?

○ Yes ◉ No

A35. What arrangements have been made to provide indemnity and/or compensation in the event of a claim by, or on behalf of, participants for *negligent* harm?

Not applicable

Please forward copies of the relevant documents.

A36. What arrangements have been made to provide indemnity and/or compensation in the event of a claim by, or on behalf of, participants for *non–negligent* harm?

Not applicable

Please forward copies of the relevant documents.

A37. How is it intended the results of the study will be reported and disseminated? *(Tick as appropriate)*

- [x] Peer reviewed scientific journals
- [x] Internal report
- [x] Conference presentation
- [x] Other publication
- [ ] Submission to regulatory authorities
- [ ] Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- [ ] Written feedback to research participants
- [x] Presentation to participants or relevant community groups
- [x] Other/none e.g. Cochrane Review, University Library

If other/none of the above, give details and justify:
Publication in "the Platelet"– the regular newsletter of the ITP suport association.

A38. How will the results of research be made available to research participants and communities from which they are drawn?

In the United Kingdom results will be circulated by updates in the ITP support association publications and at the annual ITP support national meeting.

A39. Will the research involve any of the following activities at any stage (including identification of potential research participants)? *(Tick as appropriate)*

- [ ] Examination of medical records by those outside the NHS, or within the NHS by those who would not normally have access
- [x] Electronic transfer by magnetic or optical media, e–mail or computer networks
- [x] Sharing of data with other organisations
- [x] Export of data outside the European Union
- [ ] Use of personal addresses, postcodes, faxes, e–mails or telephone numbers
- [ ] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals
- [ ] Use of audio/visual recording devices
- [x] Storage of personal data on any of the following:
  - [ ] Manual files including X–rays
  - [x] NHS computers
  - [ ] Home or other personal computers
  - [ ] University computers
  - [ ] Private company computers
  - [ ] Laptop computers

Further details:
Once patient consent and local R&D approval has been obtained, data collection forms can be downloaded by the clinician responsible for the child. The clinician will complete the form using data from the medical records. A unique study number will be allocated to the centre and refering consultant (so that the local team can retrieve data on the same patient for subsequent follow up forms). Study forms are completed without any identifiable patient data.

Data will be stored on a secure electronic database (The ITP Study will be run on the NHS fileserver). The server is kept in a locked secure room with limited access. It is configured to use three hard drives with RAID 5 so that in the event of a hard drive failure the failed drive can simply be replaced and rebuilt from the other drives with no loss of data. The server is powered through a UPS (Uninterruptible Power Supply) so that in the event of a power failure the server will continue to run

and will be shut down automatically by the UPS should the power outage be over forty minutes. The fileserver is connected and configured for web access via the trust firewall for access only to the NHSnet therefore preventing anyone external to the NHS having access to the web system. In the event of anyone attempting to access the system in an unauthorized way the server will send out notification of this and can then be configured to block access. The server has a tape backup facility which backs up the server each night. Once a week a CD backup copy of all the databases is made and these are stored in a fireproof safe.

If consenting the anonymous data returned to the UK registry will be shared with the PARC study group in Basel. This data will be transferred electronically on a dedicated secure website. The online PARC–ITP database is password protected and data is safeguarded with SSL 128bit encryption.

A40. What measures have been put in place to ensure confidentiality of personal data? Give details of whether any encryption or other anonymisation procedures have been used and at what stage:

Registrations will be accepted only from patients from whom the local clinician has obtained informed consent and local R&D approval.

The patient's name will not appear within the database (as outlined in A39); instead a unique patient number and consultant number will be allocated.

A41. Where will the analysis of the data from the study take place and by whom will it be undertaken?

Analysis of UK data will be open to the named investigators. UK data will be forwarded to the PARC study where analysis and publication will be open to the PARC publication boards.

A42. Who will have control of and act as the custodian for the data generated by the study?

Custodians of the data will be as above

A43. Who will have access to the data generated by the study?

As above

A44. For how long will data from the study be stored?

50 Years Months

Give details of where they will be stored, who will have access and the custodial arrangements for the data:
UK data for participants in this study will be held by data manager at Royal Manchester Children's Hospital. PARC, the international database, data will be stored by data managers in Basel.

A45–1. How has the scientific quality of the research been assessed? *(Tick as appropriate)*

- ☐ Independent external review
- ☐ Review within a company
- ☐ Review within a multi–centre research group
- ☑ Internal review (e.g. involving colleagues, academic supervisor)
- ☐ None external to the investigator
- ☑ Other, e.g. methodological guidelines *(give details below)*

The Ethics Committee of Basel (EKBB) has assessed in detail the PARC–ITP Study – Pediatric and Adult Intercontinental Registry on Chronic ITP during its meeting on October 21, 2003. The study was approved at this meeting.

The ITP support association has also undertaken an independent review and approved funding for the study.

The British Paediatric Haematology Forum and Royal College of Paediatricians and Child Health have also agreed to support this study

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
The ITP support association has conducted an external peer review by Professor Sir John Lilleyman and Professor Adrian Newland.

If you are in possession of any referees' comments or other scientific critique reports relevant to the proposed research, these must be enclosed with the application.

A45–2. Has the protocol submitted with this application been the subject of review by a statistician independent of the research team? *(Select one of the following)*

- ○ Yes – copy of review enclosed
- ○ Yes – details of review available from the following individual or organisation (give contact details below)
- ◉ No – justify below

The study proposed is purely a data collection exercise at present. There is no intent to randomise or compare treatment given and outcome. Should the study develop to a stage where treatments are compared then a statistical report will be submitted with any ammendmant proposal.

A48. What is the primary outcome measure for the study?

To establish a registry of children and adolescents up to the age of 16 years presenting with acute ITP.

To identify and analyse the children with persistent ITP (chronic ITP)

To analyse the heterogeneity of ITP in terms of bleeding frequency and severity

To identify clinical markers associated with a low and higher risk of life−threatening bleeding

A49. What are the secondary outcome measures? *(if any)*

To study the natural history of ITP based on a long−term follow−up

To identify patient selection criteria for future studies.

A50. How many participants will be recruited?
If there is more than one group, state how many participants will be recruited in each group. For international studies, say how many participants will be recruited in the UK and in total.

Using similar methodology the UK 1995 Audit recruited 427 patients (Assessment of UK practice for management of acute childhood idiopathic thrombocytopenic purpura against published guidelines. The Lancet, Volume 350, Issue 9078, Pages 620−623 P. Bolton−Maggs, I. Moon)

We would expect similar annual recruitmentin the current registry.

A51. How was the number of participants decided upon?

See above

If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.

A52. Will participants be allocated to groups at random?

○ Yes ◉ No

A53. Describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

Not applicable

A54. Where will the research take place? *(Tick as appropriate)*

- [x] UK
- [ ] Other states in European Union
- [x] Other countries in European Economic Area
- [ ] Other

If Other, give details:
Uk data will be anlaysed in UK but will also be forwarded to the Intercontinental Study Group based in Basel.

A55. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK, the European Union or the European Economic Area?

- ○ Yes
- ◉ No

A56. In how many and what type of host organisations (NHS or other) in the UK is it intended the proposed study will take place?

Indicate the type of organisation by ticking the box and give approximate numbers if known:

	Number of organisations
☑ Acute teaching NHS Trusts	50
☑ Acute NHS Trusts	125
☐ NHS Primary Care Trusts or Local Health Boards in Wales	
☐ NHS Trusts providing mental healthcare	
☐ NHS Health Boards in Scotland	
☐ HPSS Trusts in Northern Ireland	
☐ GP Practices	
☐ NHS Care Trusts	
☐ Social care organisations	
☐ Prisons	
☐ Independent hospitals	
☐ Educational establishments	
☐ Independent research units	
☐ Other (give details)	

Other:
The plan of investigation is that potential participants will be identified locally, from all Acute NHS Trusts, and notify investigators who will arange consent and recruitment.

A57. What arrangements are in place for monitoring and auditing the conduct of the research?

The investigators have formed a Paediatric ITP research group which will meet regularly to review the project and present updates at appropriate meetings.

Will a data monitoring committee be convened?

◉ Yes ○ No

If Yes, details of membership of the data monitoring committee (DMC), its standard operating procedures and summaries of reports of interim analyses to the DMC must be forwarded to the NHS Research Ethics Committee which gives a favourable opinion of the study.

What are the criteria for electively stopping the trial or other research prematurely?

The registry may be stopped if recruitment is unsuccessful.

A58. Has external funding for the research been secured?

(•) Yes ( ) No

If Yes, give details of funding organisation(s) and amount secured and duration:

Organisation:	ITP Support Association
Address:	Synehurste Kimbolton Road, Bolnhurst
Post Code:	MK44 2EW
UK contact:	Mrs Shirley Watson
Telephone:	08707 770559 Fax: 08707 770559
E–mail:	itpsupport.org.uk@virgin.net
Amount (£):	27500 Duration: 24 Months

A59. Has the funder of the research agreed to act as sponsor as set out in the Research Governance Framework?

( ) Yes (•) No

Has the employer of the Chief Investigator agreed to act as sponsor of the research?

(•) Yes ( ) No

Sponsor*(must be completed in all cases)*

Name of organisation which will act as sponsor for the research:

Central Manchester and Manchester Children's University Hospitals NHS Trust

Status:

(•) NHS or HPSS care organisation ( ) Academic ( ) Pharmaceutical industry ( ) Medical device industry ( ) Other

If Other, please specify:

Address:	Research and Development Royal Manchester Children's Hospital		
Post Code:	M27 4HA		
Telephone:	0161 922 2933	Fax:	0161 922 2933
E–mail:	andreaN.evans@cmmc.nhs.uk		

The responsibilities of the sponsor may be shared between co–sponsors. If this applies, name the lead sponsor for the REC application in this box and enclose a letter giving further details of co–sponsors and their responsibilities.

Sponsor's UK contact point for correspondence with the main REC

Title:	Forename/Initials: Andrea N	Surname: Evans	
Address:	Research & Development Directorate, Room G26, Giving for Living Postgraduate centre Royal Manchester Children's Hospital		
Post Code:	M27 4HA		
Telephone:	0161 922 2933	Fax:	0161 922 2933
E−mail:	andreaN.evans@cmmc.nhs.uk		

A60. Has any responsibility for the research been delegated to a subcontractor?

○ Yes ◉ No

A61. Will individual *researchers* receive any personal payment over and above normal salary for undertaking this research?

○ Yes ◉ No

A62. Will individual *researchers* receive any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A63. Will the host organisation or the researcher's department(s) or institution(s) receive any payment or benefits in excess of the costs of undertaking the research?

○ Yes ◉ No

A64. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share–holding, personal relationship etc.) in the organisation sponsoring or funding the research that may give rise to a possible conflict of interest?

◉ Yes ○ No

If Yes, give details:
Drs Paula Bolton–Maggs and Sarah Ball are memebrs of the ITP Support Association advisory board.

A65. Other relevant reference numbers if known *(give details and version numbers as appropriate):*

Applicant's/organisation's own reference number, e.g. RD(if available):
Sponsor's/protocol number:
Funder's reference number:
International Standard Randomised Controlled Trial Number (ISRCTN):
European Clinical Trials Database (EudraCT) number: NA
Project website:

A66. Other key investigators/collaborators *(all grant co−applicants should be listed)*

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PART A: Summary of Ethical Issues

A68. What do you consider to be the main ethical issues which may arise with the proposed study and what steps will be taken to address these?

The main ethical issue for this database will be the storing and transfer of medical details. To secure anonymity all participants will be allocated an individual ID number. The individual ID number and consultant number will be the only identifying data stored on the database. Consent with signatures will be stored locally in the patients notes rather thean at the registry. Confirmation that Informed consent has been given will be recorded when entering data onto the registry.

The ITP Study will be run on the NHS fileserver similary to the National Haemophilia Database. Below are set out the main points concerning the fileserver and the system :–

PHYSICAL PROTECTION: The registry server is kept in a locked secure room with limited access. It is configured to use three hard drives with RAID 5 so that in the event of a hard drive failure the failed drive can simply be replaced and rebuilt from the other drives with no loss of data. The server is powered through a UPS (Uninterruptible Power Supply) so that in the event of a power failure the server will continue to run and will be shut down automatically by the UPS should the power outage be over forty minutes.

CONNECTION TO THE SERVER: The registry fileserver is connected and configured for web access via the trust firewall for access only to the NHSnet therefore preventing anyone external to the NHS having access to the web system. In the event of anyone attempting to access the system in an unauthorized way the server will send out notification of this and can then be configured to block access.

BACKUP: The registry server has a tape backup facility which backs up the server each night. Once a week a CD backup copy of all the databases is made and these are stored in a fireproof safe.

PART B: Section 1 – Conduct of the research at local sites

From the answer given to question A6, it is assumed that:

- *Local Principal Investigators will not be appointed at each research site participating in this study.*
- *Applications for site–specific assessment by local Research Ethics Committees on Part C of the form will not be required.*
- *There will be no requirement for individual research sites to be approved by the main REC as part of the ethical review.*

The following general information should be provided to the main REC about the local conduct of the study.

1. What research procedures will be carried out at individual research sites?

Patients will be identified and approached locally.

Information sheets and consent forms will be downloaded from the registry server and given to the patient locally.

"Postal" Informed consent will be facilitated locally with the opportunity to discuss further with member of the ITP working party.

2. Are any ethical issues likely to arise at individual sites that are not covered in the protocol for the study and if so how will these be addressed?
For example, a need for particular facilities, or to notify local clinicians or departments about the research, or to arrange additional local support for participants.

No

3. How will the Chief Investigator and his/her team supervise the conduct of the research at individual sites? What responsibilities will be delegated to local collaborators?

Contact numbers for the research party are provided on patient information sheets for parents or medical staff to contact should concerns arise.

The key responsibilities for the local collaborators are facilitation of informed consent and transfer requested data from the medical records.

Management approval to proceed with the research will be required from the R D Department for each NHS care organisation in which research procedures are undertaken.

PART B: Section 7 – Declaration

– The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

– I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

– If the research is approved I undertake to adhere to the study protocol, the terms of the full application of which the main REC has given a favourable opinion and any conditions set out by the main REC in giving its favourable opinion.

– I undertake to seek an ethical opinion from the main REC before implementing substantial amendments to the protocol or to the terms of the full application of which the main REC has given a favourable opinion.

– I undertake to submit annual progress reports setting out the progress of the research.

– I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer.

– I understand that research records/data may be subject to inspection for audit purposes if required in future.

– I understand that personal data about me as a researcher in this application will be held by the relevant RECs and their operational managers and that this will be managed according to the principles established in the Data Protection Act.

– I understand that the information contained in this application, any supporting documentation and all correspondence with NHS Research Ethics Committees or their operational managers relating to the application, will be subject to the provisions of the Freedom of Information Acts. The information may be disclosed in response to requests made under the Acts except where statutory exemptions apply.

Signature: .....

Date: (dd/mm/yyyy)

Print Name: Dr John D Grainger