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:

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Full title of study:	British Association of Dermatologists Biological Interventions Register
Name of main REC:	North West England
REC reference number:	07/MRE08/9
Date study commenced:	16/08/07
Protocol reference *(if applicable)*, current version and date:	BADBIR Study Protocol – Version 13 (14/05/2009)
Amendment number and date:	Amendment Six 19/12/11

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

No

If yes, please submit <u>either</u> the revised protocol with a new version number and date, highlighting changes in bold, <u>or</u> 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.

<u>a) MREC application form A39, A40, A42</u>
Although the original BADBIR database was successful in data collection and storage, the clinical users were dissatisfied with its performance in terms of its speed and functionality. In order to satisfy the need of the users a database with a more flexible, user friendly design was required. It was decided that use of recent technological advances in this area would more adequately meet the user's needs.

The redevelopment was managed through the BADBIR co-ordinating office with support from the University of Manchester Faculty of Medical and Human Sciences IT department through 4 stages:

Collation of User Feedback

A group of users met to discuss the direction for the new database. The group was selected carefully to ensure all different types of users were represented (i.e. both administrative and clinical). The result of this process was to redevelop the BADBIR database to meet the following objectives:

- clinicians and administrators can enter data through a usable web interface with a simple and intuitive navigation structure
- clinicians can register patients and record treatments and outcomes through an efficient, fast, secure web-based management system
- users can generate reports quickly, efficiently and flexibly
- user account administration (e.g. account creation and password resets) is effective and efficient
- infrastructure is updated in order to improve performance and security
- data protection, i.e. data can be entered, processed, stored and backed-up in a secure manner
- data curation, i.e. data can be archived appropriately in line with the study protocol
- future, post-project sustainability is built in, i.e. the system can be easily and cost-effectively maintained, updated and new functionality added if required

Development

A new SQL Server database table structure was created and the supporting code for the web interface was written in the C# programming language with particular attention paid to meeting the objectives stated above.

Testing

Extensive testing took place prior to the database going live to ensure full functionality with each data field being targeted individually. Once the testing process had proved the new database to be stable, focus shifted to the migration of the existing data from the BADBIR study.

Migration

In May 2011 the original BADBIR database was closed to ensure that the data would remain static. A careful migration process then occurred to move all the data from the original tables into the new table structure. The majority of this was executed using automated electronic processes however a small amount of data was entered manually within the BADBIR office. The migration was audited continually and at length to safeguard against any data loss.

In July 2011 the database was hosted online and full access was restored to the clinical staff working with BADBIR. Details of the improved infrastructure and security can be found in the appended BADBIR System Level Security Policy (v1 25/02/2011).

c) Study Questionnaires

Minor changes in format have been made to the paper pro-forma questionnaires to reflect the design of the BADBIR database and ensure ease of entry. A date field has now been added to some items of data. The additional fields are highlighted in yellow:

- Clinician Baseline Questionnaire v7(16/11/2011)

- Clinical Follow-Up Questionnaire v7(16/11/2011)

An incremental version number has been used to indicate the small difference in the reformatted Patient Baseline Questionnaire:

- Patient Baseline Questionnaire v5.1 (30/11/2007)

The Patient follow-up questionnaire has been slightly altered on 2 occasions since it was last approved with the original MREC application. No further data is being collected but text has changed to reflect revised study practices (i.e. "Please now return it to your dermatology practitioner" has replaced "Please now return it in the pre-paid envelope provided"): These changes are highlighted in yellow

- Patient 6 monthly follow-up questionnaire v6 (08/04/2010)

<u>c) Events of Special Interest (Formerly Serious Adverse Event Further Information Forms)</u>

The original MREC application included six Serious Adverse Event Further Information Forms which acted as a guide for clinicians for the information required when reporting certain adverse events. Six events were included as these were of specific interest to the researchers.

These have now been renamed as 'Events of Special Interest' and have been expanded to 18 events. The guidance questionnaires for 13 of these are included in the application (all v1 14/11/2011):

- Aplastic Anaemia
- Cancer (not including skin)
- Central Demylination
- Congestive Heart Failure
- Hepatic Dysfunction
- Lymphoproliferative Disease
- Myocardial Infarction
- Pregnancy Outcome
- Psoriasis Flare
- Serious Infection (excl.TB)
- Skin Cancer (inc. Bowen's Disease)
- Surgery
- Tuberculosis

The following five events are considered to be of interest but have yet to have guidance questionnaires finalised:

- Progressive Multifocal Leucoencephalopathy
- Hypersensitivity
- Misuse, abuse, overdose and medication error
- Pulmonary embolism
- Cerebrovascular accident

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*
BADBIR System Level Security Policy (SLSP).docx	1	25/02/2011
Clinician Baseline Questionnaire	7	16/11/2011
Clinical Follow-Up Questionnaire	7	16/11/2011
Patient Baseline Questionnaire	5.1	30/11/2007
Patient 6 monthly follow-up questionnaire	6	08/04/2010
Aplastic Anaemia ESI	1	14/11/2011
Cancer (not including skin) ESI	1	14/11/2011
Central Demylination ESI	1	14/11/2011
Congestive Heart Failure ESI	1	14/11/2011
Hepatic Dysfunction ESI	1	14/11/2011
Lymphoproliferative Disease ESI	1	14/11/2011
Myocardial Infarction ESI	1	14/11/2011
Pregnancy Outcome ESI	1	14/11/2011
Psoriasis Flare ESI	1	14/11/2011
Serious Infection (excl.TB) ESI	1	14/11/2011
Skin Cancer (inc. Bowen's Disease) ESI	1	14/11/2011
Surgery ESI	1	14/11/2011
Tuberculosis ESI	1	14/11/2011

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: ..... CEN Smith.

Date of submission: ..... 17.1.12.