Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
Bio-markers of Systemic Treatment Outcomes in Psoriasis

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product

( ) Clinical investigation or other study of a medical device

( ) Combined trial of an investigational medicinal product and an investigational medical device

( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

( ) Basic science study involving procedures with human participants

( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

( ) Study involving qualitative methods only

(●) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

( ) Study limited to working with data (specific project only)

( ) Research tissue bank

( ) Research database

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

( ) Other study

2a. Please answer the following question(s):

a) Will you be taking new samples primarily for research purposes (i.e. not surplus or existing stored samples), including any removal of organs or tissue from the deceased?	(●) Yes	( ) No
b) Will you be using surplus tissue or existing stored samples identifiable to the researcher?	(●) Yes	( ) No
c) Will you be using only surplus tissue or existing stored samples not identifiable to the researcher?	( ) Yes	(●) No
d) Will you be processing identifiable data at any stage of the research (including in the identification of participants)?	(●) Yes	( ) No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

- [x] England
- [x] Scotland
- [x] Wales
- [ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- (•) England
- ( ) Scotland
- ( ) Wales
- ( ) Northern Ireland
- ( ) This study does not involve the NHS

4. Which applications do you require?

- [ ] IRAS Form
- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] Confidentiality Advisory Group (CAG)
- [ ] Her Majesty's Prison and Probation Service (HMPPS)

5. Will any research sites in this study be NHS organisations?

(•) Yes ( ) No

5a. Do you want your NHS R&D application(s) to be processed through the NIHR Coordinated System for gaining NHS Permission?

(•) Yes ( ) No

If yes, you must complete and submit the NIHR CSP Application Form immediately after completing this project filter, before proceeding with completing and submitting other applications.

6. Do you plan to include any participants who are children?

( ) Yes (•) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

( ) Yes (•) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

○ Yes ◉ No

9. Is the study or any part of it being undertaken as an educational project?

○ Yes ◉ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

○ Yes ◉ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

○ Yes ◉ No

NOTICE OF SUBSTANTIAL AMENDMENT

Please use this form to notify the main REC of substantial amendments to all research other than clinical trials of investigational medicinal products (CTIMPs).
The form should be completed by the Chief Investigator using language comprehensible to a lay person.

Details of Chief Investigator:

	Title	Forename/Initials	Surname
	Prof	Catherine	Smith
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For guidance on this section of the form refer to the guidance

Full title of study:	A multi-centre, prospective, cohort study to establish clinically relevant pharmaco-genetic markers of systemic treatment outcomes in patients with severe psoriasis
Lead sponsor:	Guy's and St. Thomas' NHS Foundation Trust
Name of REC:	South East London REC 2
REC reference number:	11/H0802/7

Additional reference number(s):

Ref.Number Description	Reference Number

Name of lead R&D office:	Guy's and St. Thomas' NHS Foundation Trust
Date study commenced:	2012
Protocol reference (if applicable), current version and date:	6 - 01/03/2019
Amendment number and date:	5 - 02/05/2019

Type of amendment

(a) Amendment to information previously given in IRAS

○ Yes ◉ No

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

(b) Amendment to the protocol

◉ Yes ○ No

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.

Tracked change protocol enclosed

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

◉ Yes ○ No

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

Tracked change versions enclosed.

Is this a modified version of an amendment previously notified and not approved?

○ Yes ◉ No

Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.
If this is a modified amendment, please explain how the modifications address the concerns raised previously by the ethics committee.
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.

Protocol changes-

The proposed changes do not significantly alter the research design or methodology or alter the scientific value of the study. The changes proposed relate principally to clarification of areas of ambiguity highlighted by study teams, extension of inclusion criteria in recognition of progress in treatment options made in psoriasis, additional optional sampling (skin biopsies, skin microbiome swabs, blood) and where relevant, more explicit detail and transparency over data management practice to ensure compliance with the General Data Protection Regulation.

The relevant heading and page numbers (tracked version) are included below.

1) Background and rationale updated (Sect 1, pp. 6-8)

Clinical and research advances have been made since the original application (2011). We have changed some information in this section, and added a new paragraph ('introduction update' p8) to the rationale to cover this, updating details on advances relevant to the study, for example our collaboration with the MRC funded PSORT programme (Psoriasis Stratification to Optimise Relevant Therapy), other stratified medicine initiatives and that there are now a number of new systemic therapies available for psoriasis and therefore new targets for our biomarkers of response to treatment aims. We have also referenced the optional additional samples added, specifically skin biopsies, skin microbiome swabs and peripheral blood mononuclear cells (PBMCs) which will give added value to the resource, and allow for augmentation of and comparison with existing PSORT psoriasis cohorts.

2) Trial study design updated (Sect 2.2, p.8)

Clinical advances over the last 5 years have introduced new treatments for psoriasis and additional options are likely to be licensed within the life time of this study.

The analysis approach now explicitly incorporates pharmacological and other biomarkers as an integrated, multi-dimensional approach is required to optimise discovery of clinically useful biomarkers.

3) New Section 2.3 elaborating on linkage with BADBIR (p.9)

The previous version had referred to the linkage with BADBIR. We have provided clarification about how this linkage

occurs to ensure transparency and compliance with the General Data Protection Regulations. We have also now included reference to their recent name change (from Biologic Interventions Register, to Biologics and Immunomodulators Register)

4) New Section 2.4 to explain inclusion of PSORT participants (p.10)

As part of the MRC stratified medicine consortium a deeply phenotyped, muli-omic cohort of patients initiating biologic therapy has been collected. However the follow up duration is only 12 weeks. All PSORT participants will be invited to participate in BSTOP (and also BADBIR) so that we can accrue longer term outcomes and thus enhance the value of the PSORT dataset.

5) Updated subjects' criteria (Sect 3.1, p. 10)

We have made clear that those recruited to the single sample arm should be on BADBIR, to link the data from the one-off visit to longitudinal data collected as part of the BADBIR study

6) Clarification that patients may also be recalled for further sampling if there is insufficient sample or samples have been exhausted (Sect 3.3 C, p.10)

7) Updated Section 4 Investigational Plan (pp. 12-27)

We've comprehensively reworked this section to clarify the patient cohorts and sampling strategy in light of feedback from local study teams. The existing text within the protocol was not clear regarding the patient cohorts and respective sampling requirements. The procedures themselves have not changed (namely we still collect samples at intervals during a participants' involvement) but rather the layout, format and structure on the page has been altered to make it more readable. Much of the content has not been changed, but moved.

We have also clarified the process for participants consenting to only provide a sample for DNA. These 'single sample' participants had been referred to in the previous version of the protocol, but further clarity was needed.

Within this section we have also aligned our sampling strategy with the long term data collection involved in BADBIR, ie: every 6 months for 5 years (where BADBIR go to annual follow-up after 3 years, but we continue six-monthly), or until they complete their involvement in BADBIR, whichever is longer. We share datasets with BADBIR (as previously approved) and so it is our aim to align them as much as possible to allow for cohesive analysis.

We have updated the Week 12 post-drug start description to 'Week 12-16' in line with the window for the evaluation of response to treatment specified by NICE (clinical guidelines for psoriasis assessment and management, CG153).

We hope to use our patient population to explore new sample analysis techniques and therefore have added additional samples, namely skin biopsies, skin microbiome swabs and other blood samples, to the protocol - all of which are optional to the participant. These will only be taken at specific sites and as arranged with the lead study centre. We have added further information on the techniques, and information on the maximum volume of blood per visit (not exceeding a total of 100ml per visit in addition to routine clinic bloods).

Updated Section 4.2 'Measurements and Evaluations' - addition of more patient reported outcome measures and optional sample types (p. 13). Patient reported outcomes are important and we felt it prudent to increase the number collected to augment our data analysis. We have therefore added standard of care questionnaires to our data set.

Addition of section 4.7 'Ongoing bioresource' – to clarify ongoing bioresource arrangements for patients who have consented to samples being used in this way.

8) Clarification of anonymisation and data management strategy Section 6.4 and 6.5 (pp. 28-29)

We have clarified section 6.4 regarding patient anonymisation, making the text clearer. Section 6.5 now includes reference to our collaborative work and plans to share anonymised data with our wider research team including research collaborators, who may include industry partners. They will be approved researchers within collaborative partnerships, to make use of the best technical, clinical and analytical expertise. These may include collaborators outside of the UK (including those outside of the EU, now made explicit also in patient information). To meet the terms of our data sharing agreement with BADBIR, we have made explicit the fact that any sharing would be of BSTOP data, and not BADBIR fields.

Industry partners would receive data only in accordance with a data sharing agreement, whereby the terms would restrict the use of materials to the ethically approved study activity agreed with the coordinating centre study team via an application process, whether that be for the present study or future studies in psoriasis.

The rationale for sharing data with collaborators who may include industry partners is to take advantage of additional funding streams, specialist technology and expertise, which help to get the most value out of the bioresource, or the samples and data provided by the patient. In fostering collaboration, we are then able to make the most advances with the available data to improve outcomes for patients with psoriasis. Such collaborations are beneficial to research, the NHS and the patient.

We have also added information on our new secure NHS supported database which we will be using to house all BSTOP data. This database (known as CAPTURE) is NHS hosted, behind the NHS firewall, and subject to multi-factor authentication security allows us to securely store identifiable study data for all participants. Local centres have direct access (named, delegated staff members only) to enter their data. Identifiable data is only accessible to the local study team, the Chief Investigator, and delegated study team members (e.g. database administrators). Identifiable data allows for better participant tracking (a useful tool for sites). The information governance documentation surrounding this website can be provided if helpful.

9) Increased sample numbers (Sect 2.2, p.8, and 4.6.2, p.26)

As our work has progressed and our collaborations established we have gained additional funding to support our work to allow it to continue and grow (including the MRC funded PSORT consortium, and the EC Horizon 2020 BIOMAP consortium, contractual changes pending, not referenced here but MA to extend to 31st March 2024 to follow). Additionally preliminary data from BSTOP indicate the need for at least 1000 patients per drug for genetic analyses. We therefore plan to increase our sample numbers to allow for continued research and to enable us to get the required numbers in each group for the genetic analyses - from 5500 to 9500

10) Updated safety reporting requirements (Sect 5, p.27)

The existing protocol wording was misleading in terms of the responsibility it placed on the study team for the reporting of adverse events, given that the study is observational. We have therefore provided clarity on the issue, that only adverse events which have been brought about specifically by participation on the study need be considered and reported as required. To date, no SAEs have been reported in relation to this study.

11) Removal of all appendices

We have deleted all appendices to the protocol as they are not necessary in this study document and exist separately for use by centres in the study (eg in lab manuals)

Participant Information Leaflet changes –

1) Updated 'purpose of study' statement

To bring it more in line with what we're aiming to achieve, and our original study aims

2) Clarification of visit schedule

Our original wording was not that clear. We have now clarified that participants can either agree to follow up (in line with routine clinical appointments) or just one study visit, and that long term follow up occurs during the initial weeks after starting a new treatment and then at 6 monthly intervals in line with BADBIR (if applicable). When BADBIR go to annual visits (year 3+), we continue with six-monthly visits.

We have updated the information to include reimbursement of reasonable travel expenses (max £100) for patients invited to attend research visits outside of routine clinical care, to provide additional samples.

3) Clarification of samples required

We have included new information regarding potential sampling we may carry out (e.g finger prick bloods, skin biopsies or microbiome swabs) if participants agree to donate them. We have added information about the possible risks associated with biopsy, if the patient should agree to having those additional samples taken.

4) Clarification of data storage and sharing with collaborators

The original protocol aim was to provide a bioresource that could be used by investigators to improve outcomes in psoriasis (secondary objective number 2) and required sharing of anonymised data to research investigators. However, to ensure we are in line with the new GDPR and current best practice we now wish to make this more explicit in both the Patient Information Sheet and consent form. We also wish to highlight that the new database for all BSTOP data includes identifiable data.

5) Clarification that genetic sequencing will only be to look at genes related to the research only, and will not be used to explore personal risk of developing any other diseases. Inclusion of 'skin' in relation to DNA collected.

6) Updated contact information

7) Updated procedure for those participants that withdraw. We now ask specific consent for continued access to (i) routinely collected health record data and (ii) their BADBIR record (if relevant) as these are two separate data sources with discrete implications for ongoing data management. We have removed the line regarding the 'complete withdrawal' as we are proposing to change our policy for all patients recruited to version 5 or later to enable us to retain all samples and data collected to date. The version the patient has consented to is stored in our database.

Informed Consent Form changes -

1) Clarification of samples taken (DNA for all subjects, others where applicable)

2) Addition of consent line for sharing of anonymised data with research collaborators. As per the reference above in the patient information leaflet changes, the original protocol aim was to provide a bioresource that could be used by investigators to improve outcomes in psoriasis (secondary objective number 2) and required sharing of anonymised data to research investigators. However, to ensure we are in line with the new GDPR and current best practice we now wish to make the fact that their data/samples will be shared with investigators (as part of secondary objective 2) more explicit in both the Patient Information Sheet and consent form. We have therefore made the sharing of data with investigators and collaborators a part of the consenting process, distinct from the optional items.

3) Clarification of how data will be viewed and stored – i.e. identifiable data stored and used by delegated study team members, while other staff will access anonymised data only

4) Addition of consent line for long term sample storage in approved tissue bank

5) Addition of optional consent line for contact regarding additional sampling, and/or contact regarding studies which may be of interest

6) reformatting to move 'I agree to participate' to a place where it will less likely be missed by patients during the initial review

+ general reformatting of the adult (existing) ICF into a table format to make for easier updating of trust specific headers, and large font versions where requested

+ additional ICFs (new) for child participants, including parents, and for adult participants opting to donate skin biopsies.

Patient poster -

Following feedback from teams we have created a poster which can be used in clinic settings and/or public and patient involvement events

Any other relevant information

Applicants may indicate any specific issues relating to the amendment, on which the opinion of a reviewing body is sought.

List of enclosed documents

Document	*Version*	*Date*
Patient Information Leaflet_tracked	5	01/03/2019
Patient Information Leaflet_clean	5	01/03/2019
Informed Consent Form_tracked	5	01/03/2019
Informed Consent Form_clean	5	01/03/2018
Patient invite letter_tracked	2	31/01/2019

Patient invite letter_clean	2	31/01/2019
Patient withdrawal of consent form_tracked	2	31/01/2019
Patient withdrawal of consent form_clean	2	31/01/2019
Protocol_tracked	6	06/06/2019
Protocol_clean	6	06/06/2019
Patient_poster	1	31/01/2019
Cover letter	NA	31/01/2019
Skin biopsy ICF (supplementary)	1	31/01/2019

Declaration by Chief Investigator

1. *I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.*
2. *I consider that it would be reasonable for the proposed amendment to be implemented.*

This section was signed electronically by Professor Catherine Smith on 06/06/2019 15:56.

Job Title/Post:	Prof of Dermatology & Therapeutics
Organisation:	GSTT/KCL
Email:	catherine.smith@kcl.ac.uk

Declaration by the sponsor's representative

I confirm the sponsor's support for this substantial amendment.

This section was signed electronically by R&D Department Elizabeth Bruna on 06/06/2019 16:05.

Job Title/Post:	Acting R&D Governance Manager
Organisation:	Guy's and St Thomas' NHS Foundation Trust
Email:	r&d@gstt.nhs.uk