PROFILE

CRF Completion Guidelines

Trial Title:	PRedicting Outcomes For Crohn's dIsease using a moLecular biomarkEr (PROFILE) trial
IRAS ID:	220851
Chief Investigator:	Dr Miles Parkes
Trial Sponsor:	Cambridge University Hospitals NHS Foundation Trust and University of Cambridge

Email all completed CRFs to the Data Manager at the following:

Karlena Champion – Data Manager
Cambridge Clinical Trials Unit
Email:add-tr.profile@nhs.net

Weeks 4, 16, 32 & 48 CRF pages should be sent within five weeks of the end of a trial visit.

Screening, Baseline & SAE forms have more urgent timelines, detailed in Section 4.8.

Remember to retain a copy of each completed CRF for your site records.

Remember that CRFs (and any other study-related documentation) sent to the trial coordinator MUST NOT contain patient-identifiable data.

Contents

1. List of PROFILE Case Report Forms

Title
Adalimumab Administration
Adverse Event Log
Adverse Event and Concomitant Medications Review
Azathioprine, Mercaptopurine and Methotrexate Administration
Blood Results
Blood Results Review
Colonoscopy
Concomitant Medications Log
Exclusion Criteria and Eligibility
Harvey Bradshaw Index (HBI) & Perianal Disease
Height
Inclusion Criteria
Infliximab Administration
Medical History - Baseline
Medical History - Screening
MRE
Pregnancy
Primary Outcome Week 4
Primary Outcome Weeks 16/32/48
Randomisation
Research bloods - Weeks 16/32/48
Serious Adverse Event
Screening Blood Results
Screening – Demographics
Screening Research Bloods
Stool Sample
Screening Visit – Sign Off
Thiopurine Monitoring
TPMT
Visit Confirmation
Visit
Weight & Physical Exam
Week 16 Stool Sample
Week 32 Stool Sample
Week 48 Stool Sample
Withdrawal

2. List of PROFILE Participant Questionnaires

Title
EQ-5D-5L
IDBQ
Resource Usage – Baseline
Resource Usage – Week 16, 32 & 48

3. Abbreviations

Abbreviation	Full Term
AE	Adverse Event
CCTU	Cambridge Clinical Trials Unit
CRF	Case Report Form
MedDRA	Medical Dictionary for Regulatory Activities
MRE	Magnetic Resonance Enterography
NA	Not Applicable
ND	Not Done
SAE	Serious Adverse Event
NK	Not Known

4. Visit Schedule Overview

Procedure	Screening Wk -2	Baseline Wk 0	Wk 4	Wk 16	Wk 32	Wk 48	Ad-hoc Visit
Consent	✓						
Disease assessment - Harvey Bradshaw Index (HBI)	✓	✓	✓	✓	✓	✓	✓
Concomitant medication	✓	✓	✓	✓	✓	✓	✓
Weight in Kg	✓	✓	✓	✓	✓	✓	✓
Physical examination	✓	✓	✓	✓	✓	✓	✓ (exc height)
Eligibility confirmed		✓					
Randomisation		✓					
PAXgene RNA tube for biomarker assessment	✓						
PAXgene RNA tube for research sample	✓			✓	✓	✓	
Serum tube	✓			✓	✓	✓	
EDTA tube	✓					✓	
Bloods (FBC, CRP, U&E, Creatinine, LFT)	✓†	✓	✓	✓	✓	✓	✓
Bloods (Hepatitis B & C, VZV, TPMT and Tuberculosis testing)	✓						
Bloods (6-TGN and 6-MMP = thiopurine metabolites)			✓ α	✓ α	✓ α	✓ α	✓ α
Stool sample for faecal Calprotectin	✓	†		✓	✓	✓	
Buffered stool sample	✓					✓	
Patient rated Questionnaires	✓	✓		✓	✓	✓	
Colonoscopy	✓*					✓	✓
Magnetic Resonance Enterography (MRE)	✓¥					✓	
Adverse event reporting		✓	✓	✓	✓	✓	✓

α 6-TGN and 6-MMP Thiopurine metabolites only to be measured if participants are taking either Azathioprine or 6-Mercaptopurine.

† Results of blood tests and faecal Calprotectin performed as part of standard care can be used for eligibility provided performed within 4 weeks of screening visit –however a repeat stool sample should still be sent for central processing (as Central lab results will be used in subsequent analyses). Sample pot for faecal Calprotectin will be provided at screening visit and patients advised to provide sample promptly so that central Calprotectin result is available at the baseline visit.

*** Screening colonoscopy results can be taken from the participants index colonoscopy performed as part of their standard care within 3 months of the screening visit. Ideally a video of the colonoscopy should be recorded for central reading to allow comparison with the colonoscopy at week 48.**

¥ It is anticipated that all patients newly diagnosed with Crohn's disease will undergo MRE. An MRE performed as part of standard of care can be used; and if not already performed should be undertaken within 3 months of the screening visit. The results of this index MRE will be collected at the week 16 visit. It will be used for central reading and allow comparison with MRE at week 48.

5. General Completion Guidelines

4.1 General Principles for CRF Completion

- All CRF pages must be clear and legible
    - Important as 1 and 7 can be misrepresented if the writing is not clear
        - 1 or I and 7 or ~~7~~
- The correct version of the CRF form must be completed.
- Once a patient is randomised, please label a CRF pack with the subject ID number
- Data reported on the CRF must be extracted from, and be consistent with, documented source data
- Where selection boxes indicate a selection of Y or N or numerical options (i.e. 1, 2, 3), only ONE entry should be recorded per box
- The CRFs must be completed, dated and initialled/signed by an Investigator or designee as appropriate
- **COPIES** of CRF pages should be returned or emailed promptly to the Data Manager at add-tr.PROFILE@nhs.net
- The investigator site should always retain a copy of each completed form
- Source data should always remain at the participating site
- Any changes made to the CRF pages once the copy has been returned to the Trial Coordinating centre must be sent to the Data Manager within one month - see section 4.9 Correcting Errors
- CRFs must only be completed by authorised personnel. They should have completed and signed the site's trial Delegation Log
- The timely completion, legibility and accuracy of the CRFs remain the responsibility of the Principal Investigator
- The PI should retain regular oversight and timely sign off of the CRFs, particularly those relating to a patient's eligibility
- An INVESTIGATOR is any person that has been delegated an activity.

4.2 Header Boxes

- The following data must be completed in the header of every completed CRF:
    - Patient Initials: First and last initials only
    - Patient Date of Birth: Enter using the DD/MMM/YYYY format (e.g. 13 AUG 2013)
    - Site Code: The four-digit site number allocated at site initiation (e.g. N001)
    - Subject ID number: Each subject will receive a unique 3-digit trial number upon randomisation (e.g. 001) – hence their trial number will be a 7 digit composite of Site Code and Subject ID number N001_001

4.3 Participant Data

- CRFs (and any other study-related documentation) sent to the Trial Coordinator **MUST NOT** contain any patient-identifiable information e.g. names, hospital number, NHS Number
- Please use partial identifiers ONLY e.g. the patient's initials, date of birth and subject ID number when communicating with the coordination team

4.4 Completion of Dates

- All dates are to be completed in the sequence day/month/year (DD/MMM/YYYY) with the month written using **LETTERS** not numbers
- If the day or month is unknown/not known complete the boxes with NK

4.5 Entering numbers

- Enter a digit in each box provided, if three boxes are provided but only two are required please enter a preceding 0

E.g. | 0 | 2 | 3 |

4.6 Unavailable Data

- **All** applicable questions must be answered
- Where data are not available **please do not leave the answer blank** as this will create unnecessary data queries
- Please include one of the following abbreviations instead:
  - NK = Not known
  - NA = Not applicable
  - ND = Not done

4.7 Correcting Errors

- Errors should be crossed out with a single line (i.e. ~~mistake~~), the correction inserted and the change initialled and dated by the investigator or designee
- Typing correction fluid should **NOT** be used
- If it is not clear why a change has been made, an explanation should be written next to the change

4.8 Sending CRFs to the Trial Coordinating site

✓ Please email COPIES of CRF forms to:

Karlena Champion
Email: add-tr.profile@nhs.net

- Ensure that the form is scanned, with the copy sent to the Data Manager and the original kept at your site.
- Please send the Screening visit CRF's no later than two weeks after the visit date.
- Please send the Baseline visit CRF's no later than four weeks after the visit date.
- Other CRF pages should be sent in a timely manner, ideally within five weeks after the end of a visit.

- Completed **SAE** forms should be sent to the trial coordinator by email (add-tr.profile@nhs.net) **within 24 hours** of becoming aware of the event.

6. CRF Completion Guidelines

Note: Not all questions on the CRFs are covered by these guidelines. Please contact the Trial Coordinator if you require clarification on any questions. All CRFs to follow in alphabetical order:

ADALIMUMAB ADMINISTRATION

Complete this form at the following point in the trial:

- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

ADVERSE EVENT LOG

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

- At each visit time point following consent adverse events should be reported.
- A copy of the adverse event log should be provided with the CRFs to the central coordinating site after each visit.
- One continuous log should be maintained for the duration of the participant's enrolment in the trial.
- Resolution should remain blank until an end date has been entered. An event should only be completed as on-going at the end of the trial visit at Week 48.

ADVERSE EVENT AND CONCOMITANT MEDICATIONS REVIEW

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

AZATHIOPRINE, MERCAPTOPURINE AND METHOTREXATE ADMINISTRATION

Complete this form at the following point in the trial:

- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32

- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

  - Ensure all relevant questions are completed.

BLOOD RESULTS

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

  - Ensure all relevant questions are completed.
  - Check units of values entered to ensure these match the units listed on the form. Enter 'ND' for those tests that were not done

BLOOD RESULTS REVIEW

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

  - Ensure all relevant questions are completed.

COLONOSCOPY

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

  - Ensure all relevant questions are completed.
  - The time displayed on the endoscope output should be noted at the start of the recording and at each point that the endoscope transfers from one section of the bowel to the next i.e. when moving from the ileum to the caecum.

CONCOMITANT MEDICATIONS LOG

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16

✓ Visit 4 - Week 32
✓ Visit 5 - Week 48
✓ Ad-hoc Visit

- Ensure all relevant questions are completed.
- Enter only ONE value per field (e.g. do not enter a range such as '100-200' for Dose).
- If the medication is on-going, leave blank until week 48.
- If the medication is NOT on-going, enter '0' in the 'On-going' field AND PROVIDE THE STOP DATE.
- At Week 48 ensure medication on-going field is completed.

EXCLUSION CRITERIA AND ELIGIBILITY

Complete this form at the following point in the trial:

✓ Visit 1 - Baseline

- Tick the box confirming that the patient meets all exclusion criteria
- Please ensure this form is signed and dated by the principal investigator or an appropriately delegated member of staff prior to sending to the central coordinating site.

HARVEY BRADSHAW INDEX (HBI) & PERIANAL DISEASE

Complete this form at the following point in the trial:

✓ Screening Visit
✓ Visit 1 - Baseline
✓ Visit 2 - Week 4
✓ Visit 3 - Week 16
✓ Visit 4 - Week 32
✓ Visit 5 - Week 48
✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

HEIGHT

Complete this form at the following point in the trial:

✓ Screening Visit

- Height is only mandatory at screening visit
- Ensure all relevant questions are completed.

INCLUSION CRITERIA

Complete this form at the following point in the trial:

✓ Visit 1 - Baseline

- Tick the boxes confirming that the patient meets all inclusion criteria

INFLIXIMAB ADMINISTRATION

Complete this form at the following point in the trial:

✓ Visit 2 - Week 4

✓ Visit 3 - Week 16
✓ Visit 4 - Week 32
✓ Visit 5 - Week 48
✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

MEDICAL HISTORY - BASELINE

Complete this form at the following point in the trial:

✓ Visit 1 - Baseline

- Ensure all questions are completed.
- Measurements are **MANDATORY**. If any information is not known, please mark as NK, clearly stating the reason on the CRF.

MEDICAL HISTORY - SCREENING

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all questions are completed.
- Measurements are **MANDATORY**. If any information is not known, please mark as NK, clearly stating the reason on the CRF.

MRE

Complete this form at the following point in the trial:

✓ Visit 3 - Week 16
✓ Visit 5 - Week 48

- Ensure all relevant questions are completed

PREGNANCY

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all relevant questions are completed.

PRIMARY OUTCOMES – WEEK 4

Complete this form at the following point in the trial:

✓ Visit 2 – Week 4

- Ensure all relevant questions are completed.

PRIMARY OUTCOMES – Week16/32/48

Complete this form at the following points in the trial:

✓ Visit 3 – Week 16
✓ Visit 4 – Week 32
✓ Visit 5 – Week 48

✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

RANDOMISATION

Complete this form at the following point in the trial:

✓ Visit 1 - Baseline

- Ensure all questions are completed.

RESEARCH BLOODS - WEEKS 16/32/48

Complete this form at the following point in the trial:

✓ Visit 3 - Week 16
✓ Visit 4 - Week 32
✓ Visit 5 - Week 48

- Ensure all relevant questions are completed.

SERIOUS ADVERSE EVENTS

Complete this form as appropriate during the trial:

- Complete all sections of the form.
- Deaths should be reported using the SAE form.
- Report the SAE to the Trial Coordinating site as defined in the protocol.

The form should be sent to the trial coordinating site **within 24 hours** of becoming aware of the event. Provide a clear, chronological, clinical course of events from presentation to current time—including symptoms and signs at presentation/vital signs/examination findings. Please specify the severity or grade for all related symptoms (mild, moderate or severe).

Reporting Requirements:
For all initial reporting of any SAEs this form must be completed fully or with as much information as possible.

New SAE information after an initial submission should be indicated on an SAE follow up report and forwarded to the PROFILE Trial Coordinating Site as soon as possible. All SAEs must be followed up until resolution. There are two options for subsequent follow-up reporting of an SAE:

1. If only minimal follow-up data is being submitted (e.g. 2 or 3 fields): The site may submit the initial SAE form updated as a follow-up. In this case a reporter should add all new or missing information to the initial SAE form.

2. If significant or many changes are being submitted: A new SAE Reporting form should be completed with the following information provided as a minimum: trial and participant details (SAE form header), SAE term, SAE onset date and all new or missing information.

MedDRA coding will be assigned by the Cambridge Clinical Trials Unit.

SCREENING BLOOD RESULTS

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all questions are completed.

SCREENING – DEMOGRAPHICS

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all questions are completed.

SCREENING RESEARCH BLOODS

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all questions are completed.

STOOL SAMPLE

Complete this form at the following point in the trial:

✓ Screening Visit
✓ Visit 1 - Baseline Visit
✓ Visit 2 - Week 4 Visit
✓ Visit 3 - Week 16 Visit
✓ Visit 4 - Week 32 Visit
✓ Visit 5 - Week 48 Visit

- Ensure all questions are completed.

SCREENING VISIT – SIGN OFF

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all questions are completed.

THIOPURINE MONITORING

Complete this form at the following point in the trial:

✓ Visit 2 - Week 4
✓ Visit 3 - Week 16
✓ Visit 4 - Week 32
✓ Visit 5 - Week 48
✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

TPMT

Complete this form at the following point in the trial:

✓ Screening Visit

- Ensure all relevant questions are completed.

VISIT CONFIRMATION

Complete this form at the following point in the trial:

- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

- Ensure all questions are completed.

WEIGHT & PHYSICAL EXAM

Complete this form at the following point in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 2 - Week 4
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48
- ✓ Ad-hoc Visit

- Ensure all relevant questions are completed.

WITHDRAWAL

Complete this form as appropriate during the trial if:

- ✓ The participant withdraws consent for any reason

- Participants may withdraw from either treatment, or follow up or both.
- Multiple forms can be used for a participant withdrawing consent for differing activities over time.
- Return this form to the Trial Coordinating site as soon as possible after the patient has withdrawn consent from an activity.

7. Particpant Questionnaires Completion Guidelines

Complete the questionnaires cover before releasing the documents to the participant.

QUESTIONNAIRE: EQ-5D-5L

Ensure these forms are completed by the patient at the following points in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48

- Complete the headers of the questionnaires before releasing the documents to the patient.
- Only use first and last initials in header and cover.
- Review the completed form to ensure all questions have been answered

QUESTIONNAIRE: IBDQ

Ensure these forms are completed by the patient at the following points in the trial:

- ✓ Screening Visit
- ✓ Visit 1 - Baseline
- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48

- Complete the headers of the questionnaires before releasing the documents to the patient.
- Only use first and last initials in header and cover.
- Review the completed form to ensure all questions have been answered

QUESTIONNAIRE: RESOURCE USAGE – BASELINE

Ensure these forms are completed by the patient at the following points in the trial:

- ✓ Visit 1 - Baseline

- Complete the headers of the questionnaires before releasing the documents to the patient.
- Only use first and last initials in header and cover.
- Review the completed form to ensure all questions have been answered

QUESTIONNAIRE: RESOURCE USAGE – WEEK 16, 32 & 48

Ensure these forms are completed by the patient at the following points in the trial:

- ✓ Visit 3 - Week 16
- ✓ Visit 4 - Week 32
- ✓ Visit 5 - Week 48

- Complete the headers of the questionnaires before releasing the documents to the patient.
- Only use first and last initials in header and cover.
- Review the completed form to ensure all questions have been answered