Exeter Clinical and Health Research

Standard Operating Procedure:
StartRight Study – Visit 1 Recruitment, Data & Sample Collection & Sample Processing
(All Sites apart from Exeter central site)

SOP Number: NIHRexe251STARTRIGHT **Version Number & Date:** v4.0 03 November 2017 **Superseded Version Number & Date:** v3.0 09May2017	**Effective Date: 06 Nov 2017** **Review Date: 06 Nov 2018**

Author:

Name: Anita Hill **Position:** Research Project Manager

Approved By:

Name: Dr Angus Jones **Position:** Chief Investigator

Senior Management Agreement:
I agree that appropriate members of my workforce (as named above) have written and approved this SOP for use in clinical research.

Name: Dr Bea Knight **Position:** Research Midwife & CRF Senior Manager

CONTENTS

BACKGROUND & SCOPE:

It is not always easy for doctors to be able to say for certain what kind of diabetes a person has (particularly in adults aged under 50), where the distinction between the types is less clear. Getting the right diagnosis is important to know what treatment will be most effective; for example patients with Type 1 diabetes need insulin, whereas most patients with type 2 diabetes may be effectively treated without insulin.

The purpose of this research is to determine whether blood tests can help us improve treatment by identifying which patients have Type 1 diabetes, and will need very early insulin treatment, and which patients are unlikely to need insulin treatment at diagnosis. These tests include antibodies against the cells that make insulin (often seen in Type 1 diabetes), and a new test which assesses genetic risk of diabetes.

Purpose of this SOP:
To ensure correct and uniform data / sample collection from participants in the StartRight study.

Location:
Research recruitment site, secondary care, primary care or community setting (e.g. GP practice or participant's home).

Skill level:
All personnel should be appropriately trained to carry out the procedures detailed in this SOP. All staff working on the project must be listed on the study delegation log and signed off by the appropriate study PI or CI.

Scope:
This SOP applies to all individuals involved in the following activities relating to the recruitment of participants to the StartRight study:

- Patient contact and informed consent.
- Sample & data collection
- Sample processing and recording on CRF Tracker
- Sample despatch to local laboratory and the CI site in Exeter
- Scanning and transfer of completed DCFs, consent forms & local biochemistry results to the CI site in Exeter.

Responsibilities:
It is the responsibility of staff involved in the activities listed above to read and use this SOP.

Expected outcome:
Complete and accurate collection, recording and transfer of Visit 1 samples and data for all participants recruited to the StartRight study.

EQUIPMENT REQUIRED:

a.	**Current versions of the following StartRight study specific paperwork:**
	• Participant Referral & Contact Form • Visit 1 data collection form (DCF) • Consent form • Hypoglycaemia questionnaire • Quality of life questionnaire (SF12 & CD10)
b.	**Anthropometry equipment:**
	• Weighing scales (should be calibrated class 3 scales) • Stadiometer • Blood pressure machine • Tape measure suitable for waist & hips (Please see local policies for acceptable equipment at your site)
c.	**StartRight Visit 1 Blood Sample Pack comprising:**
	Research Blood Tubes in Plastic Bag with part-filled Biochem form listing CPep etc. • 1 large (7.5ml) Serum Gel tube • 1 large (7.5ml) EDTA tube • 1 Paxgene RNA tube (clear/orange top) • 1 Elkay tube (with blue lid) • 1 Pasteur pipette • 1 Butterfly needle • 1 BD Vacutainer One Use Holder • 1 Sarstedt Multi-adaptor • 1 Chem MTO instruction form **DNA Blood tube in plastic bag with Genetic request form** • 1 Exeter Genetic form (DNA) • 1 Roche Cell free DNA tube • 1 small (2.7ml) EDTA tube
d.	**Standard local venipuncture equipment & the following local tubes:**
	• 1 small (2.7ml) fluoride tube (Glucose analysis at local lab) • 1 small (2.7ml) EDTA tube (FBC analysis at local lab) **If no Renal results in patient record (at least a Creatinine result) dated no more than 6 months prior to the research visit then you will also require:** • 1 small (4.9ml) serum tube (renal function)
e.	**StartRight Visit 1 Participant Home Urine Pack containing:**
	• 1 urine collection container (red top) • 1 Exeter biochemistry form (green) with plastic bag attached • 1 participant home urine collection instruction sheet • 1 postage-paid padded envelope for sample transfer to Exeter
f.	**StartRight Visit 1 Sample Barcode Label Set**
g.	**Centrifuge** • Please refer to Appendix 4 on page 15 for required centrifuge settings

1.	**Initial contact with participant following identification or referral by clinician**
	• Using the StartRight Participant Referral & Contact form, confirm eligibility to one of the following groups: a) diagnosed with diabetes within the last 12 months and aged between 18 and 50 years at the time of diagnosis b) diagnosed with diabetes within the last 12 months, aged > 50 years at diagnosis and insulin treated at the time of recruitment. c) diagnosed with diabetes within the last 12 months, aged >50 years at diagnosis and treated without insulin at the time of recruitment. • Explain procedures for study participation and agree date for Visit 1 **Important Note: To ensure that the posted samples do not arrive in Exeter at the weekend, it is preferable to arrange the visit on a Monday, Tuesday or Wednesday. If a Thursday morning appointment is necessary, please ensure that the bloods are in the post before by 1pm on the day of collection.** • Complete the participant referral and contact form in full and sign and date. • Send appointment confirmation, with a copy of the participant information sheet (PIS), to the participant by email or letter, ensuring that you re-confirm instructions to eat a meal containing carbohydrates within 1 to 5 hours before their appointment time. • Assign your next site specific study ID to the participant (as listed in your recruitment log). • Log the participant onto the CRF Tracker system (see Items 1 to 4 in Appendix 2 on page 9 of this SOP). • A study barcode set may be assigned to the participant at this stage. Study documents may be labelled with the appropriate barcode labels in advance of the patient visit but **it is best to label research tubes & forms with the barcode labels at the time of the appointment.**
2.	**Informed Consent**
	• Prior to any data/sample collection ensure the participant is fully informed about the project, is given an opportunity to ask any questions, and is happy to proceed. • Ensure written informed consent is obtained on the current version of the study consent form. • The patient needs to add their initials in the boxes to confirm their consent as well as dating and signing the form. • The person taking consent must then counter-sign the form and provide the participant with a copy of the signed consent form. (The original signed consent form must be filed in your local study site file). • Label consent form & participant referral form with the appropriate barcode labels and add participant study ID where indicated
3.	**Prior To Data & Sample Collection**
	• **CONFIRM THAT THE PARTICIPANT HAS EATEN A MEAL CONTAINING CARBOHYDRATE WITHIN THE LAST 1 TO 5 HOURS** • **If the participant is insulin treated** please ask them to check a capillary blood glucose before you collect blood samples. • Hypoglycemia will make C-peptide results invalid. Therefore if the glucose is below 4 please ask the participant to treat hypoglycemia as they would normally (with fast acting carbohydrates), and then follow the instructions for 'if the participant has not eaten' below. • If the participant has already tested capillary glucose within 1 hour of the visit, and this is >8mmol/L, no repeat is required.

- **IF THE PARTICIPANT HAS NOT EATEN OR HAS HYPOGLYCAEMIA, THE OPTIONS ARE AS FOLLOWS:**

  a) IF THE PARTICIPANT IS HAPPY TO STAY FOR A FURTHER HOUR, offer a carbohydrate meal (e.g. toast), record the details of the meal, and time consumed, in the relevant section of the DCF and collect the blood samples after 1 hour.

  b) IF THE PARTICIPANT CANNOT WAIT FOR A FURTHER HOUR please arrange another appointment for blood collection.

4. Data Collection

- Please ensure you use the current version of the Visit 1Data Collection Form (DCF) which will be pre-filled with your 4 digit site ID (e.g. Exeter site ID = EXET).
- Label DCF with the appropriate barcode label and add participant study ID where indicated on each page.
- The DCF is designed in 'Teleform' and the data will be scanned and transferred to the study database electronically. The scanning process is extremely sensitive so please write as clearly as possible and keep within the boxes provided.
- Please answer **all** questions.
- **If your research scales do not provide body fat % please mark that field 'N/A'.**
- Further information about **Acanthosis-Nigricans** is available at: http://www.nhs.uk/conditions/acanthosis-nigricans/Pages/Introduction.aspx
- If any errors are made completing the DCF, cross through the incorrect answer with a single line and complete the correct answer. Please initial and date any amendments.
- Following the study visit, please collect the required details relating to condition at diagnosis from the patient's records (hospital and/or GP).
-

5. Blood sample collection

- Ensure participant is relaxed and comfortable, either sitting in a chair or supine on a bed, depending on their preference.
- Explain the procedure fully to the participant.
- Following local venepuncture guidelines collect the following blood samples **in the priority order listed below:**

  1. Research Plasma (7.5ml EDTA – red top)
  2. Research Serum (7.5ml Serum Gel tube – orangey brown top)
  3. Research HbA1c (2.7ml EDTA – red top)
  4. Research DNA (2.7ml EDTA – red top)
  5. Research Cell-free DNA (Roche tube – white top)
  6. Local Fluoride tube (for local glucose analysis)
  7. Local small EDTA tube (FBC analysis)
  8. Local Serum Gel tube (local renal function **if required**)
  9. Research RNA (Paxgene tube)
     Important Note: When collecting blood directly into a Paxgene tube, ensure that a butterfly is used and that the tube remains below the arm during blood collection. Shake the Paxgene tube vigorously immediately after blood collection.

	• Remove needle, ensure puncture site is covered and participant is comfortable.
6.	**Research Blood Sample Processing**
	• Please follow the detailed instructions in: **Appendix 2 (pages 9-12) – CRF Tracker logging instructions** **Appendix 3 (page 13) – Generic Guidance for Sample Processing** **Appendix 4 (page 14) – Sample Processing & Labeling Table** • **EXAMPLES OF COMPLETED RESEARCH BLOOD AND URINE FORMS ARE PROVIDED AT THE END OF THIS SOP.** • **WHEN WRITING THE PARTICIPANT NAME AND DOB ON THE TUBE LABELS, TAKE CARE NOT TO WRITE OVER THE 2D BARCODE ON THE RIGHT HAND SIDE OF THE LABEL . (Fine permanent marker pens are provided for writing on the study labels).** ***First Initial and Surname is acceptable if there is insufficient space to fit full name (e.g. J. Harrison-Potter).*** • **SAMPLES MUST BE <u>IN THE POST</u> ON THE DAY OF COLLECTION TO ENSURE THAT THEY ARRIVE AT THE CI SITE IN EXETER NO LATER THAN 48 HOURS AFTER COLLECTION.**
7.	**Local Blood Processing & Results**
	• Send blood samples for Glucose & FBC analysis in accordance with local site protocols. • If patient's latest renal function result (at least a Creatinine result) is >6 months prior to the research visit, please send serum sample to local lab for Renal Function analysis (eGFR & Creatinine)
8.	**Questionnaires**
	If participant has consented to complete the Hypoglycaemia & Quality of Life questionnaires, provide them with the questionnaires and ask them to complete them (as independently as possible). Label completed questionnaires with the appropriate labels from the participant barcode set and add participant study ID where indicated.
9.	**Participant Home Urine Test**
	Discuss the home urine collection with the participant and check that they are happy to collect the sample and post it to the lab at the CI site in Exeter **within 7 to 10 days of the study visit.** **Prepare the urine collection pack by** • Labeling the Exeter biochemistry form with the participant's details (name, NHS number & date of birth) and the '2hr home urine' biochemistry form barcode label. *An example of a completed and labeled form is provided at the end of this SOP.* • Labeling the urine collection tube with the participant's name and date of birth and the '2hr home urine' primary tube label. **Please ensure that:** **a.** The participant is familiar with the contents of the pack and collection procedure. Full instructions are in the pack, **please ensure that your local team contact number has been added at the end of the instructions.** b. The participant understands that the sample must be collected 2hrs after their MAIN MEAL.

	c. **THE PARTICIPANT IS ASKED TO WRITE THE DATE AND TIME THE SAMPLE IS COLLECTED ON BOTH THE TUBE AND THE FORM.** d. The participant understands that the sample must be posted on the day of collection (or the next morning if taken in the evening) as it must reach Exeter within 3 days of collection. e. The participant is asked to collect the urine sample **WITHIN THE NEXT 7 TO 10 DAYS AND POSTED BETWEEN SUNDAY AND WEDNESDAY** TO ENSURE THAT IT DOES NOT ARRIVE AT THE EXETER LABORATORY AT THE WEEKEND.
10	**Participant Follow Up Arrangements**
	Explain to the participant that they will be contacted in 10 to 12 months time to collect information about their diabetes & treatment and to ask them to collect and post another home urine sample. Ensure the participant still has their copy of the PIS and ask them to notify you if their contact details change. Thank the participant for their time and ensure they know how to contact the study team if they need to.
11	**Transferring Data To Exeter For Processing**
	Ensure that all fields on the study paperwork have been completed and that all biochemistry results have been received and recorded. Ensure that all study paperwork (participant contact form, consent form, DCF and questionnaires) have both barcode label and participant study ID. Send scanned copies (in PDF format) of patient contact form, data collection form, consent form, questionnaires and biochemistry results (in electronic format) to the StartRight central coordinating team by secure NHS email to **rde-tr.DiabetesResearch@nhs.net** **PLEASE SEND ALL DOCUMENTS TO EXETER WITHIN 10 WORKING DAYS OF THE STUDY VISIT.**

Appendix 1

Coding For Ethnic Group

Please use the standard coding for ethnic groups as shown below:

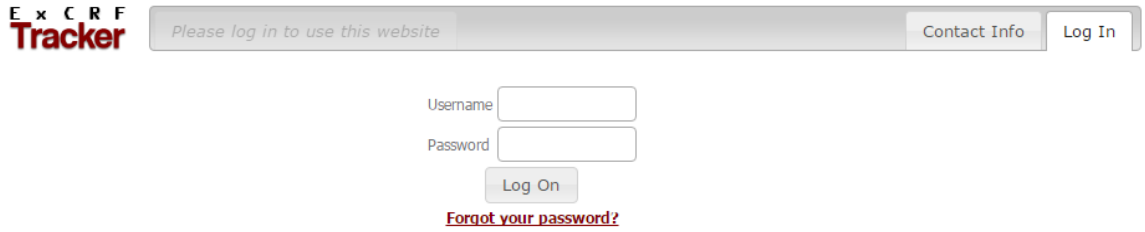
White:	**A** White British	**B** White Irish	**C** Other White	
Mixed:	**D** White & Black Caribbean	**E** White & Black African	**F** White & Asian	**G** Other Mixed
Asian or Asian British:	**H** Indian	**J** Pakistani	**K** Bangladeshi	**L** Other Asian
Black or Black British:	**M** Black Caribbean	**N** Black African	**P** Other Black	
Other Ethnic Groups:	**R** Chinese	**S** Any other group		

Appendix 2: CRF Tracker Instructions

Please use the instructions below to register StartRight participants & study samples into CRF Tracker.

Opening CRF Tracker

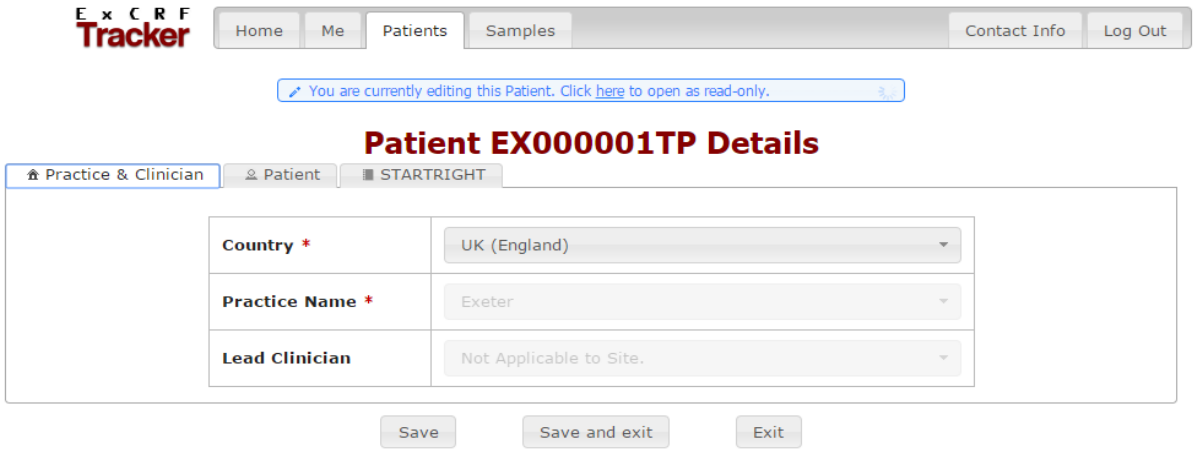
- To open CRF Tracker enter the following URL into an internet browser https://crf.exeter.ac.uk/tracker
- Log in with your personal username and password emailed to you by the CI site in Exeter.



Creating a new patient

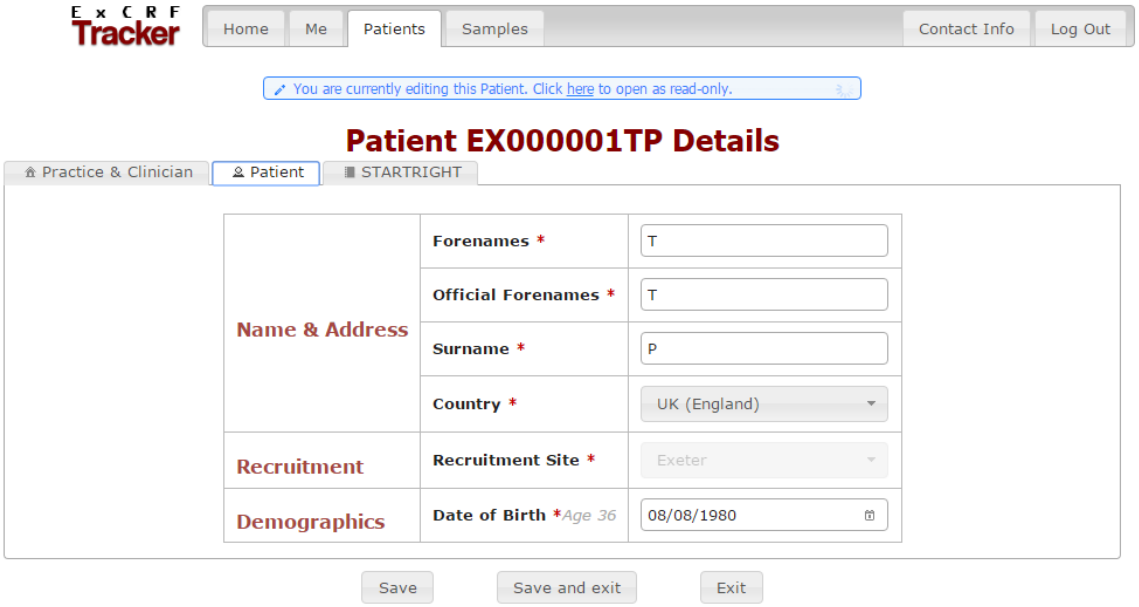
1. Once logged in to CRF Tracker select the "Patients" tab, then the "Add a new patient" button.

2. Select the "Practice & Clinician" subtab and complete the required fields as shown in the example below.
   - **Country** = select from the drop down list.
   - **Practice Name** = this field will be auto filled with your site name.
   - **Lead Clinician** = not applicable.

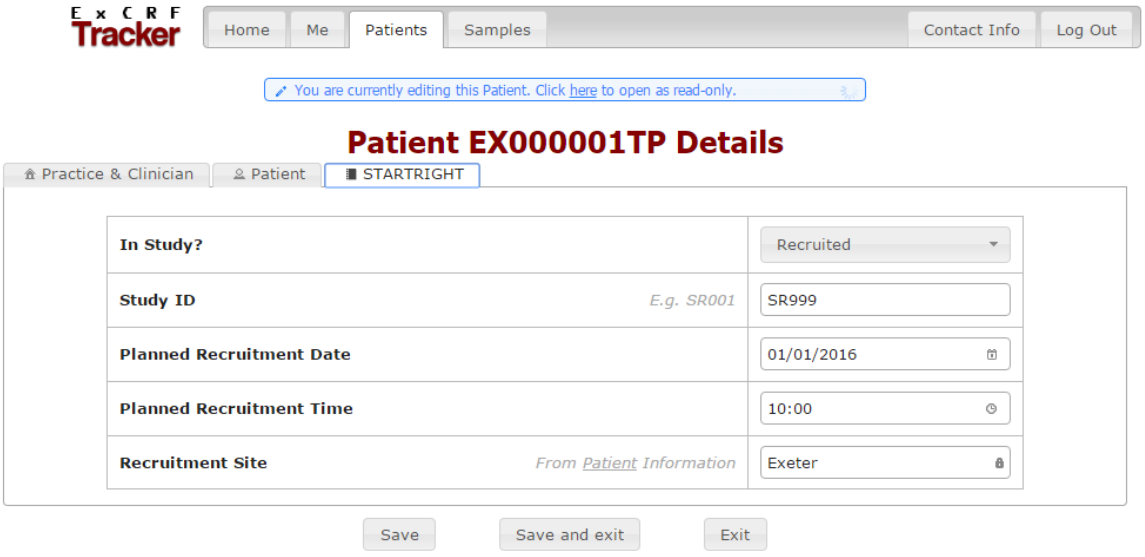


3. Select the "Patient" subtab and complete fields as shown in the example below.
   - **Forenames** = initial of first name.
   - **Official Forenames** = initial of first name.
   - **Surname** = initial of Surname
   - **Country** = select from the drop down list.
   - **Recruitment Site** = this field will be auto filled with your site name.

- **Date of Birth** = enter the participant's date of birth in the format dd/mm/yyyy.

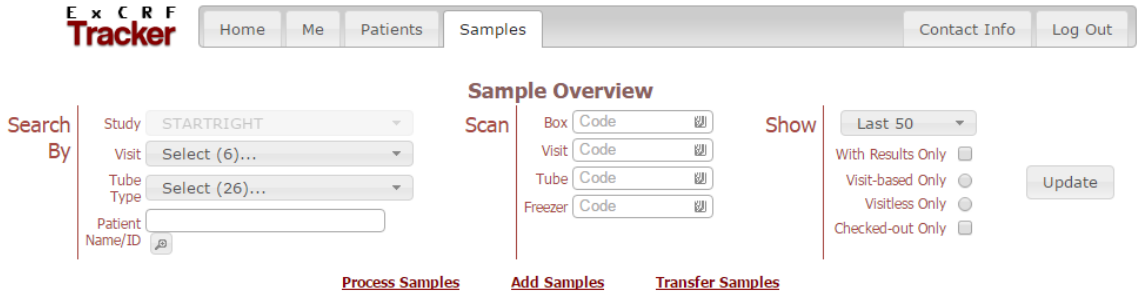


4. Select the "STARTRIGHT" subtab and complete as shown in the example below. Click the "Save and exit" button once all of the fields have been completed.
   - **In Study?** = select "On Hold" from the drop down list if registering the patient before the study visit **OR** "Recruited" if you have already seen the patient and you are logging the patient at the same time as the samples.
   - **Study ID** = enter the 5 digit Study ID, please note that each patient will be assigned a unique study ID which can be found on the recruitment log.
   - **Planned Recruitment Date** = date of Visit 1.
   - **Planned Recruitment Time** = time of Visit 1.
   - **Recruitment Site** = this field will auto fill with your site name.



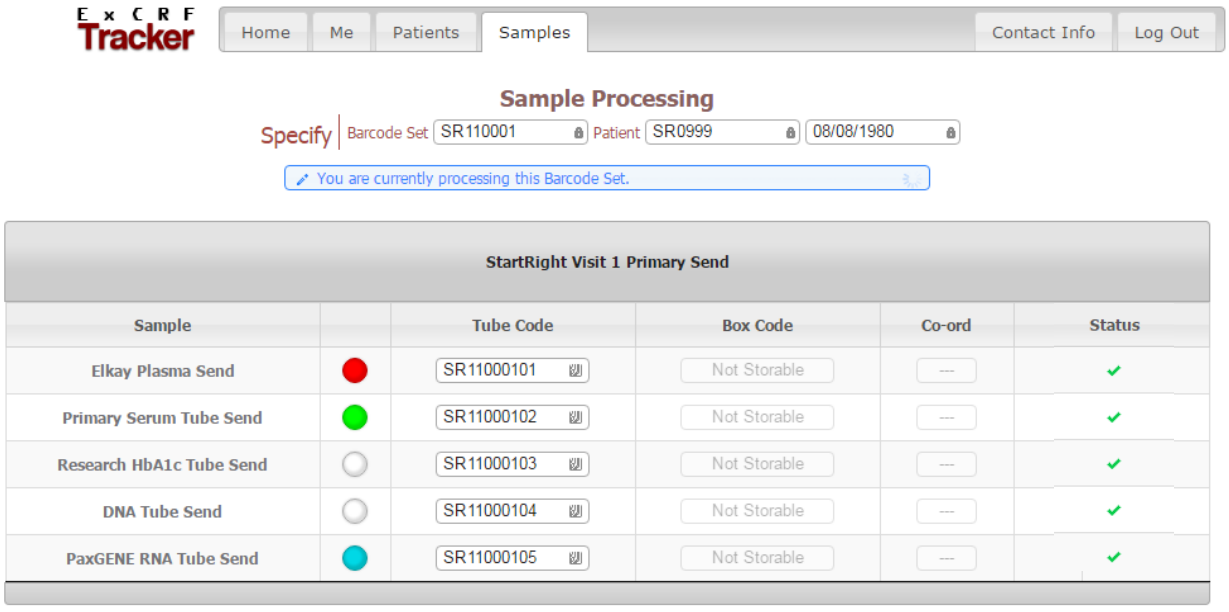
Sample registration

5. Samples can be logged onto the CRF tracking system once a participant has been created. To process the samples select the “Samples” tab, then the “Process Samples” button.

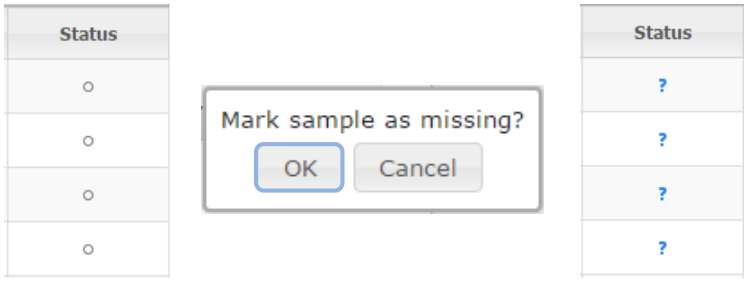


6. Scan or manually enter the 8 digit Barcode Set which can be found on the eye readable barcode labels on all of the participant’s documents including the consent form, DCF and questionnaires (if you are manually entering the number, do not include any hyphens), press the ‘return’ or ‘enter’ key on your keyboard, then type in the Patient ID, followed by ‘return’ or ‘enter’ and participant’s date of birth, in the format dd/mm/yyyy.

7. Scan or manually enter the barcodes from the Plasma Elkay tube, the 7.5ml Primary Serum tube, the 2.7mL EDTA Research HbA1c tube, the Roche DNA tube and the Paxgene RNA tube into the appropriate fields in the “Visit 1 Primary Send” section (if you are manually entering the number, do not include any hyphens). Once each sample has been registered, press the ‘return’ or ‘enter’ key on your keyboard and a tick will appear in the “Status” column as shown below.



8. If any of the above samples have not been collected then please mark the sample as missing on CRF Tracker:
   a. Click on the circle in the “Status” column that corresponds with the missing sample.
   b. Select “OK” when asked if you would like to “Mark sample as missing?”
   c. A question mark will appear in the “Status” column as shown below.



Appendix 3

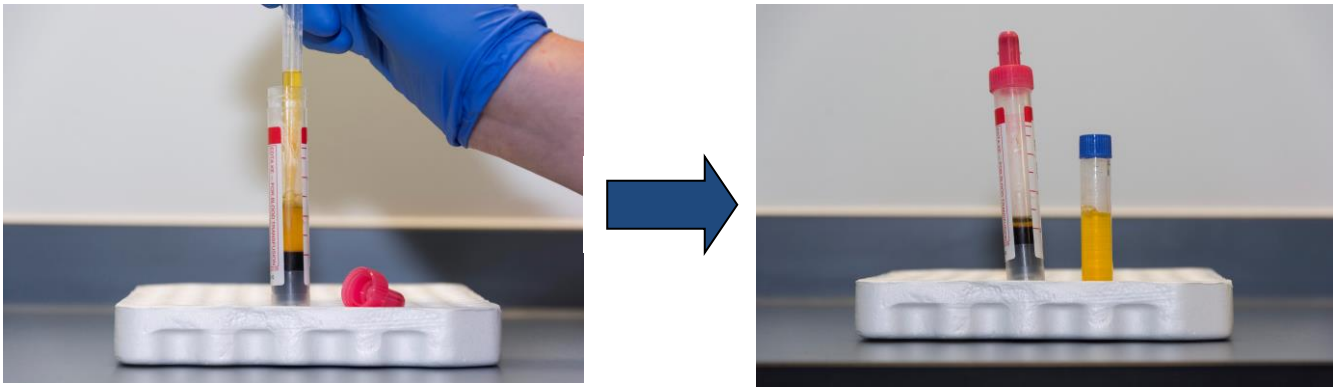
IMPORTANT GENERIC GUIDANCE FOR SAMPLE PROCESSING

- **Centrifuge conditions**: Please ensure that you have your centrifuge set at the correct rpm to obtain the 2500g required for this protocol. This will differ between individual rotors. While many centrifuges can be set to g directly, for some you will need to calculate the rpm required to give 2500. If you are not familiar with this please see the manufacturer's instructions for your centrifuge and/or discuss with a laboratory technician. If your centrifuge has a temperature setting please set to 20^{o}c.

- **Time from patient to centrifuge**: The gold standard is to have samples centrifuged within 30 minutes of being taken from the patient. In situations where community visits are necessary, samples must be processed in the shortest time possible and within 6 hours of being taken from the patient.
  SAMPLES MUST BE DISPATCHED ON THE DAY OF COLLECTION TO ENSURE THAT THEY ARRIVE AT THE CI SITE IN EXETER PREFERABLY THE NEXT DAY BUT NO LATER THAN 48 HOURS AFTER COLLECTION.

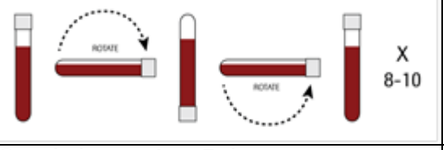
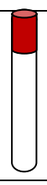
- **Serum Samples:** Please ensure that serum tubes are well mixed and allowed to clot for 10-15 minutes in an upright position prior to centrifugation.

- **Plasma Separation**: When taking the plasma supernatant, be very careful that you don't accidently pipette-up the white cells (buffy coat) on top of the red bottom layer.



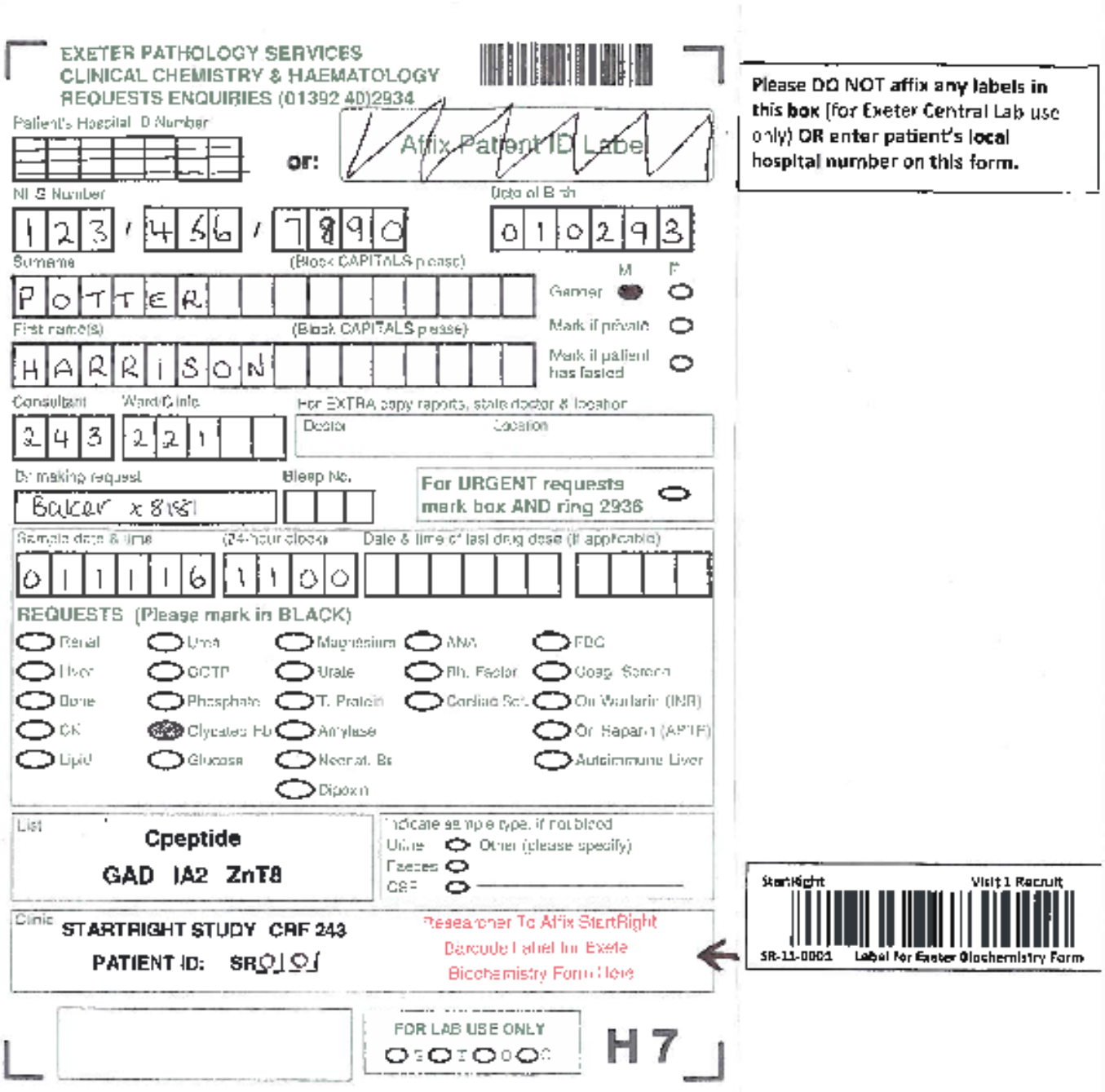
APPENDIX 4. STARTRIGHT STUDY RESEARCH BLOODS PROCESSING TABLE

PLEASE FOLLOW TUBE PROCESS FROM LEFT → RIGHT

Tube Name	Primary Tube Description	Label Tube with:	Processing	Scan or enter barcode to CRF Tracker	Form To Use:	Label Form With:	Package	Dispatch on day of collection
7.5ml EDTA Primary Tube for Plasma Extraction		Label for Research Primary Plasma Tube	Gently invert 4 or 5 times to ensure blood mixes with tube additives. Stand for 10 mins. Centrifuge at 2500g for 10 minutes. **(See centrifuge conditions in Appendix 3)** Use the pipette to transfer the plasma from the primary tube into the Elkay tube provided & seal securely with the blue lid provided. (Dispose of the EDTA tube & remaining contents in accordance with local protocol)					
Elkay Plasma Tube		Label for Elkay Plasma Tube AND Patient Name AND Patient Date of Birth		YES Elkay Plasma Send	Exeter Biochemistry Request Form	Patient Surname, First Name, NHS Number & Date of Birth. AND Sample Date & Time. AND StartRIght Study ID AND Label for Exeter Biochemistry Form	Place the 4 tubes in the absorbent pocket provided and then into the plastic sample bag with the completed and labelled Exeter Biochemistry Form. Label the 'Urgent Research Samples for Chem MTO' form (the A4 sheet in red type) with the Label For Exeter Lab Instruction Form.	Place the 2 bags of Exeter samples in the postage paid absorbent envelope provided with the labelled Exeter Biochem Lab Instruction form. **THE SAMPLES MUST BE SENT TO EXETER BY FIRST CLASS POST ON THE DAY OF COLLECTION.** **PLEASE ENSURE THAT THE SAMPLES ARE 'IN TRANSIT' ON THE DAY OF COLLECTION AND DO NOT REMAIN IN A POST BOX OR HOSPITAL POST ROOM OVERNIGHT.**
7.5ml Serum Tube		Label for Research Primary Serum Tube AND Patient Name AND Patient Date of Birth	Gently invert 4 or 5 times. Stand for 10 minutes Centrifuge at 2500g for 10 minutes **(See centrifuge conditions in Appendix 3)**	YES Primary Serum Tube Send				
Paxgene RNA Tube		Label for Research Paxgene RNA Label	Shake vigorously for a few seconds.	YES Paxgene RNA Tube Send				
2.7ml EDTA for Research HbA1c		Label for Research HbA1c Tube AND Patient Name AND Date of Birth	Gently invert 4 or 5 times.	YES EDTA HbA1c Send				
Roche CfD DNA Tube		Label for Research DNA Tube	Gently invert 8 to10 times to ensure adequate mixing of the chemical additives with the blood sample. 	YES DNA Tube Send	Exeter Molecular Genetics Form	Label for Exeter Genetics From (DNA)	Place both tubes in absorbent pockets and then into the plastic sample bag with the labelled Exeter Genetics Form	
2.7ml EDTA DNA Tube		SPARE Barcode Set Label	Gently invert 4 or 5 times.	NO				

STARTRIGHT STUDY – VISIT 1

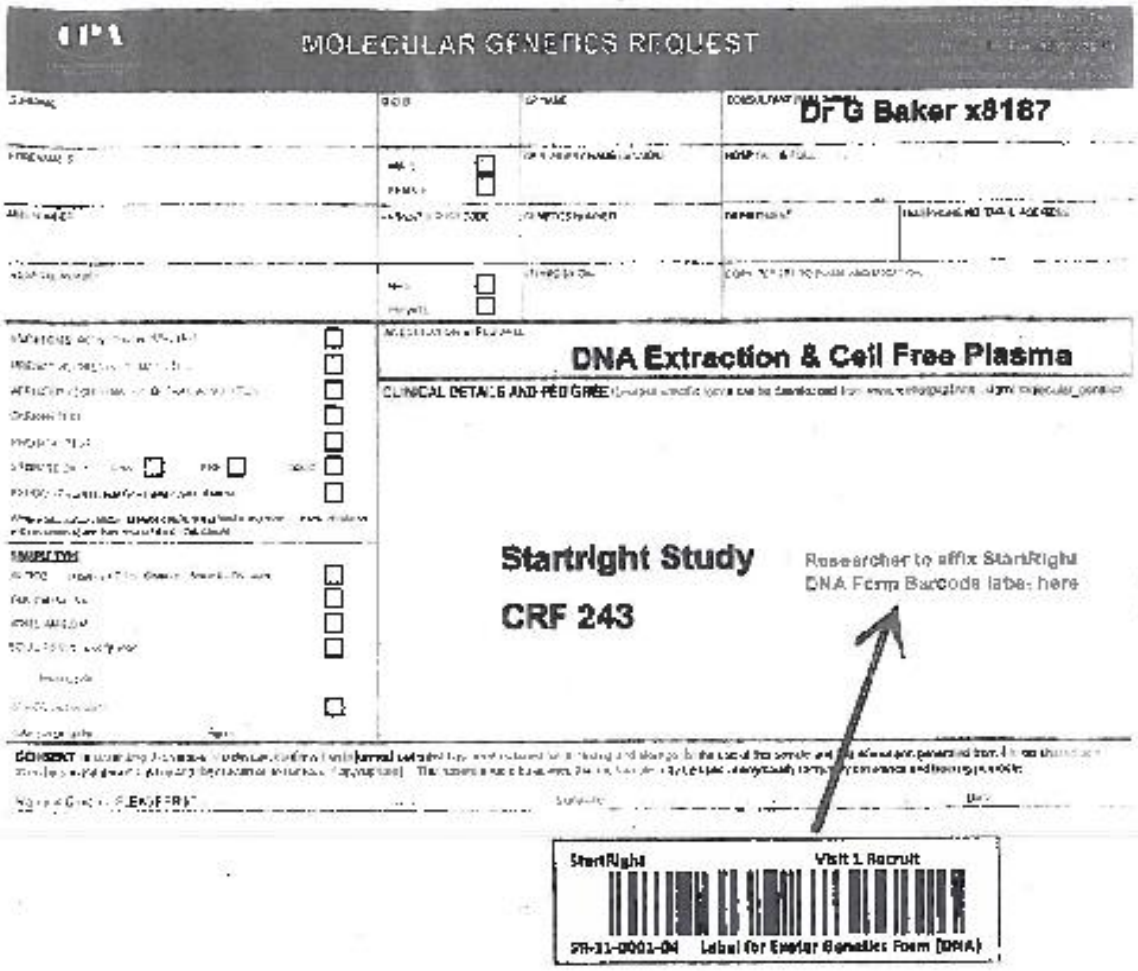
EXAMPLE OF COMPLETED FORM FOR RESEARCH BLOOD SAMPLES



Please DO NOT affix any labels in this box (for Exeter Central Lab use only) OR enter patient's local hospital number on this form.

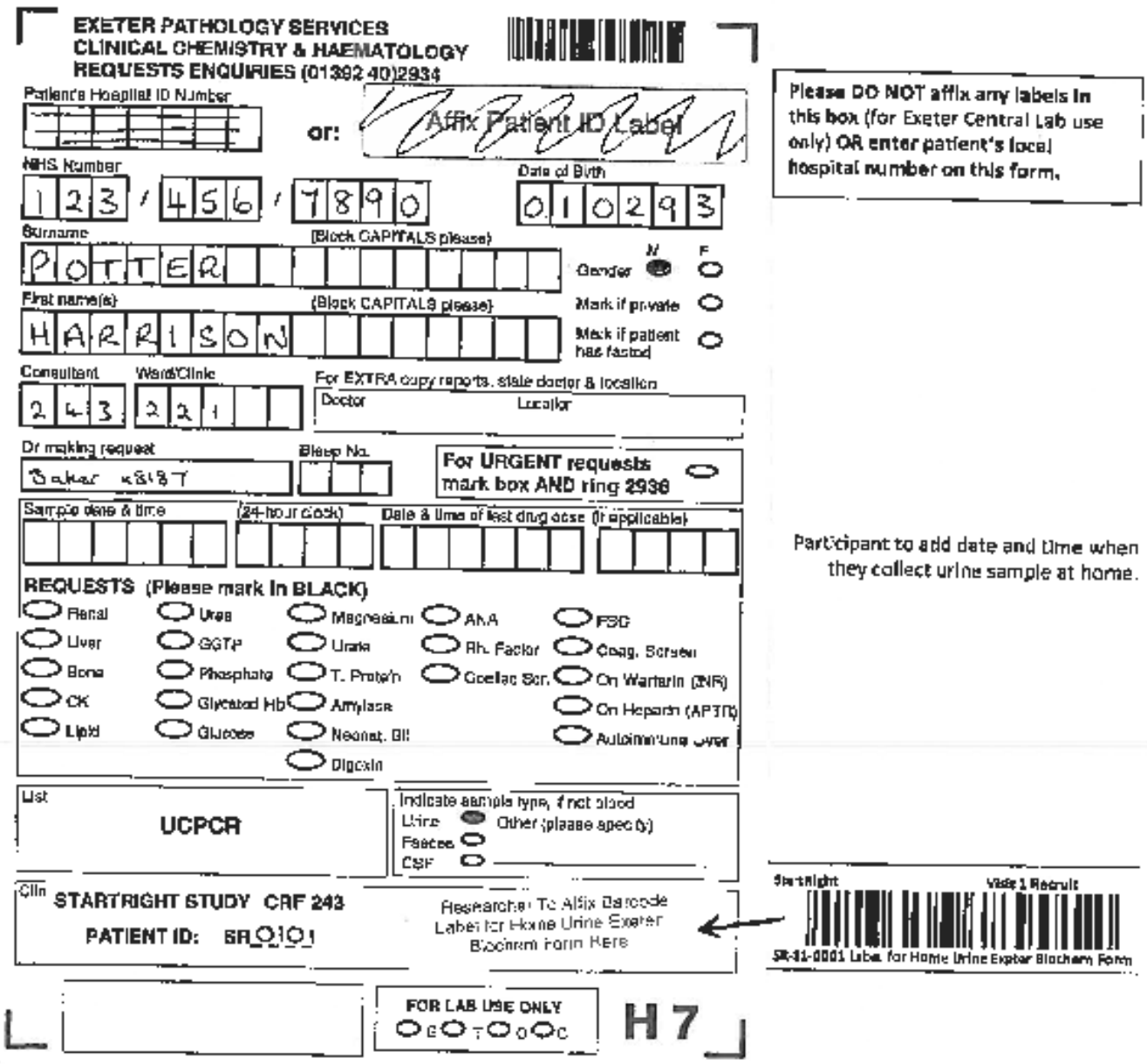
STARTRIGHT STUDY – VISIT 1

EXAMPLE OF COMPLETED FORM FOR EXETER GENETICS FORM (DNA)



STARTRIGHT STUDY – VISIT 1

EXAMPLE OF COMPLETED FORM FOR RESEARCH HOME URINE SAMPLE



EXETER PATHOLOGY SERVICES
CLINICAL CHEMISTRY & HAEMATOLOGY
REQUESTS ENQUIRIES (01392 40)2934

Patient's Hospital ID Number

or: Affix Patient ID Label

Please DO NOT affix any labels in this box (for Exeter Central Lab use only) OR enter patient's local hospital number on this form.

NHS Number: 123 / 456 / 7890

Date of Birth: 01 02 93

Surname (Block CAPITALS please): POTTER

Gender: M ● F ○

First name(s) (Block CAPITALS please): HARRISON

Mark if private ○

Mark if patient has fasted ○

Consultant: 243

Ward/Clinic: 221

For EXTRA copy reports, state doctor & location

Doctor Location

Dr making request: Baker KBT

Bleep No.

For URGENT requests mark box AND ring 2936 ○

Sample date & time (24-hour clock)

Date & time of last drug dose (if applicable)

Participant to add date and time when they collect urine sample at home.

REQUESTS (Please mark in BLACK)

○ Renal	○ Urea	○ Magnesium	○ ANA	○ FSC
○ Liver	○ GGTP	○ Urate	○ Rh. Factor	○ Coag. Screen
○ Bone	○ Phosphate	○ T. Prot/n	○ Coeliac Scr.	○ On Warfarin (INR)
○ CK	○ Glycated Hb	○ Amylase		○ On Heparin (APTT)
○ Lipid	○ Glucose	○ Neonat. Bil		○ Autoimmune Over
		○ Digoxin		

List: UCPCR

Indicate sample type, if not blood: Urine ● Other (please specify) Faeces ○ CSF ○

Clin STARTRIGHT STUDY CRF 243

PATIENT ID: SR_0101

Researcher To Affix Barcode Label for Home Urine Exeter Biochem Form Here

StartRight Visit 1 Recruit

SR-01-0001 Labs for Home Urine Exeter Biochem Form

FOR LAB USE ONLY ○ G ○ T ○ O ○ C

H 7