Work Instruction Title: CRF Completion, source data and clinical record entry

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Review History

Version No.	Reviewer	Amendments
	20/06/2012	Under review
WI 16 V.2	02/07/2012	5
V3	BD	Author title formerly PCRN-EoE Research Nurse. Minor changes throughout
V4	CP/RO/ HM	Major addition to include entry in Practice Patient Electronic Records about Research Participation

1. Introduction, Background and Purpose

ICH Good Clinical Practice Guidelines define a **Case Report Form** (CRF) as:

"A printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject" (Section 1.11, ICH GCP, 2006).

This may include information about:
- The participant
- Study interventions
- Administration of the Investigational Product (if applicable)
- Study procedures
- Outcome of assessment/tests
- Adverse events

Throughout this Work Instruction (WI) the term CRF will be used to include both paper and electronic data collection tools.

CRFs are the official documentation of the trial for both sponsors and regulatory authorities, and together with the source documents (Refer to: WI 10 Study files and filing) will be closely examined during audits and inspections. The data collected on the CRF is used directly as the basis for the trial report and any publications, as well as contributing to the Summary of Product Characteristics, for regulatory approval of a new drug.

In addition to entering data on the study team CRF, it will also be necessary to document in the participant's clinical patient record as detailed in Section 6 below. Prior to entering data onto the clinical records it is advised to confirm with the Practice how it would prefer the data to be entered. Free-texting the information will not affect the Practice's Quality Outcomes Framework (QOF) data collection whereas entering data into templates the Practice has established will do so. For the purposes of MHRA inspection it is recommended that reference to data entry into patient electronic records is fully referenced and documented to ensure a complete audit trail of source data. Practices should also be aware that MHRA inspectors may require access to paper "Lloyd George" notes to confirm eligibility of participants or extraction from source data if the participant has changed Practices during the duration of a study.

If any clinical concerns about the participant arise the patient should be advised to see their usual GP and the research practitioner should document in the clinical records, task the patient's usual GP and also email via nhs.net account (as an additional measure) about the nature of the concern and the recommendation made to their patient.

The purpose of this Work Instruction is to describe the procedure for completing, signing and correcting CRFs.

2. Abbreviations

See Reference Document: CRN Glossary of Terms and Abbreviations.

3. Scope

All staff making entries into CRFs and seeing patients for trial related visits should follow the procedure set out in this WI.

4. Responsibilities

Training in study specific CRF completion should be provided by the sponsor, or delegate, as agreed. Staff must also be trained and competent in accessing the required source data and recording into the clinical record.

Prior to study initiation/start-up, it is the responsibility of a designated member of staff to ensure there is an adequate access to CRFs at the research site to conduct the study. The delegation of responsibility of CRF completion by the Investigator should be documented on the Study Delegation Log/Site Responsibility Log and only these individuals may enter data in a CRF.

5. Procedures

5.1 CRF completion

The participant's identity should remain confidential at all times. The participant should only be identified by a study number and/or initials only on the CRF. A record must be kept by the Investigator of participants in the study, consisting of the patient's full name and study participant number. This is the Subject Identification Log, or Enrolment Log, to be retained in the Site File (Refer to WI 10 Study Files and Filing)

- CRFs should be completed according to the specifications of each study. Laboratory values and other measurements should be entered as specified by the protocol or the CRF.
- CRFs should be completed during the visit, or in exceptional circumstances as soon as possible after the associated visit/ patient assessment to ensure the information is accurate and up to date. The study specific protocol will dictate if CRF data must be captured during consultation.

5.1.1 Guidelines for completion

- Always use a black ballpoint pen.
- If the CRFs are printed on carbonless duplication paper, always make sure that a suitable separator is inserted under the page being completed.
- If electronic CRFs are being used for data capture, passwords will be provided by the Sponsor to each individual who has been delegated with CRF completion by the PI.
- Passwords are unique to each individual and clinicians must use their own password to enter or correct data.
- Many studies will provide a demo electronic data collection site for training purposes. Care must be taken to access the demo site only during training.
- Ensure data entry is as complete as possible with no omissions. If data are unavailable write, for example, 'unknown', missing', 'test not done', etc as

defined by CRF Completion Guidelines (if applicable). Avoid using the ambiguous phrase, 'not available'.

- Ensure all entries are accurate, legible and verifiable with the source data in the medical record. The intentional entry of invalid data is fraud.
- Any discrepancies with source data should be explained and the significance noted in the CRF and/or participant's clinical record.
- Never over-write an entry.
- Data added to a CRF at a later date after PI sign off, should be initialled and dated, with the comment 'added retrospectively'

5.1.2 Corrections to CRF entries

- Cross out the incorrect entry with a single line so that the original entry is still legible.
- Never use correction fluid or obliterate entries made on the CRF – if a correction is made, the original entry and subsequent correction must always be fully legible.
- Enter the correct data
- Initial and date the correction, inserting a reason for the correction. (e.g. error in entry).

5.1.3 Data queries

- Data queries arise when the study monitor raises a query about an entry in the CRF.
- The procedure to be followed for the resolution of data queries should be agreed with the study Sponsor and these should be completed by study site staff in a timely fashion.

5.1.4 Sign-off of CRFs

- The CRF must be signed where indicated, by the Principal Investigator (PI) or designee (as appropriate) to assert that s/he believes they are complete and correct according to set time points dictated by the sponsor. Any further changes will require completion of a Data Clarification Form (DCF).
- CRFs should be kept in a secure location during the course of the study. CRFs should then be archived when the study has finished. Refer to: WI 18 Archiving and destroying documents.

5.2 Entry into Patient's Clinical Records held by the Practice

The individual involved in research is referred to as the "participant" for the purposes of the research study and the "patient" for their usual NHS standard care.
All relevant data collected on case report forms should be entered into the patient's clinical record unless specifically stated otherwise in the study protocol. The use of the research templates enables this to happen. Patient responses to study questionnaires do not have to be copied in the the clinical record but a note that each questionnaire has been completed and the way it is transferred to the study team should be noted. A check should be made to ensure that the data in the CRF and clinical record is accurate to prevent data corrections later.

5.2.1 Read Coding Patient Invitation, Participation and Study Closure

CRN nurses will be trained to input research data into the clinical record. The templates found in the appendix of this document will be completed as part of the clinical record clinical trial process. The templates can be accessed once the template is shared with the practice and can be found by searching for the template on the search facility (bottom left hand corner) of the clinical system. The templates help to collect basic data of the trial participant and also helps the practice to easily search for trial activity by patient. The CPMS number is entered onto the template and the study name entered by free text - including the accronym. If the CPMS is not available the IRAS number should be used with pre determined pre fix number. The CPMS and IRAS numbers can be identified on the study RISP sheet for searching purposes.

5.2.2 Documenting Informed Consent

- If pre-consent access to patient records for the purpose of NHS research has been permitted then the nature and reason for this access should be fully documented by the person accessing the record so as to be transparent and justifiable to the patient.
- Informed consent should be received and reconfirmed at every study intervention. This activity should be documented as follows:
    - Date;
    - Study ID;
    - Study team contact details;
    - How consent has been obtained;
    - Medication implications for the patient if the study involves a medicinal product.
    - Duration of study;
    - Period of Adverse Event Reporting;
    - Principal Investigator Contact.

  The above data entry will ensure that whoever accesses the record has easy access to the detail required to ensure participant safety.

5.2.3 Documenting clinical decisions and concerns

- If there are any concerns about continuing eligibility of the patient these should be queried with the PI and documented in the site file and patient record as appropriate.
- If any clinical concerns about the participant arise the patient should be advised to see their usual GP and the research practitioner should document in the clinical records, task the patient's usual GP and also email via nhs.net account (as an additional measure) about the nature of the concern and the recommendation made to their patient.
- Entering into further discussion about aspects of standard care is beyond the remit of the research practitioner.

5.3 Use of Alert on patient record

Alerts can be added to clinical systems to flag to other clinicians and the Out Of Hours service that a patient is on a clinical trial. Ideally the alerts should be linked to the study patient information sheet to help the clinician understand more about the study and who to contact if they have concerns. Pop-Ups can be used to alert clinicans that a patient may be eligible to be invited into a trial.

5.4 QOF data

Some data collected for clinical trials which has been read coded in the clinical record will automatically be extracted from the clinical system by primary care commissioners to facilitate payments to the practice. Therefore before collecting data for a study whch may be read coded, it is important to check with the practice how this data needs to be collected.

6.Related SOPs, Work Instructions and Documents

6.1 SOPs

SOP 01 Informed consent
SOP 03 Study set up
SOP 04 Study conduct
SOP 05 Safety reporting

6.2 Work Instructions

WI 08 Initiation visit
WI 10 Study files and filing
WI 12 Data protection
WI 16 Audit and inspection
WI 17 Monitoring visit
WI 18 Archiving and destroying documents
WI 19 Study Close-down
WI 20 Adverse Event Reporting
WI 21 Serious Adverse Event Reporting

6.3 Reference Documents

Declaration of Helsinki
ICH Good Clinical Practice (GCP)
EU Directive
Research Governance
CRN Glossary of terms and abbreviations
Research Ethics Committees and IRAS
Incident reporting

7. Appendices

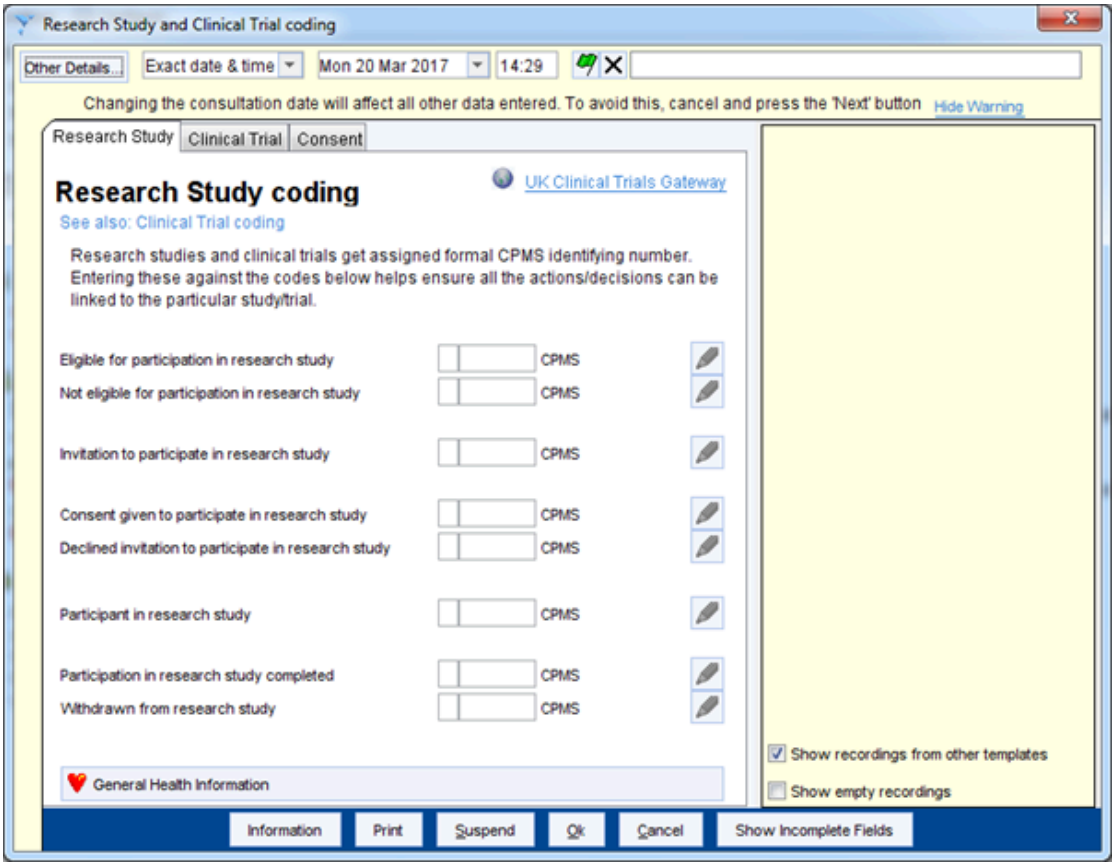
Appendix 1: Research Administration Codes

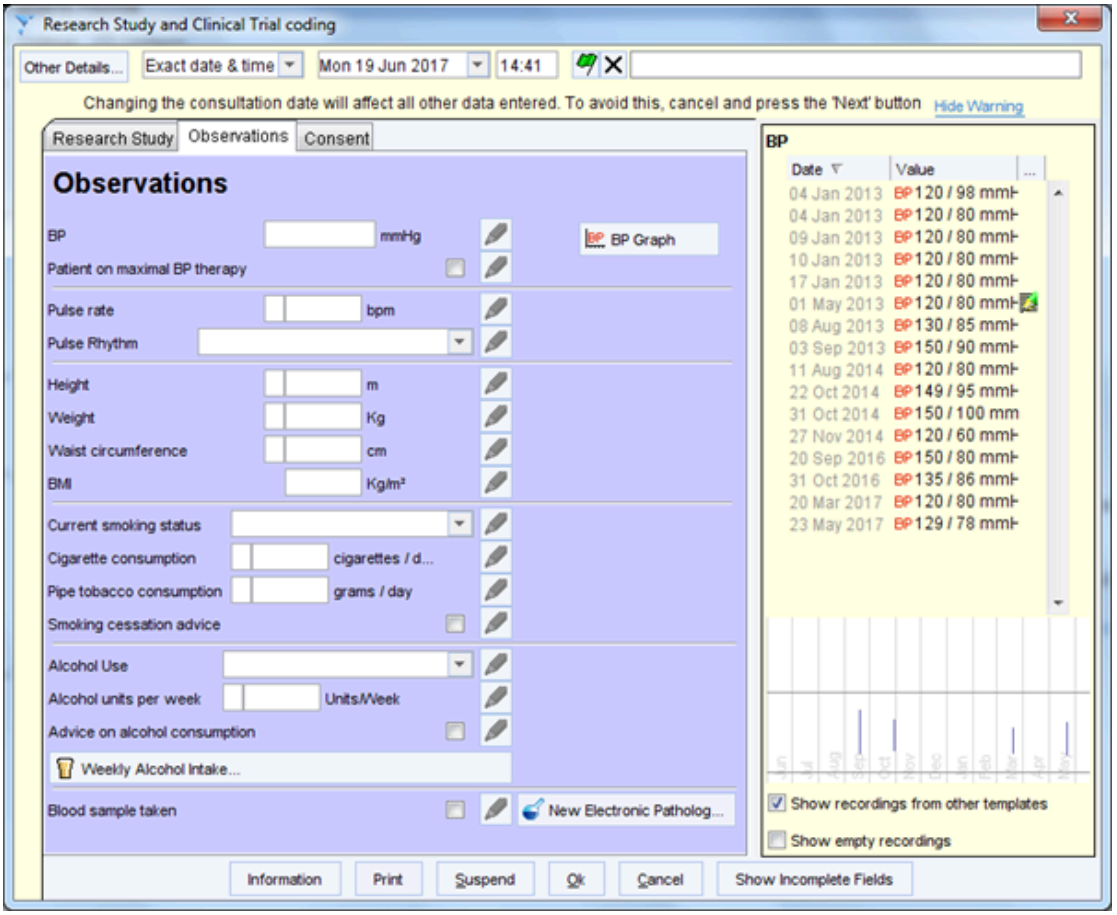
Appendix 2: Template example

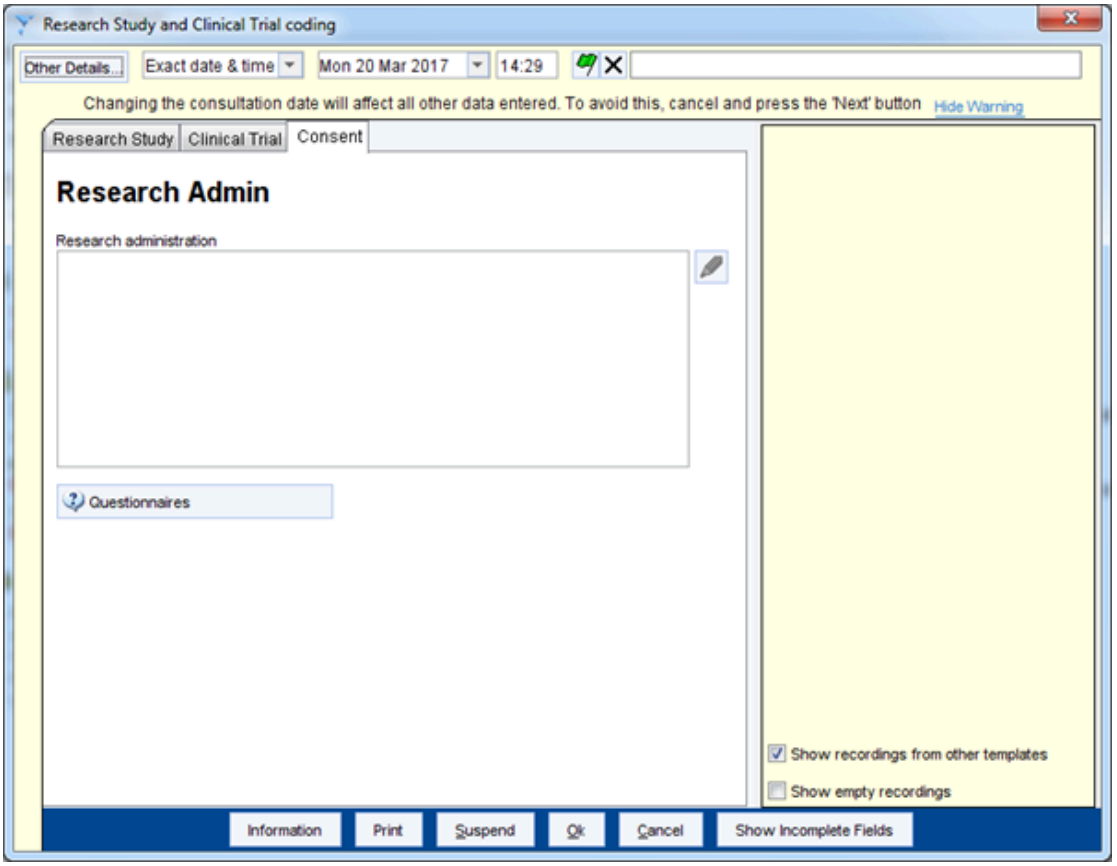
RESEARCH ADMINISTRATION CODES

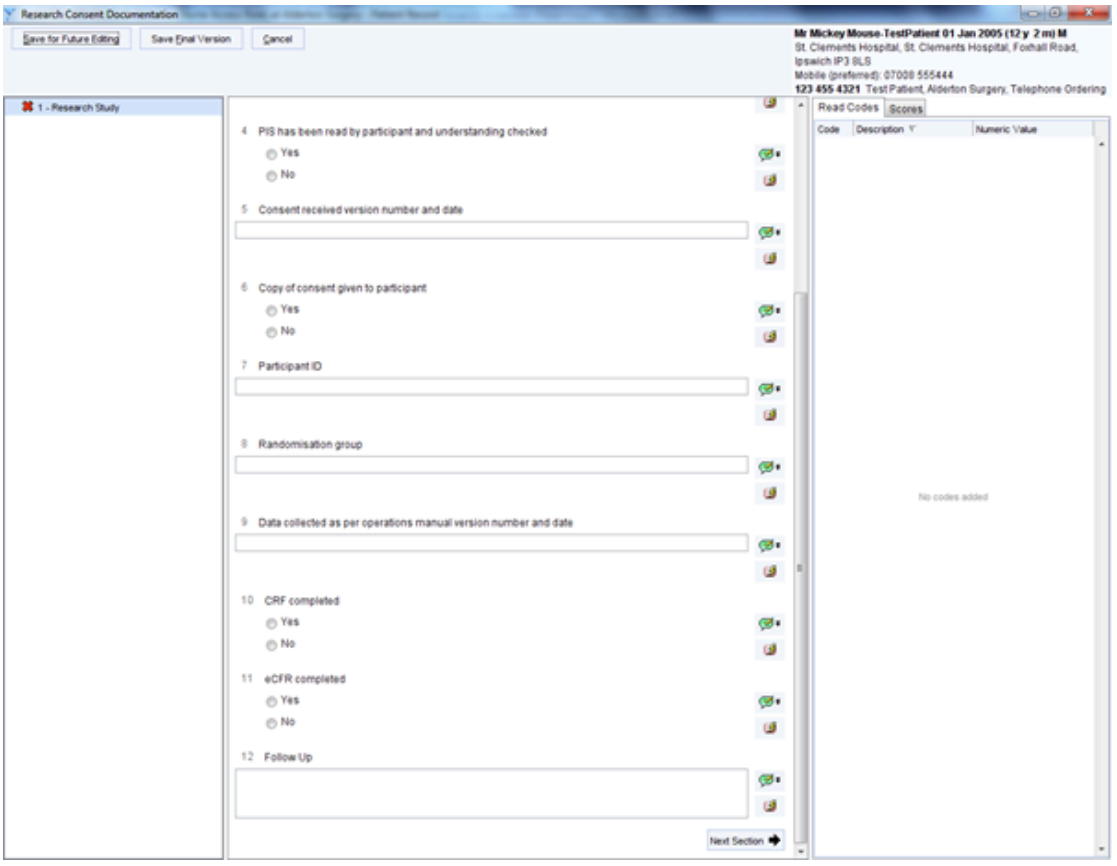
EMIS/ SYSMONE CODE	**Description**	**SYSONE CODE**	***Comment***
9Q	Research Admin		*Traditionally used*
9QJ	Eligible for participation in research study		*to confirm eligibility.*
9Q9	Invitation to participate in research study		*used*
9QM	Consent given to review medical record in research study		*used for pre-consent access permission recording*
9QB	Declined invitation to participate in research study		*Useful to remove patients from follow-up mailouts*
9QL	Consent given to participate in research study	XaaGy	*Necessary- restrict to participants where express consent is obtained by the coder.*
9QC	Participant in research study		*Useful for studies where consent is obtained outside of the Practice.*
9QD	Withdrawn from research study	XaaDd	*Useful*
9QF	Participation in research study complete		*Necessary for study closure.*

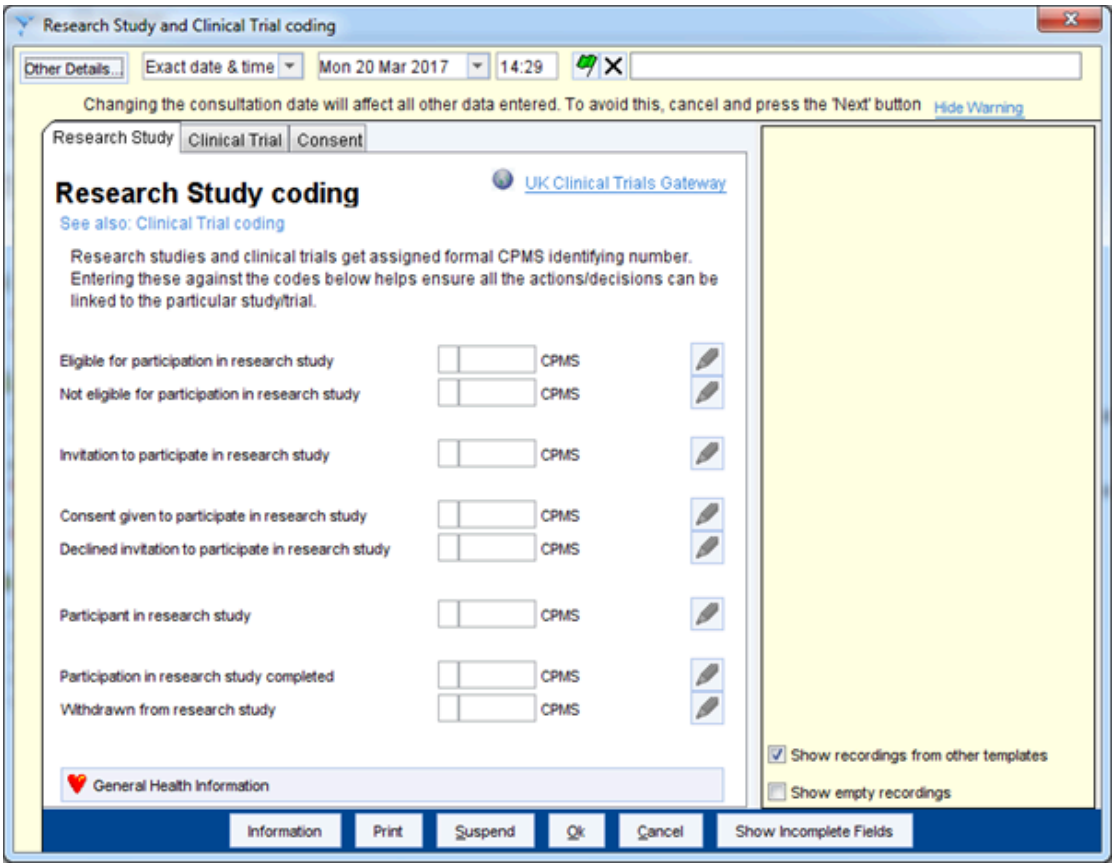
Below you will find an example of a research template. Current templates are found on the research organisational group. Always draw template from the group to ensure you are accessing the current version.

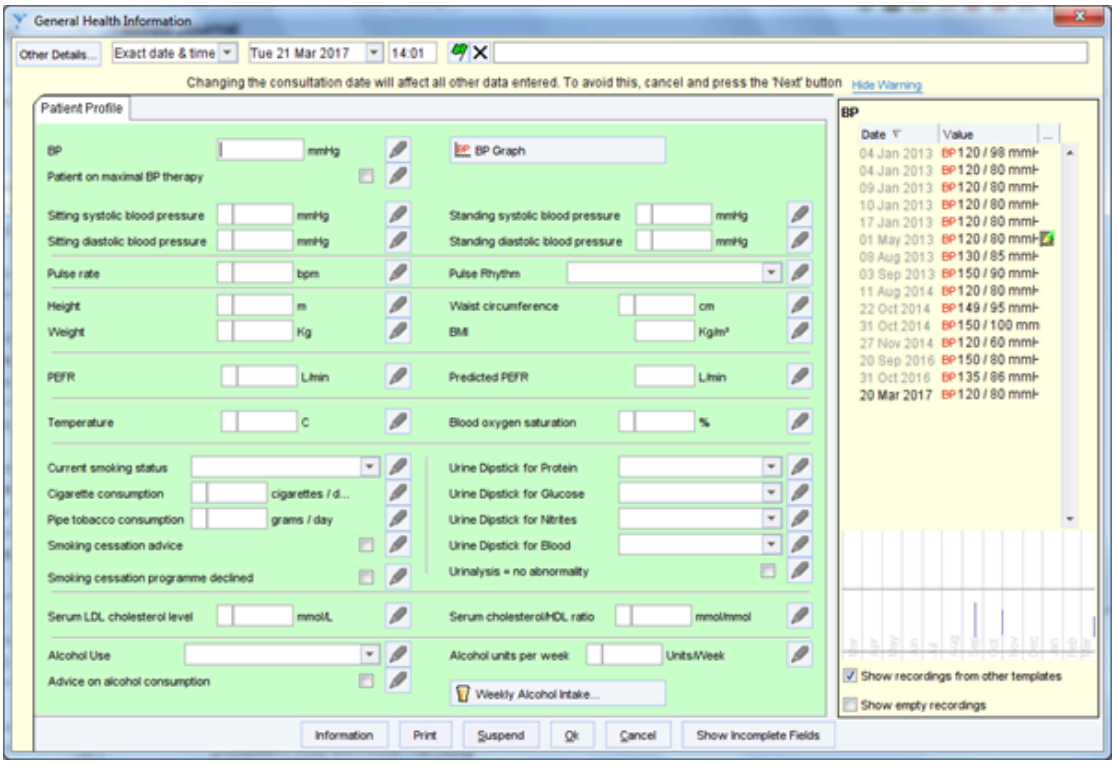

Research Study and Clinical Trial coding
Other Details...
Exact date & time
Mon 20 Mar 2017
14:29
Changing the consultation date will affect all other data entered. To avoid this, cancel and press the 'Next' button
Hide Warning
Research Study
Clinical Trial
Consent
Research Study coding
UK Clinical Trials Gateway
See also: Clinical Trial coding
Research studies and clinical trials get assigned formal CPMS identifying number. Entering these against the codes below helps ensure all the actions/decisions can be linked to the particular study/trial.
Eligible for participation in research study
Not eligible for participation in research study
Invitation to participate in research study
Consent given to participate in research study
Declined invitation to participate in research study
Participant in research study
Participation in research study completed
Withdrawn from research study
CPMS
General Health Information
Show recordings from other templates
Show empty recordings
Information
Print
Suspend
Ok
Cancel
Show Incomplete Fields


Research Study and Clinical Trial coding
Other Details...
Exact date & time
Mon 19 Jun 2017
14:41
Changing the consultation date will affect all other data entered. To avoid this, cancel and press the 'Next' button
Hide Warning
Research Study
Observations
Consent
Observations
BP
mmHg
BP Graph
Patient on maximal BP therapy
Pulse rate
bpm
Pulse Rhythm
Height
m
Weight
Kg
Waist circumference
cm
BMI
Kg/m²
Current smoking status
Cigarette consumption
cigarettes / d...
Pipe tobacco consumption
grams / day
Smoking cessation advice
Alcohol Use
Alcohol units per week
Units/Week
Advice on alcohol consumption
Weekly Alcohol Intake...
Blood sample taken
New Electronic Patholog...
BP
Date
Value
04 Jan 2013 BP 120 / 98 mmHg
04 Jan 2013 BP 120 / 80 mmHg
09 Jan 2013 BP 120 / 80 mmHg
10 Jan 2013 BP 120 / 80 mmHg
17 Jan 2013 BP 120 / 80 mmHg
01 May 2013 BP 120 / 80 mmHg
08 Aug 2013 BP 130 / 85 mmHg
03 Sep 2013 BP 150 / 90 mmHg
11 Aug 2014 BP 120 / 80 mmHg
22 Oct 2014 BP 149 / 95 mmHg
31 Oct 2014 BP 150 / 100 mm
27 Nov 2014 BP 120 / 60 mmHg
20 Sep 2016 BP 150 / 80 mmHg
31 Oct 2016 BP 135 / 86 mmHg
20 Mar 2017 BP 120 / 80 mmHg
23 May 2017 BP 129 / 78 mmHg
Show recordings from other templates
Show empty recordings
Information
Print
Suspend
Ok
Cancel
Show Incomplete Fields


Research Study and Clinical Trial coding
Other Details...
Exact date & time
Mon 20 Mar 2017
14:29
Changing the consultation date will affect all other data entered. To avoid this, cancel and press the 'Next' button
Hide Warning
Research Study
Clinical Trial
Consent
Research Admin
Research administration
Questionnaires
Show recordings from other templates
Show empty recordings
Information
Print
Suspend
Ok
Cancel
Show Incomplete Fields


Research Consent Documentation
Save for Future Editing
Save Final Version
Cancel
1 - Research Study
4 PIS has been read by participant and understanding checked
Yes
No
5 Consent received version number and date
6 Copy of consent given to participant
Yes
No
7 Participant ID
8 Randomisation group
9 Data collected as per operations manual version number and date
10 CRF completed
Yes
No
11 eCFR completed
Yes
No
12 Follow Up
Next Section
Read Codes
Scores
Code
Description
Numeric Value


Research Study and Clinical Trial coding
Other Details...
Exact date & time
Mon 20 Mar 2017
14:29
Changing the consultation date will affect all other data entered. To avoid this, cancel and press the 'Next' button
Hide Warning
Research Study
Clinical Trial
Consent
Research Study coding
UK Clinical Trials Gateway
See also: Clinical Trial coding
Research studies and clinical trials get assigned formal CPMS identifying number. Entering these against the codes below helps ensure all the actions/decisions can be linked to the particular study/trial.
Eligible for participation in research study
Not eligible for participation in research study
Invitation to participate in research study
Consent given to participate in research study
Declined invitation to participate in research study
Participant in research study
Participation in research study completed
Withdrawn from research study
CPMS
General Health Information
Show recordings from other templates
Show empty recordings
Information
Print
Suspend
Ok
Cancel
Show Incomplete Fields


General Health Information
Other Details...
Exact date & time
Tue 21 Mar 2017
14:01
Changing the consultation date will affect all other data entered. To avoid this, cancel and press the 'Next' button
Hide Warning
Patient Profile
BP
BP Graph
Patient on maximal BP therapy
Sitting systolic blood pressure
Sitting diastolic blood pressure
Standing systolic blood pressure
Standing diastolic blood pressure
Pulse rate
Pulse Rhythm
Height
Weight
Waist circumference
BMI
PEFR
Predicted PEFR
Temperature
Blood oxygen saturation
Current smoking status
Cigarette consumption
Pipe tobacco consumption
Smoking cessation advice
Smoking cessation programme declined
Urine Dipstick for Protein
Urine Dipstick for Glucose
Urine Dipstick for Nitrites
Urine Dipstick for Blood
Urinalysis = no abnormality
Serum LDL cholesterol level
Serum cholesterol/HDL ratio
Alcohol Use
Alcohol units per week
Advice on alcohol consumption
Weekly Alcohol Intake...
Date
Value
Show recordings from other templates
Show empty recordings
Information
Print
Suspend
Ok
Cancel
Show Incomplete Fields