UNIVERSITY OF WARWICK

STANDARD OPERATING PROCEDURE 16

Case Report Forms (CRFs)

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Revision Chronology:	Effective date:	Reason for change:
Version 5.0	12 June 2026	Biennial review: very minor additions to text. Some amendments to ensure text is concise. Move to new SOP template.
Version 4.0	07 March 2024	Minor update by the QA team to reflect implementation of 'Data Items List' Template to aid CRF cross checking and data minimisation.
Version 3.0	17 March 2022	Biennial review: Additional information about CRF annotation, a unit wide preventative action for ensuring appropriate access to data fields within the CRF. Replaced references to 'Database' with CDMS for consistency across SOPs. Slight amendment to flow to demonstrate that development of the CRFs often occurs alongside the programming of the CDMS. Multiple minor clarifications to text and expansion of the definition section.
Version 2.1	20 January 2020	Minor amendments to responsibilities for Trial Managers and Programming team. Change of order to process. Update to new format.
Version 2.0	20 March 2019	Biennial review: Rewrite with change to process flow. Addition of requirement for documented cross check of CRF with the protocol. Expansion of scope to include patient facing data collection forms.
Version 1.5	25 July 2016	Biennial review: Minor changes to guidance document and SOP text to include eCRFs. Change to new format.
Version 1.4	6 January 2014	Addition of process of generation, review and approval of documentation.
Version 1.3	5 March 2012	Format change to comply with SOP 1.
Version 1.2	1 February 2010	Biennial review. Web page links updated. Definition of source data and note re; design of CRF added.
Version 1.1	8 February 2008	Biennial review: Format change. Slight amendments to text.
Version 1.0	March 2006	

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CONTENTS

1 Purpose and Scope

This SOP describes the process for developing and implementing tools to capture participant data, ensuring accuracy, data verification and compliance with relevant data protection regulations. For guidance on the development of a CDMS, refer to SOP 42 'CDMS Planning and Maintenance'. This SOP is for Warwick Sponsored studies or where the creation of data capture tools is delegated to Warwick by an external sponsor.

2 Acronyms

CI	Chief Investigator
CDMS	Clinical Data Management System
CRF	Case Report Form
DCF	Data Clarification Form
DMP	Data Management Plan
eCRF	Electronic Case Report Form
eQMS	Electronic Quality Management System
EDC	Electronic Data Capture
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
ISF	Investigator Site File
pCRF	Paper CRF
PI	Principal Investigator
QA	Quality Assurance
R&IS	Research and Impact Services
SAE	Serious Adverse Event
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
TM/TC	Trial Manager/Trial Coordinator
TMF	Trial Master File
WCTU	Warwick Clinical Trials Unit

3 Definitions

Case Report Form (CRF)	Form on which individual participant data required by the study protocol are recorded. It may be a paper document or a computer application, commonly a web-based portal system, where site staff enter data into an electronic case report form (eCRF). This could be an in house or 3rd party system. This type of system may be referred to as electronic data capture (EDC). For this procedure, the term CRF will be used to refer to all data capture tools, including participant questionnaires and diaries.
On entry validation	Automated check built into the application to ensure the validity or accuracy of a data item.
Clinical Data Management System (CDMS)	A tool used for the collection, tracking, processing, and storage of data used in clinical research. Where EDC will be used, entry of data may occur straight into the CDMS.

Source data	Source data is where a data point is first captured and is therefore the original record of information (e.g. hospital records, concomitant medication, laboratory results, ECGs, patient diaries, x-rays etc.)

4 Background

CRFs are typically used to record data transcribed from source documents such as medical notes, laboratory reports, and imaging reports. In some cases, the CRF serves as the source document, for example, questionnaires or diaries completed by participants.

The method of data collection directly affects data quality, therefore, CRFs must be designed to ensure data capture is clear, precise and unambiguous. This supports consistency of data quality, enables adequate data collection for protocol defined analyses, and ensures appropriate audit trails to demonstrate data validity and integrity.

As data analysis, reporting and potential audit or inspection may occur long after study completion and after study personnel have changed, it is essential that CRFs are well designed, that the design process is documented and that the completed CRFs are appropriately maintained and archived.

5 Responsibilities

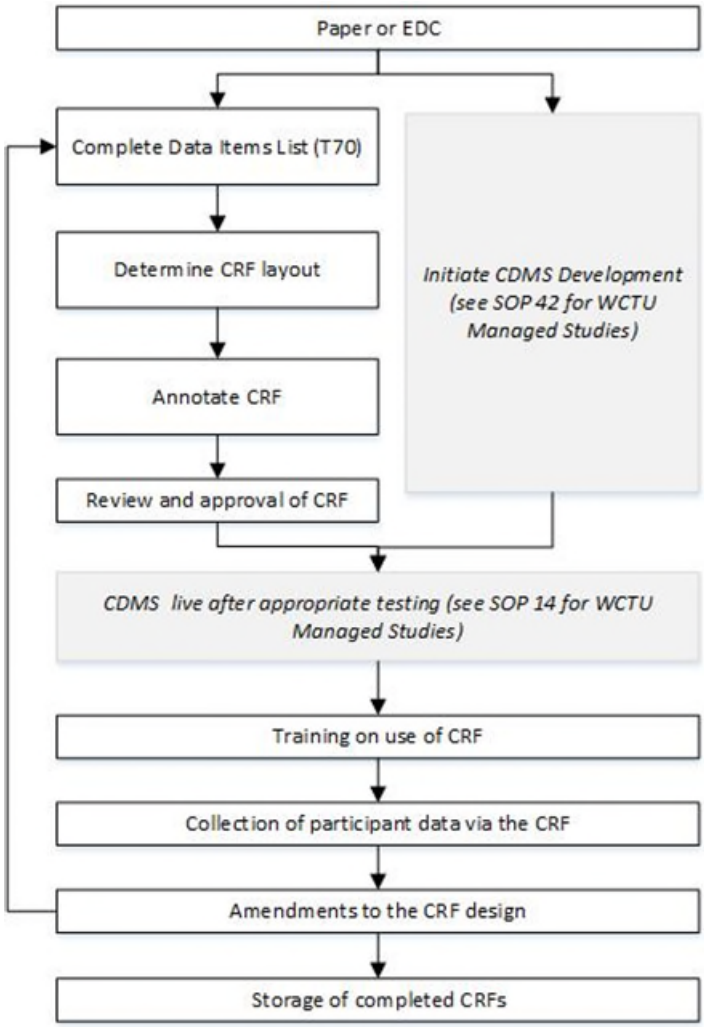
CI	• The Sponsor typically delegates overall responsibility for the design of CRF to the CI. Who will ensure that the CRF is designed to capture the required data and that the information gathered is appropriate to the aims of the study and will not adversely affect recruitment. • Ensure validated questionnaires are used within the terms of the license. The coordination of this process can be delegated but the CI retains overall responsibility and therefore final approval.
Statistician & Health Economist	• Review of CRFs to assure that data collection will enable the analysis specified in the protocol.
TM/TC	• Coordinate the design of the CRF and acting on the instructions of the CI, statistician, and programmers.
QA	• Should be involved in the development and review of CRFs related to Serious Adverse Event (SAE) reporting.
Programmer	• Program CRF in accordance with instructions from the study team. To check acceptability and logic for programming against requirements.

6 When

CRF design should be initiated alongside protocol development and should always reflect the current version of the protocol. For studies managed by WCTU, CRFs must be reviewed and approved prior to CDMS release.

7 How

Process for development of the CRF is summarised below, see subsections for more information.



7.1 Paper or EDC

Consideration should be made at study outset as to whether paper or EDC, or a combination of both, will be used and the potential advantages and disadvantages for the study. Where EDC is used, paper CRFs (pCRFs) will often need to be created as a backup in case of system failures or in situations where an individual's signature is required who does not have individual access to the CDMS application.

7.2 Complete Data Items List

- Template **T70**, Data Items List, should be completed using the protocol to ensure all data items required for the safe conduct of the trial and analysis of the primary and secondary outcomes are identified. Critical data items should be agreed upon and recorded in the designated section of the risk assessment and monitoring plan to ensure team alignment.
- This template documents alignment with the protocol and aids the concept of data protection by design by encouraging the minimisation of data.
- Use of the template also supports quality by design and effective and proportionate monitoring.
- Excessive data capture that is surplus to data analysis can increase resource burden, reduce data accuracy, completeness and ability to identify non-compliance.
- The completed template can then be used to inform the CRF content.

- At CDMS release, CRF content should align to the outcomes and analysis specified in the current approved version of the protocol.

7.3 Design layout of CRF

- Participant facing data capture tools such as questionnaires or diaries will require ethical approval in line with the guidance in SOPs 5 part 1 'Gaining initial ethical approval for research studies' & 6 'Modifications to approved study documents'.
- Where validated questionnaires are used, cost, permission or licence requirements should be considered at an early stage. Evidence of permission should be filed in the TMF. Where a validated questionnaire will be collected using different methods e.g., direct entry onto a form or collected over the phone by trial/site staff, separate licences may be required.
- For non-validated CRFs, the design should ensure that language and layout are appropriate, intuitive and accessible. Where CRFs are patient facing, input from PPI representatives should be considered.
- The programming team should be consulted at an early stage to determine technical feasibility and support efficient design.
- Appropriate **version control** should be applied throughout. Decimal increments should be reserved for each draft revision and whole integers for final approved documents. Further information is available in guidance document SOP 45: Document Management.

7.4 Annotation of the CRF

- CRF annotation supports CDMS design alongside the Data Items List (**T70**). This helps ensure that validation and access requirements have been considered.
- Annotations may consist of simple notes for each CRF field and should be retained in the TMF as evidence that these considerations have been applied.
- The table below lists the required considerations for each CRF field during the annotation process.

Access to the CRF	On entry validations
Does access need to be restricted to certain roles?	Variable length
Does the protocol, ethics application or PIS state that certain people will not see data?	Variable format
Does the requirement for robust blinding mean information should be restricted?	Data Categories or codes
	Variable constraints (e.g. range restrictions)
	Skip logic

7.5 Review and approval of CRF

- Draft CRFs should be circulated for review to relevant individuals with sufficient knowledge or experience to comment on content and suitability.
- Version control and tracked changes should be used to coordinate the review process. If possible, a CRF review meeting may be held to agree the final CRF.
- The CI must approve all changes to the CRF prior to submission to ethics (where it is applicable for participant facing CRFs) and for all CRFs prior to implementation.
- All CRFs should have appropriate review before they are approved. Minimum suggested reviewers are listed in the table below.

Role	Scope of review
Statistician	To check all required data are being collected and in the correct format to be able to conduct the analysis as per the approved protocol. To ensure validations are appropriate.
Clinically qualified investigator(s):	To ensure all data are being collected in line with the clinical data flow and that items are included to ensure effective monitoring of participant safety. To ensure validations are appropriate and data collection is adequate and not excessive.

Other appropriate reviewers include, but are not limited to:

Quality Assurance: specifically in relation to the SAE reporting CRFs.

Health Economist: to check that all the required data is being collected and in the correct format to be able to conduct the planned health economic analysis.

Senior Project Manager: it is strongly recommended that the Senior Project Manager reviews CRFs in order to facilitate consistency and lessons learnt across the portfolio.

For **WCTU managed studies**, documentation of appropriate review and approval of CRFs should be captured using an appropriate method. If email approval will be used, there is guidance in **G33**.

Only after CRFs have been reviewed and approved as per the process above, can the CDMS be released.

7.6 Training on use of CRF

https://warwick.ac.uk/fac/sci/med/research/ctu/ctuintranet/qa/sop/Training requirements for CRF completion must be identified and appropriate guidance provided via the CRF, approved working instructions or study manuals, or at an SIV. Relevant WCTU training requirements must be documented in the DMP. CDMS access must only be granted once appropriate training has been completed and documented.

7.7 Collection of participant data via the CRF

CRFs based on source data should be completed as soon as the source data become available.

Source data should remain in a participant's medical records in a manner that allows retrieval for audit or regulatory inspection, including long after study completion. The medical record should clearly indicate the participants' involvement in a clinical trial.

Data transcribed onto the CRF should be consistent with the source documents. Any discrepancies should be explained and documented, for example through Data Clarification Forms (DCFs) or explanatory notes, either filed with the CRF or incorporated within CDMS functionality or associated guidance.

7.7.1 CRFs that are also source data

Where CRFs act as source data, relevant data items/forms and procedures must be specified in the protocol and personnel must be appropriately trained. Completion methods, missing data strategies, submission format, and site retention arrangements must be defined, with any deviations clearly documented and justified in the protocol.

7.8 Amendments to CRF design

https://warwick.ac.uk/fac/sci/med/research/ctu/ctuintranet/qa/sop/All CRF amendments must follow the approved review and approval process, with a summary of changes and justification retained in the TMF. Change control procedures must ensure site awareness and correct implementation, including retraining where required. Implementation dates, ethical approvals, and updates to the DMP and working instructions must be managed in accordance with SOP 15 Part 1 and SOP 34.

7.9 Storage of completed CRFs

Completed CRFs must be stored securely within the ISF during the study and archived by the site following notification. For EDC studies, site access is usually maintained until data lock, after which site-specific data should be provided for archiving. CRFs held at WCTU must be securely stored and accessed only by authorised personnel.

For more information on storage of CRFs, see SOP 20 'Closing Research Study Recruitment Sites' and SOP 23 'Archiving'.

8 Associated Templates and Documents

T70	Data Items List
G33	Email approval guidance