## Case Report Forms

<table>
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<th>Version</th>
<th>Date</th>
<th>Reason for Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final 1.0</td>
<td>03.07.2006</td>
<td>Annual review</td>
</tr>
<tr>
<td>Final 2.0</td>
<td>25.06.2007</td>
<td>Annual review</td>
</tr>
<tr>
<td>Final 3.0</td>
<td>26.06.2008</td>
<td>Annual review</td>
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<td>Final 4.0</td>
<td>08.02.2010</td>
<td>Formations of Joint Research Compliance Office</td>
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<tr>
<td>Final 5.0</td>
<td>14/07/11</td>
<td>Annual review</td>
</tr>
<tr>
<td>Final 6.0</td>
<td>30/11/12</td>
<td>Annual review</td>
</tr>
<tr>
<td>Final 7.0</td>
<td>18 Feb 2015</td>
<td>Scheduled review</td>
</tr>
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1. PURPOSE

The purpose of this guide is to aid in the design of paper Case Report Forms (CRFs). Electronic CRFs (eCRF) will be detailed in a separate SOP. CRFs are the official instrument to collect data from clinical trials and are a key component of quality assurance and control. It is aimed at researchers, trial coordinators, research nurses, and any other staff who design CRFs for a study.

2. INTRODUCTION

CRFs are used to collect data generated for a trial subject, in accordance with the protocol, during the course of their participation in a trial. They also ensure compliance with regulatory requirements. A CRF should collect only appropriate trial data, in an appropriate format, as set out in the protocol and for anticipated analyses. Data collection in excess of that required by the protocol and analysis plan is undesirable. Collaboration with a trial statistician is recommended.

Standard CRFs usually include the following forms:

- Randomisation/registration form (Appendix 2)
- Entry form (collects baseline data)
- Treatment form (doses, AEs, toxicity)
- End of Treatment form (end result of study?)
- Death
- Relapse / recurrence
- Serious Adverse Event (Appendix 3)
- Follow-ups

3. PROCEDURE

3.1 General Principles

Each CRF should be dated and have a clear version number. Any changes to the final CRFs used during a trial should be documented.

The CRF layout should have a logical ordering that follows the schedule of clinic visits, should ask unambiguous questions and should be consistent with the protocol. Thought should be given in advance as to whether any data collected on the CRF can be validated through monitoring of the original source document if required or if the CRF is the source document.

CRFs should be reviewed and signed off by the Chief Investigator and Trial Statistician, if available before they are used in the trial. It is good practice for data managers, monitors, CRAs and research nurses to view the CRFs prior to sign off as they will have a clear perspective.
Ideally a well-designed CRF will remind the principal investigators at local sites to perform specific evaluations. Research nurses or monitors can verify that the protocol is being followed and compare with source documents, and the database developer will be able to build in edit checks to help with data management and analysis.

The CRF package that is circulated to all local sites should include:
- General instructions
  - Use permanent Black ink when completing
  - Complete all items
  - Provide glossary of abbreviations
  - Contact information
  - Procedure for corrections and amendments
- CRF study schedule
- Checklist and section dividers, preferably by visit

3.2 Design Guide
For ease of completion:
- Provide definitions
- Specify units if appropriate
- Avoid requesting unnecessary calculations
- Consider grading visual analogue scales

For ease of understanding:
- Avoid double negatives
- Ask explicit questions
- Use absolutes if possible. For examples when describing levels of pain, use: None, Mild, Moderate, Severe; rather than: Better, Same, Worse
- Give constant baselines for comparisons
- Avoid compound questions

3.2.1 Layout
Keep adequate amounts of free space on the CRF page. Ensure alignment, margins, spacing and fonts are consistent throughout the CRF booklet. Margins should be large enough to accommodate hole punching/binding.

As much as possible, align text to the right with boxes to the left or centred so it is easily understood which tick box is associated to which question:

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Married?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Driving licence?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any children?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good health?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Layout of CRF should allow for ease of completion, as well as ease of data entry. Things to look for with data entry include adding dropdown choices/menu onto a database, grouping same type of data together on
the same form, e.g. dropdown answers together, numeric together and alpha numeric together.

### 3.2.1.1 Header
The header of each CRF should include:
- Name of study or study number
- Subject identification number
- Initials
- Site/centre number (if not included in the subject number)
- Name of form
- If CRF goes to 2 pages, indicate page 1 of 2 and 2 of 2

It is easier to access this vital information when looking through a stack of CRFs if located in the upper right hand corner

<table>
<thead>
<tr>
<th>&lt;Name of study&gt;</th>
<th>&lt;subject ID number&gt;</th>
<th>&lt;Name of form&gt; (page 1 of 2)</th>
</tr>
</thead>
</table>

### 3.2.1.2 Footer
Signatures and dates should be included at the bottom of each CRF. Each CRF should include the address to return form to on the bottom of the form

<table>
<thead>
<tr>
<th>Completed by:</th>
<th>Date completed:</th>
</tr>
</thead>
</table>

Please return to: <Trial Coordinator>, Imperial College AHSC, <address>

### 3.2.2 Data Collection
For data analysis purposes, avoid unnecessary textual data, pictorial data and obtaining data from diary cards. Provide choices for each question, this makes it easier at analysis.

Provide units to ensure comparable values and provide instructions to reduce misinterpretations.

Collect raw data rather than calculated data, e.g. for age, collect birth date and visit date. When collecting toxicity data, it is more valuable to have the exact value of the blood result, e.g. haemoglobin 5.2 g/dl rather than a CTCAE toxicity grade of 3

There are different types of data collection responses:
- Open: text, number, alpha numeric
- Closed: Check box, multiple choice
- Combination: open and closed
- Analogue / rating scales

#### 3.2.2.1 Open
Avoid free text if possible as it is almost impossible to analyse. For date / time, add characters to boxes to ensure that the dates
are collected in a uniform fashion (MMM/DD/YYYY). This is especially important with international trials.

3.2.2.2 Closed
Provides a list of options e.g. yes/no. Checkbox is the clearest option. If using coding, be consistent across all CRFs, e.g. ‘Yes’ is always 1, ‘No’ is always 2.

This is the best choice for collecting and analysing data.

3.2.2.3 Combination
Generally used with closed type questions when one of the possible responses is ‘Other’, or ‘Specify’. This information could be used for future studies as it gives the investigator additional options.

3.2.2.4 Analogue/rating scales
Use only validated instruments, e.g. Quality of Life. They are used to measure one’s perception of a situation.

Text boxes should have a consistent design throughout, e.g. utilise box combing, box dividing or free text areas (avoid if possible).

Box combing: 1 1 1 1 1 1 1

Box dividing: [ ] [ ] [ ] [ ] [ ]

Free text: ______________________

Use a standardised answer mode throughout all the CRFs, e.g.:

Married? Yes[No] by circling

Driving licence? Yes / No by underlining

Any children? Yes / No by deleting

Good health? Yes □ /No [ ] by ticking a box

Smoker? Yes (Y) / No (N) [N] by using a code

Tick boxes tend to be the easiest to complete and utilise for data entry.

3.3 Completing CRFs
No fields should be left blank. ND (not done) should be used if data is unavailable either because a measure was not taken or test was not performed. N/A (not applicable) should be used if a measure was not required at the particular time point the form relates to. NK (not known) should be used if the data is unknown, and every effort has been made to
find the data. CRFs should be signed by all site personnel completing the CRF. The Principal Investigator at the local site is responsible for the accuracy of the CRF.

3.4 Amendments
As a general rule, amendments to data recorded on CRFs should always be handled at the local site. Exceptionally, the Chief Investigator or Trial Coordinator could amend a CRF if this is agreed in writing or verbally AND a copy of the changed CRF is then sent to the local site.

Corrections should be made by drawing a single line through the incorrect item and dating and initialling all correction. Tippex should not be used.

When completing a query, attach an amended copy of the CRF and return either by post or fax to the coordinating centre.

3.5 Electronic data capture
Electronic data capture (EDC) will allow the local sites to transcribe subject details direct onto a web-based database, thus saving time and trees. They also offer an advantage as it ensures a standardised format for data entry and can code events. Possible disadvantages include training of staff at local sites to complete online, ensuring that all staff have access to the internet and the need for a paper backup in case of system failure. Imperial College Academic Health Science Centre (AHSC) has implemented a Clinical Trial eCRF (InForm) that will allow for the design and use of EDC. This system is mandatory for all Imperial College AHSC sponsored clinical trials of an IMP. For further information on the eCRF, please contact Sandra Griffiths: s.e.griffiths@imperial.ac.uk

4. REFERENCES
Medicines for Human Use (Clinical Trials) Regulations 2004
5. APPENDICES

5.1 Appendix 1: Example CRF sign-off sheet

<table>
<thead>
<tr>
<th>Trial form</th>
<th>Version number</th>
<th>Version date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I have reviewed the trial's CRFs and approve the use of the above documents.

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Statistician</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>___ / ___ / ___</td>
</tr>
<tr>
<td>Chief Investigator</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>___ / ___ / ___</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Planned implementation date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
</tr>
<tr>
<td>Position:</td>
</tr>
<tr>
<td>Signature:</td>
</tr>
<tr>
<td>Date:</td>
</tr>
</tbody>
</table>
5.2 Appendix 2: Example randomisation form

Section 1 - Clinician Details
Randomising centre: ___________________________ Randomising consultant: ___________________________

Section 2 - Eligibility Checklist
These should be based on the inclusion/exclusion criteria set out in the protocol

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has a diagnosis of xxx been histologically confirmed?</td>
<td>☐</td>
</tr>
<tr>
<td>Is the patient aged between 18 and 88?</td>
<td>☐</td>
</tr>
<tr>
<td>Has the patient signed the consent form?</td>
<td>☐</td>
</tr>
</tbody>
</table>

Is the patient eligible for the xxx Trial? ☐ ☐

Section 3 - Patient and Tumour Characteristics
Ideally you should capture as much vital information as possible at randomisation/registration

Tumour Details

<table>
<thead>
<tr>
<th>Site</th>
<th>T Stage</th>
<th>Nodal Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper (10-15cm)</td>
<td>T0</td>
<td>N0</td>
</tr>
<tr>
<td>Middle (5-9.9cm)</td>
<td>T1</td>
<td>N1</td>
</tr>
<tr>
<td>Lower (0-4.9cm)</td>
<td>T2</td>
<td>N2</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N3</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>N4</td>
</tr>
</tbody>
</table>

Patient Details
Surname: ________________________
First name: ________________________
Sex: Male ☐ Female ☐
Initials: ________________________
Date of birth: mm/dd/yyyy
Hospital no: ________________________

Section 4 - Randomisation Details
A ☐ Drug combination A and B
B ☐ Drug combination C and D

Trial Number: ________________________

Completed by: ________________________ Date completed: ________________________
5.3 Appendix 3: Example Serious Adverse Event form

### Details of SAE

**Serious Adverse Event Name:** [Please code using these criteria from AE criteria used]

**Duration of SAE:** (dd mm yy)

**SAE Status:**
- 1=Resolved
- 2=Resolved with sequelae
- 3=Persisting
- 4=Resolved with sequelae
- 5=Fatal
- 6=Not assessable

**Expectedness:**
- 1=Expected
- 2=Unassessable

### Treatment

**Trial drugs patient was receiving when SAE started:**

**Total Daily Dose:**

**Start Date of Most Recent Cycle:**

**Currently Ongoing:**
- 0=No
- 1=Yes

**End Date:**

**Causal Relationship to Event:**
- 1=Definitely
- 2= Probably
- 3= Possibly
- 4= Unlikely
- 5= Not related
- 6= Not assessable

**Action Taken:**
- 0=None
- 1=Treatment delayed
- 2=Treatment withdrawn
- 3=Cure
- 4=Death

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### Other treatments at time of event (include concomitant medication, radiotherapy, surgery, palliative care, continue on a separate sheet if necessary. Exclude any therapy given for management of SAE)

<table>
<thead>
<tr>
<th>Treatment given</th>
<th>Total Daily Dose</th>
<th>Route of Administration</th>
<th>Start Date (dd mm yyyy)</th>
<th>Currently Ongoing?</th>
<th>End Date (dd mm yyyy)</th>
<th>Action Taken</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

### Other relevant information to facilitate assessment

(include medical history, drug or alcohol abuse, family history, findings from special investigations)

Was this event expected in view of the patient's clinical history?

☐ No

☐ Yes

### Additional information:

Signature: 

Authorised Health Professional: 

Print name: 

Contact telephone no: 

Date of report: d d m m y y

### OFFICE USE ONLY

Was SAE drug related?

Yes ☐ No ☐

Was event unexpected?

Yes ☐ No ☐

Was the event a SUSAR?

Yes ☐ No ☐

Date sent to MHRA: d d m m y y

Date entered on database: d d m m y y

MEDRA code: 

Form checked by xxx staff (signature): 

Checked by clinical reviewer (signature): 

Event No: 

Comments: 

Date: d d m m y y