Introduction

Hard copy case report forms (CRFs) are still the most commonly used method of capturing clinical trial data at investigational sites and transferring it to the trial sponsor or contracted data management organisation. From a records management perspective this approach generally works well. When problems do occur it is quite likely that they will relate to additional CRF pages received by the Sponsor or unused CRF pages and/or modules* that are either not returned or are returned without any data. This paper recommends that the sponsor defines a process which ensures documentation and reconciliation of the additional or 'missing' pages/modules while avoiding the unnecessary transfer to the archive of pages which contain no data. This is consistent with GCP audit trail principles.

The use of consecutive page numbering throughout the CRF will further facilitate this process and avoid ambiguous page numbering across modules. Consecutive page numbering is strongly recommended, particularly in an electronic environment, where pages of data are created or scanned and indexed as electronic images.

Proposed process

There are 3 potential situations that need to be addressed:

- additional individual pages or individual pages which are not used
- additional entire modules* or entire modules* which are not used
- entire CRFs which were issued to the investigational site and are not used

Reasons for the first two situations can include: subject withdrawal; additional concomitant medication pages used; more pages provided than actually needed e.g. adverse events pages. Reasons for the third situation can include: oversupply of CRF books to the site; lower than forecasted subject recruitment.

The essential component of any process to address these problems is maintenance of adequate documentation. This applies whether the sponsor's preferred process allows unused pages and/or modules and/or CRFs which will remain unused to be destroyed on site or returned to the sponsor for destruction. Sponsors should decide whether to eliminate all unused CRF pages from the Trial Master File or alternatively, eliminate all unused modules. In addition, reconciliation of additional CRF pages is also vital to ensure the completeness of the Trial Master File.

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* ***Definition of module:*** *A component of the overall CRF consisting of one or more pages, containing sets of data as agreed for the study in question eg visit or other data set such as AEs.*

The key activities in this process are:

1. Document the number of CRFs supplied to each investigational site (including pre-printed randomisation numbers, if applicable).

2. When collecting CRFs/modules, the monitor undertakes the following for each subject:

- confirms that all used CRFs/modules for the subject are collected and handled in accordance with current practices and documents this;

- confirms, by reviewing the used CRFs, which CRF modules or pages remain unused and documents this;

- ensures that any additional pages are accounted for.

In addition, at the end of the study, the monitor confirms and documents which CRF *books* remain unused and reconciles with the number allocated to the investigational site.

Example of forms which may be used as is or adapted for use to document these activities are shown in the attached appendices.

3. Following completion of each form, obtain the agreement and signature of the investigator or authorised member of the study team; this will usually be the person authorised to complete CRFs.

4. If the sponsor permits local destruction of unused pages/modules/CRFs, remove the pages/modules and ensure their secure destruction. Otherwise, return unused pages/modules/CRFs to the sponsor's site for destruction according to documented working practices.

5. The investigator should retain a copy of the appropriate form(s) with the CRFs.

6. Return completed CRF modules to the sponsor, together with all of the completed CRF accountability forms.

Appendices A - C below are examples of forms which may be used and/or adapted for this purpose. One form will be completed for each subject with additional/missing pages/modules and may be pre-printed and sent out as part of the CRF. Appendices D - F show the forms completed with sample data. Appendix G is an example of a form to document the reconciliation of used/unused CRFs with the initial number of CRFs issued to the investigational site together with a sample form completed (Appendix H). These forms are examples only and should be modified as necessary to meet the specific needs of the sponsor. Completed forms will be filed with the corresponding completed CRFs by the sponsor and investigator.

Appendix A
CRF Page Reconciliation - Sample Form

Protocol Number | **Subject Number**

Page Count

- Complete this page for all subjects
- Return this page with the CRF transmission
- Indicate in the notes section below if this subject was a screen failure
- Place an "X" through the page number of those pages that have no data recorded on them and will not be transmitted
- Enter any additional page numbers in the empty boxes below

Notes:

Investigator/Responsible person signature *day* *month* *year*

Appendix B
Unused CRF Pages/Modules - Sample Form

Accountability of unused CRF pages/modules

Protocol: | | | | | | | | | | | | |

Investigator/Centre: | | | | | | | | | | | | |

CRF/Subject initials/Identifier: | | | | | | | | | | | | |

No information was entered on the following pages:

Module/Visit	**Pages**	**Justification** *(see key below)*

These pages are not archived in the Trial Master File and:

have been destroyed at site ☐

are returned to sponsor for destruction ☐ *(check one)*

_____ _____

(Investigator signature) (Date)

Key:
1 Unused adverse event page
2 Unused concomitant medication page
3 Withdrawn from study
4 Other - clearly specify reason

Assumptions:

CRF design is the same for all patients entered in study.
The term "blank" CRF often refers to the template or master; therefore, pages not filled in will be called "unused" rather than "blank" to avoid confusion.

Appendix C
Unused CRF Pages - Sample Form

Unused Page Form

Protocol:												
Investigator/Centre:												
CRF/Subject initials/Identifier:												
Module/visit:												

No data have been entered on the following pages:

	Pages		**Pages**
[1]	_____	**to**	_____
[2]	_____	**to**	_____
[3]	_____	**to**	_____

Reason(s): *(must be completed)*

[1] _____

[2] _____

[3] _____

_____ _____

(Investigator signature) (Date)

The present form, filled out, signed and dated by the investigator, replaces the above-mentioned empty pages in the Trial Master File. The present form will be filed at the start of the relevant module/visit. The empty pages will not be retained.

Assumptions:

CRF design is the same for all patients entered in study.
The term "blank" CRF often refers to the template or master; therefore, pages not filled in will be called "unused" rather than "blank" to avoid confusion.

Appendix D
Accountability of unused CRF pages - Sample form with example data

Protocol Number

ABCD-1234

Subject Number

0003561

Page Count

- Complete this page for all subjects
- Return this page with the CRF transmission
- Indicate in the notes section below if this subject was a screen failure
- Place an "X" through the page number of those pages that have no data recorded on them and will not be transmitted
- Enter any additional page numbers in the empty boxes below

1	2	3	4	5	6	7	8	9	10
10.1	10.2	10.3	10.4	10.5	10.6				
11	12	13	14	15	16	17	18 X	19 X	20
21	22	23	24	24.1	24.2	24.3	24.4		
25	26	27 X	28	29	30	31	32	33	34
35	36	37	38	39	40	40.1			
41	42	43	44	45	46	47	48	49	50
51	52	53	54						

Notes: _____

J. Doyle _____ 0 2 F E B 9 9

Investigator/Responsible person signature *day* *month* *year*

Appendix E
Unused CRF pages - Sample form with example data

Accountability of unused CRF pages/modules

Protocol:	X	X	X	1	2	3	4					
Investigator/Centre:	D	O	Y	L	E	/	1	5				
CRF/Subject initials/Identifier:	2	0	2	A	B							

No information was entered on the following pages:

Module/Visit	**Pages**	**Justification** *(see key below)*
3	30-31, 39	1
4	40-41, 49	1
5	59-60	3
6	All	3
7	All	3
8	All	3

These pages are not archived in the Trial Master File and:

have been destroyed at site ☒
are returned to sponsor for destruction ☐ *(check one)*

A. Doyle _____ 10-Mar-1999 _____
(Investigator signature) (Date)

Key:
1 Unused adverse event page
2 Unused concomitant medication page
3 Withdrawn from study
4 Other - clearly specify reason

Appendix F
Unused CRF pages - Sample form with example data

Unused Page Form

Protocol:	X	X	X	X	1	2	3	4				
Investigator/Centre:	D	O	Y	L	E	/	0	0	1	5		
CRF/Subject initials/Identifier:	2	0	2	/	A	B						
Module/visit:	0	3										

No data have been entered on the following pages:

	Pages		**Pages**
[1]	39	**to**	40
[2]	49	**to**	-
[3]	-	**to**	-

Reason(s): *(must be completed)*

[1] Subject did not keep laboratory appointment

[2] Subject did not keep laboratory appointment

[3]

A. Doyle (Investigator signature)

10-Mar-1999 (Date)

The present form, filled out, signed and dated by the investigator, replaces the above-mentioned empty pages in the Trial Master File. The present form will be filed at the start of the relevant module/visit. The empty pages will not be retained.

Appendix G
Accountability of issued CRF books - Sample Form

Accountability of Issued CRF Books

Protocol: | | | | | | | | | | | | |

Investigator/Centre: | | | | | | | | | | | | |

Number of CRF books issued to site: [ ]

Number of CRF books returned used: [ ]

Number of CRF books returned unused: [ ]

All unused CRF books have been returned to the sponsor for destruction/re-use, as appropriate.

_____ _____

(Monitor/CRA signature) (Date)

The present form will be filed in the study file for this protocol. The empty CRF books will not be retained.

Appendix H
Accountability of issued CRF books - Sample form with example data

Accountability of Issued CRF Books

Protocol:	X	X	X	X	1	2	3	4			
Investigator/Centre:	D	O	Y	L	E	/	0	0	1	5	

Number of CRF books issued to site:	14
Number of CRF books returned used:	12
Number of CRF books returned unused:	2

All unused CRF books have been returned to the sponsor for destruction/re-use, as appropriate.

C. Burnett (Monitor/CRA signature)

10-Mar-1999 (Date)

The present form will be filed in the study file for this protocol. The empty CRF books will not be retained.