Development of an Internal Quality Review Process for Essential Study Documents

Maria Spillane, MSc[1]; Ruben Keane, PhD[1]; Niamh Kelly, RN[1]; Maeve Kelsey, RN[1]
[1]HRB-Clinical Research Facility-Cork

Introduction

Maintaining study documentation and source documents is an area that can be easily postponed by busy study staff, but errors and omissions in this area are one of the most common findings in GCP inspections.[1]

The Clinical Research Facility Cork (CRF-C) has recently developed a system for conducting Internal Quality Reviews of ongoing research studies being run by its Operations team. The main reason for introducing this system is to maintain the high quality standards of research carried out by the CRF-C; to minimise findings from monitoring visits and audits; and to ensure that studies are inspection-ready at all times.

The Internal Quality Reviews involve checking the Investigator Site Files (ISF's) and Source Documents of research studies being carried out by CRF-C staff. The reviews are conducted to the relevant quality standards, including ICH-Good Clinical Practice (GCP), the study protocol, the terms of the research ethics approval, the applicable regulatory requirements, and relevant sponsor or CRF-C Standard Operating Procedures (SOP's).

This report outlines the process developed for conducting Internal Quality Reviews, and the most common findings identified during the reviews.

Methods

Once per quarter the Clinical Management Team (CMT) meet and decide which studies should be reviewed. This list is approved by the Quality & Regulatory Affairs Director (QRAD), who appoints a member of the Quality team to carry out the reviews. The review process is detailed in Figure 1 below.

The following risk-based criteria are used when deciding which studies will be reviewed in the next quarter:

- Type of study (i.e. Regulated/Non-Regulated)
- Complexity and phase of study (Phase I-IV)
- Upcoming monitoring visits and Sponsor audits
- Level and rate of recruitment
- Duration of the study
- Experience of staff involved
- Protocol deviations or issues with the study

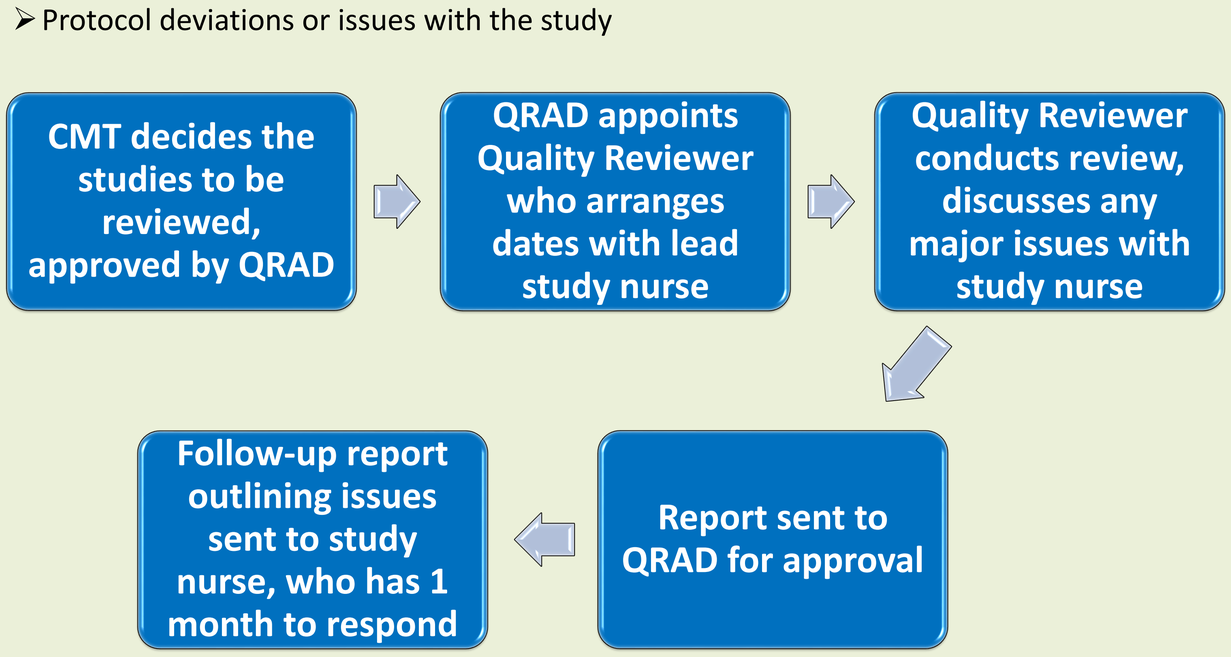

Figure 1: Internal Quality Review Process

The reviewer looks at the following documents:

Investigator Site File:

- Study logs, including Delegation Log and Training Log; CV's and GCP certificates
- Ethics and Regulatory approvals
- Adverse Event (AE)/Serious Adverse Event (SAE) Reports
- Insurance certificates
- Protocol deviations

Source Documents:

- Informed Consent/re-consent process documentation
- Study visit documentation and CRF's
- Signed Consent Forms
- IMP dispensing
- Laboratory results
- Safety reporting

Results

Between September 2018 and April 2019, 21 reviews were completed on 18 studies; with three studies being reviewed twice in the eight month period. The common findings noted from all of the initial reviews were categorised, and the number of findings per category were counted. In total, there were 74 findings in the ISF's, and 27 findings in the Source Documents. The frequency of the findings are detailed in Figures 2 & 3.

Results continued

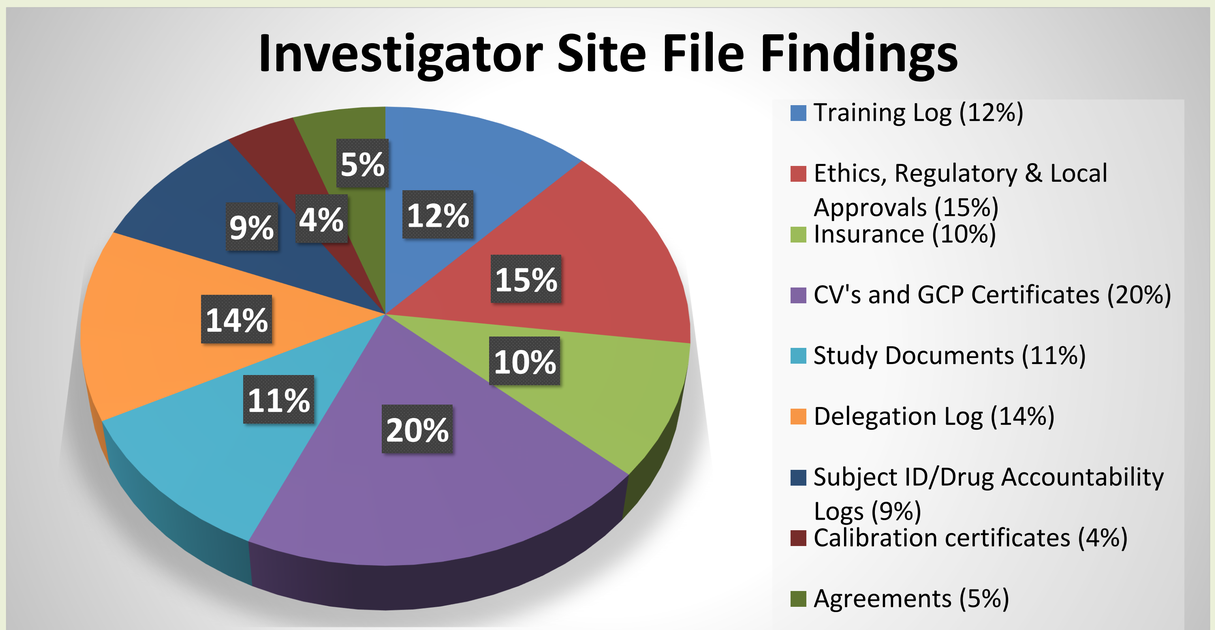

Figure 2: Common findings in Investigator Site File reviews (n=8 Regulated and n=10 Non-Regulated studies).

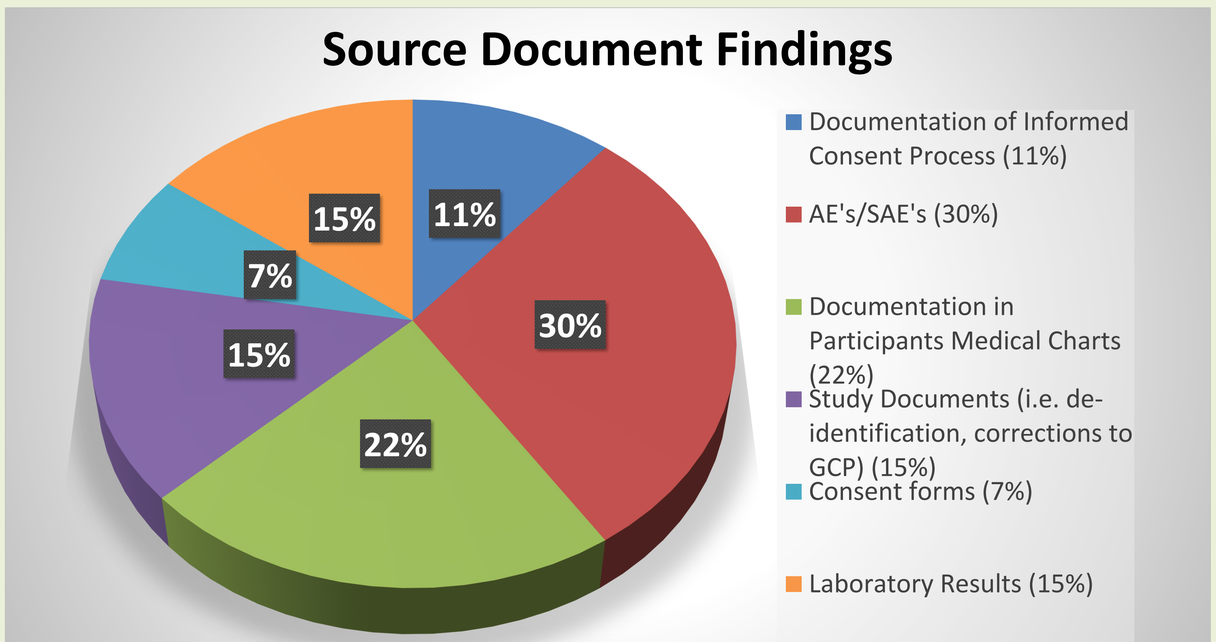

Figure 3: Common errors in Source Document reviews (n=8 Regulated and n=10 Non-Regulated studies)

The main findings with the ISF were: updated or relevant CV's/GCP certificates not filed; relevant Ethics and Regulatory approvals not filed; incorrectly completed Delegation Logs and staff training documentation.

The main findings with the Source Documents included: insufficient or no documentation of AE's/SAE's; poor documentation of study visits and consent process in participants' medical charts; not filing relevant study documents or correspondence; and study Investigators not signing laboratory results or prescriptions.

After the first three months of piloting the Internal Quality Reviews, a Work Instruction and Standardised Form for conducting the reviews was developed by the Quality Reviewer, QRAD and CMT.

Conclusions

- Study staff have reported favourably on the reviews, and study Site Files are better maintained as a result
- Study staff are now more aware of the importance of maintaining study documentation throughout the life-cycle of a study
- Development of an Internal Quality Review process has raised the quality of research study documentation at the CRF-C, giving added value to Sponsors.

Recommendations

- Develop Education sessions with the CRF-C Operations Team to outline the major issues identified, in order to focus on these problem areas.
- Review the process after 1 year to determine how it has affected the quality of study documentation, and identify areas where the process needs changing or improving.
- Conduct reviews of studies in the set-up stage to ensure all essential documents are in place.

References

[1] 'Overview of GCP inspections including common findings', presented at HPRA Information Day, Dublin, 23rd October 2018 https://www.eiseverywhere.com/ehome/345191

For more information please contact us at: CRF-C, Mercy University Hospital, Grenville Place, Cork, Ireland • **T** 021 493 5150 • **E** crfc@ucc.ie www.ucc.ie/en/crfc