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Information and guidance for primary care sites on how to maintain an Investigator Site File (ISF)

The purpose of this guide is to provide primary care sites with guidance on how to maintain an Investigator Site File (ISF).

1. What is an investigator site file?

The Investigator Site File (ISF) contains essential documents which shows that the clinical trial site and Investigator are following the regulatory requirements, from initiation to closeout. The sponsor may provide the ISF but if not, one should be set up at site.

Please see website to access the templates for investigator site file index primary care CTIMP and Non-CTIMP. To request the file templates for Investigator site file -Primary Care CTIMP and non – CTIMP and for more information, contact rdu@shsc.nhs.uk.

2. Is there a difference between paper and electronic site files management?

There is no legal difference between management of paper and electronic site files. Hence, all the basic requirements are the same for both formats or when used in combination as a hybrid site file. It is usually the sponsor that decides whether a site will use electronic or paper site files and will provide you with the guidance on how to maintain it.

3. Why is it important to keep an ISF?

It tells the entire story of the research study from start to finish. It outlines the exact conduct of a research study, integrity of the study data and compliance with Good Clinical Practice (GCP) standards. It also assists with monitoring, audit and inspection process and ensures participant safety and wellbeing.

4. Who is responsible for the investigator site file?

The Principal Investigator (PI) is responsible for ensuring an ISF is established prior to the start of a study at their site and updating the file with relevant and applicable documents as the study progresses. The PI is also responsible for archiving the ISF at the end of the study. These duties maybe delegated by means of the Delegation Log.

5. Does an ISF differ between studies?

Your site file will differ depending on whether the study is a Clinical Trial of an Investigational Medicinal Product (CTIMP), non-CTIMP study and a PICs and who has issued it. You should always use the one provided by the sponsor as a preference.

6. What is a CTIMP and non-CTIMP?

A CTIMP is a clinical trial or study that is evaluating the safety or efficacy of a drug (Investigational Medicinal Product) or obtaining any other information about the drug. CTIMPs are studies governed by UK law through The Medicines for Human Use (Clinical Trials) Regulations 2004. An example is *"assessing whether paracetamol relieves headaches is a CTIMP and paracetamol is the Investigational Medicinal Product (IMP)"*

A non-CTIMP is a study that does not involve an Investigational Medicinal Product (IMP). An example is - *a study of blood flow which involves the infusion of a vasoactive drug to monitor or establish the effects of this vasoactive drug to see if it is effective in achieving a particular physiological effect.*

If the trial is being conducted for a reason other than ascertaining the effects of, or reactions to, a product it is simply being used as an aid or tool in the study and is not a CTIMP.

7. Do PICs need to maintain an ISF?

A full ISF as par research sites is not necessary for PICs. It is the responsibility of the research team to maintain a PIC site file for current documentation to be stored and to provide local information on the research staff, contact details, training records and referrals. See below documents that can be found in PIC site file.

Please see website to access the list of documents that can be found within a PIC site file.

8. Where is the ISF kept?

The file should be stored in a secure location at the research site with access limited to research staff involved in running the study at the site only. While the study is still ongoing, the ISF must be kept securely with restricted access e.g in a locked cupboard in a locked room. This is the PI's responsibility but can be delegated via the Delegation of Duties Log. Access should be 24 hrs of the day.

9. What documents are always included in the ISF?

Essential documents included are the protocol, Delegation Log and Participant Identification Log. There are however lots of other essential documents that you may find in your ISF e.g file notes.

10. What is a file note?

It is a document that records any site-specific or protocol related process that is not documented in any previously approved procedures. You can find more information about file notes on the file notes Q&A.

11. What is version control and why is it important?

Version control is how we can make sure that we are using the latest approved version of our essential documents and means we have a record of any amendments that have been made. New documents must have the new version numbers and accompanying date stated in the header or footer of the document.

12. How are superseded documents filed?

You may cross through superseded documents, initial, and date them.

13. What should I do with the ISF when the study ends?

This will be decided by the sponsor and will be described in the protocol. As a guide, CTIMPs are normally archived for 25 years and non-CTIMPs for 5 years after the end of the study.

14. How do I find out more about maintaining an ISF

Maintaining a Site File training can be found on the NIHR Learn website in the section called Practical Research Delivery Skills. https://learn.nihr.ac.uk/ (accessed 04/01/2023)

NHS site set-up in England https://www.hra.nhs.uk/planning-and-improving-research/best-practice/nhs-site-set-up-in-england/ (accessed 02/05/2023)

15. Who do I contact if I have further questions?

For any questions, please email: rdu@shsc.nhs.uk