Strategic Quality Assurance and Quality Control Plan

Protocol Number: TRI08889

REGISTRY TITLE: Global Anticoagulation Registry in the FIELD observing treatment and outcomes in patients with treated acute Venous Thromboembolic Events in the real world.

SHORT TITLE: Global Anticoagulant Registry in the FIELD (GARFIELD) – Venous Thromboembolic Events (GARFIELD –VTE)

REGISTRY NUMBER: TRI08889
SPONSOR: Thrombosis Research Institute (TRI)
VERSION: Version 2.0 October 05th 2016

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ABBREVIATIONS

ToC	Table of Content
CRO	Clinical Research Organisation
DMP	Data Management plan
MVR	Monitoring Visit Report
QA	Quality Assurance
QC	Quality Control
SDV	Source Data Verification
eCRF	Electronic Case Report Form
iCRA	International Clinical Research Associate

1 Introduction and Scope

The purpose of this document is to describe the Quality Assurance (QA) and Quality control (QC) used for managing the quality and accuracy of the study data for protocol No TRI08889. The plan will be used to achieve good practice for QA and QC in accordance with ICH GCP Guidelines.

The strategic monitoring plan and the Data Management Plan (DMP) are required to ensure appropriate management and oversight of data through the duration of the trial and to assure a high-quality data. Quality assurance also aims to ensure that the data are collected in accordance with the protocol.

The accuracy of registry data depends on the accurate transcription of the participants' clinical data by staff at the selected clinical sites. A major criticism of patient registries is they often lack the stringent quality controls applied to clinical trials. In TRI08889 we have introduced a number of quality control steps to be able to more accurately monitor the data quality and accuracy.

The process for assessing data quality within clinical trials is similar whether observational or interventional. This typically involves quality and consistency checks of the electronic database using validation and edit checks, remote or online monitoring and more conventional onsite monitoring including SDV. The quality of data is frequently assessed using Kappa summary statistics or by dividing the number of errors observed by the number of data fields inspected.

Studies have shown that only a small percentage of data is changed due to 100% SDV, and the effect of this change on the primary analysis is negligible. Robust sampling strategies with smaller percentages of SDV (e.g. 10-20%) may be substituted for 100% SDV without clinically significant differences in the error rates. Many of the data issues are identified and queried by Data Management following the application of screening rules and internal consistency checks without the extra effort required to check every variable against its source. Therefore, methods used to ensure database quality are not solely dependent on 100% SDV of the data but increasingly on various remote monitoring techniques.

The main focus of the GARFIELD VTE Registry is to capture the real-life management of Venous Thromboembolism (VTE) from the time of diagnosis and to follow up on outcomes in national care settings that treat VTE patients in the long term. This prospective multicentre registry will include 10,000 + VTE patients at 442 centres in 28 countries.

The registry protocol requires that:

- 10% of all CRFs are monitored against source documentation at sites
- All data modifications to the database will be recorded electronically in an audit trail
- Critical variables will be subjected to 5% audit during statistical analysis at study completion
- Registry will be conducted in accordance with the spirit of the Declaration of Helsinki

The document aims to provide an overview of the monitoring activities and QA processes which have been implemented to ensure the quality and accuracy of the data held in the TRI08889 registry. It has been developed to outline how data quality and accuracy are to be measured during the study period.

It is proposed GARFIELD VTE will employ a combination of QA and QC control techniques. These are:

1) Electronic database monitoring
2) Remote monitoring conducted by a Contract Research Organisation (CRO) – International Clinical Research Associates (iCRAs) and Study managers
3) Onsite monitoring, involving source data verification (SDV) protocol compliance and other quality assurance techniques.

2 Overview of TRI08889 Monitoring Strategy

2.1 Electronic database monitoring

Conducted on an ongoing basis at all sites, central statistical or remote electronic monitoring is designed to optimize on-site monitoring by providing information on common data entry errors, omissions and data quality. It represents a cost-effective approach to quality control and regulatory compliance. All patient data will undergo central monitoring at different intervals. The purpose of this activity is to:

- Identify outlying sites or implausible data.
- Identify sites with possible issues with data quality, completeness and late locking of data.
- To identify, target and select high risk sites for onsite monitoring.

2.1.1 Identification of implausible or outlying data

Although research misconduct may be difficult to detect, implausible data may be discovered using statistical techniques. Manipulated data tend to have little variance, no outliers or an abnormally flat or non-contiguous distribution. In this context we will undergo routine examinations for outliers and implausible values by examining univariate continuous data (i.e. Blood pressure, weight etc.) at sites.

2.1.2 Exploring data quality and completeness at site

The volume of data reported by different sites can vary considerably. Although in the majority of cases this will reflect variation in case mix or care settings, it may also indicate possible issues with underreporting. For example, summary statistics quantifying volumes of critical and non-critical data may help to identify poorly performing or less experienced sites with lower event and higher error rates than those of their counterparts.

On a quarterly basis, a surrogate measure of data quality and under-reporting (Alpha Score) will be evaluated for each Investigator site. A composite site performance score will be generated from Alpha scores, site recruitment against target, volume of unlocked data, volume of missing data, site inactivity and quality of site communication and a ranking produced of the best and worst performing sites.

2.2 Remote monitoring

Remote monitoring will be conducted by a CRO using data from 2 primary sources:

- The study database (CRF data located in an eCRF, Clinpal)
- The study site performance tracker containing information on recruitment rates, data query status and site CRO communications.

2.3 Onsite Monitoring

Approximately 42 sites will be selected globally for the Phase I face to face site monitoring. Monitoring for this phase is to be completed approximately by end of December 2016.

A minimum of 6 and maximum of 10 cases (patient medical records) will be identified within the eCRF that are critical to the clinical dataset and statistical analyses. These are known as critical variables. During a monitoring visit to the study site (onsite monitoring), source data verification (SDV) will be performed.

Cases will be selected using an electronic random case selection tool designed for this purpose. A list of these selected sites and patients ID will be provided to the monitor. When notified of the sites to be visited the monitor must complete the site visit tracker in SharePoint and must be updated twice a week.

A site may also be selected for an onsite monitoring visit including SDV if the study monitors or TRI Project Managers have concerns about the quality, accuracy or GCP compliance at that particular site.

Onsite monitoring, including SDV, will occur in multiple phases as depicted below:

Phase	Start Date	Cohort	Countries	*No. of Sites	No. of cases per site	Variables SDV'd	Total Cases SDV'd
1	Sep- 16	C1,C2	All, except Brazil, Mexico, UAE	42 (~10%)	6-10	100% SDV on first patient data following by partial SDV (Critical Variable)	~400 (40%)
2	Sep- 17	C1,C2	All	32 (~7%)	6-10	partial SDV (Critical Variable)	~300 (30%)
3	Sep- 18	C1,C2	All	32 (~7%)	6-10	partial SDV (Critical Variable)	~300 (30%)

*Final No. of sites and number of patients per sites will be determined during the randomization process.

The table depicts either actual or approximate start dates for each of the onsite monitoring phases. It should be noted that the number of cases monitored per site will vary dependent on the complexity of the cases and volume of data.

- Sites will be selected using a combination of Risk based selection and random selection
  - Site with more than 10 patients, patients ID will be further randomly selected.

2.4 Pre – Visit

Site visit request/confirmation letter requesting a site visit for on-site monitoring to include the following:

- ✓ Date of Visit
- ✓ Patient Medical Records to be monitored
- ✓ ISF Review
- ✓ Familiarize yourself with the Garfield VTE ISF Table of Content (ToC)
- ✓ Review eCRF
- ✓ Review Screening Log
- ✓ Review (CRO specific) template MVR

2.4.1 On site Visit Preparation

To prepare for on-site visits:

- ✓ Send site visit confirmation letter, per the company guidelines and as soon as the visit date is confirmed with site
- ✓ Inform sites patient ID's for the patients that will be monitored and data locked for SDV(at least 3 days prior to the visit)
- ✓ Establish whether any of the source data is in electronic format and whether access can be granted.
- ✓ Review the GARFIELD VTE ISF template in preparation for ISF review. This is placed on SharePoint or eTMF.
- ✓ Review eCRF

2.4.2 On-site Visit Plan

It is reported that on average, at least 6 patients could be source data verified during a one day monitoring visit. Assuming the onsite Monitoring Visit duration is 6 hours a typical day would be split as follows:

- ✓ **30 minutes:** introduction and closure
- ✓ **1 hour:** Investigator Site File review
- ✓ **4.5 hours:** SDV – 6-10 cases at each site. (**Please contact TRI if a longer monitoring visit is required)

2.5 Case selection strategy: All other Phases

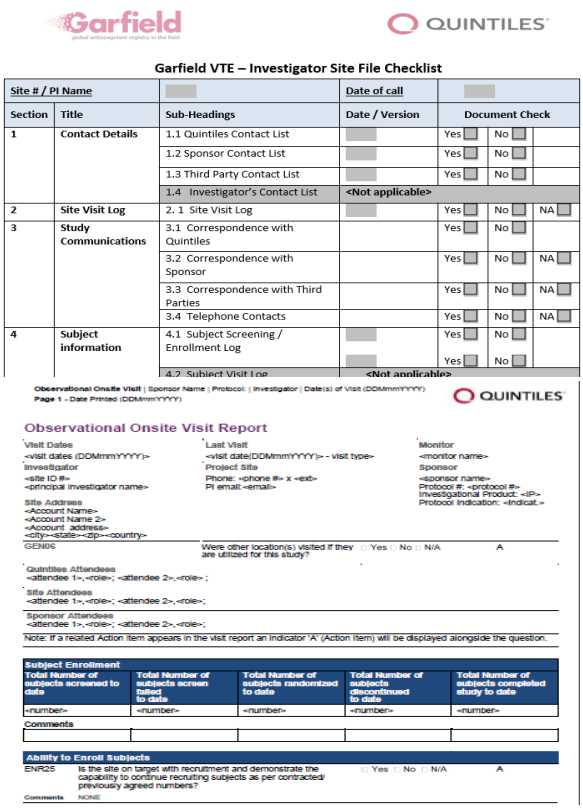
As shown in section 2.3 – A minimum of 6 patients will undergo SDV at a specific number of sites between September 2016 and September 2018 in order for the audit reports to be ready to be presented to the Audit Committee. There are 3 phases planned.

- **Protocol:** Source Data Verification will be undertaken in a minimum of 10% of all cases (n=1000 – As target number of patients is 10,000)
- **Solution**
  - 25% SDV Based on Random selection
  - 75% SDV Based on Risk assessment tool
- **Phase 1**
  - Random Site selection and Risk based site selection at 42 sites in 25 countries (100% SDV first patient Case Report Form following by partial SDV of), ~400 patients
- **Phase 2**
  - Targeted SDV based on risk based assessment tool at 32 sites in 28 countries, ~300 patients.
- **Phase 3**
  - Targeted SDV based on a modified risk based assessment tool at 32 sites in 28 countries, ~300 patients.

2.6 SDV and the eCRF database

2.6.1 Source Data Verification

1. Only cases (patient medical records) with locked data/milestones will be SDVd.
2. All locked data in the patient eCRF will be flagged to be source data verified.
   a) All deaths, events and lost to follow-up must be SDVd even if the record is not locked
   **Note: Treatment at diagnosis (baseline), treatment change/interruption for follow up events and missing events are critical data variables to be monitored on all selected patients.
3. If a blank field exists in the CRF
   a) The monitor is not required to search for the missing data in the source documentation.
   b) Missing data queries will be resolved using centralized monitoring procedures post the monitoring visit.
4. Variables to be checked are those data populated in Clinpal.
5. Key critical data variables to be checked are those data populated in Clinpal.
6. All cases (patient medical records) will be SDVd on critical variables in section 3.
7. Garfield VTE ISF Checklist and Onsite Visit Report will be used for the site level information. These documents must be completed only once per site. [CRO specific ISF checklist and Onsite Visit Report will be provided]



Garfield QUINTILES

Garfield VTE – Investigator Site File Checklist

Site # / PI Name			Date of call				
Section	**Title**	**Sub-Headings**	**Date / Version**	**Document Check**			
1	**Contact Details**	1.1 Quintiles Contact List		Yes ☐	No ☐		
		1.2 Sponsor Contact List		Yes ☐	No ☐		
		1.3 Third Party Contact List		Yes ☐	No ☐		
		1.4 Investigator's Contact List	<Not applicable>				
2	**Site Visit Log**	2. 1 Site Visit Log		Yes ☐	No ☐	NA ☐	
3	**Study Communications**	3.1 Correspondence with Quintiles		Yes ☐	No ☐		
		3.2 Correspondence with Sponsor		Yes ☐	No ☐	NA ☐	
		3.3 Correspondence with Third Parties		Yes ☐	No ☐	NA ☐	
		3.4 Telephone Contacts		Yes ☐	No ☐	NA ☐	
4	**Subject information**	4.1 Subject Screening / Enrollment Log		Yes ☐	No ☐		
		4.2 Subject Visit Log	<Not applicable>	Yes ☐	No ☐		

Observational Onsite Visit | Sponsor Name | Protocol: | Investigator | Date(s) of Visit (DDMmmYYYY)
Page 1 - Date Printed (DDMmmYYYY)

QUINTILES

Observational Onsite Visit Report

Visit Dates
<visit dates (DDMmmYYYY)>
Investigator
<site ID #>
<principal investigator name>
Site Address
<Account Name>
<Account Name 2>
<Account address>
<city><state><zip><country>

Last Visit
<visit date(DDMmmYYYY)> - visit type>
Project Site
Phone: <phone #> x <ext>
PI email:<email>

Monitor
<monitor name>
Sponsor
<sponsor name>
Protocol #: <protocol #>
Investigational Product: <IP>
Protocol Indication: <indicat.>

GEN06 Were other location(s) visited if they are utilized for this study? ☐ Yes ☐ No ☐ N/A A

Quintiles Attendees
<attendee 1>,<role>; <attendee 2>,<role> ;
Site Attendees
<attendee 1>,<role>; <attendee 2>,<role>;
Sponsor Attendees
<attendee 1>,<role>; <attendee 2>,<role>;

Note: If a related Action item appears in the visit report an indicator 'A' (Action Item) will be displayed alongside the question.

Subject Enrollment

Total Number of subjects screened to date	Total Number of subjects screen failed to date	Total Number of subjects randomized to date	Total Number of subjects discontinued to date	Total Number of subjects completed study to date
<number>	<number>	<number>	<number>	<number>

Comments

Ability to Enroll Subjects

ENR25 Is the site on target with recruitment and demonstrate the capability to continue recruiting subjects as per contracted/ previously agreed numbers? ☐ Yes ☐ No ☐ N/A A

Comments NONE

2.6.2 Post Visit Guidelines

Once the visit is completed:

- ✓ The completed checklist is to be posted on TRI SharePoint or CRO specific eTMF within 3 working days.
- ✓ The completed MVR is to be posted on SharePoint or CRO specific eTMF.
- ✓ Any critical findings should be reported to the Regional Project Managers at TRI immediately via email.
- ✓ Any follow up letters, TRI shall be copied in all correspondence.
- ✓ The sites must acknowledge the receipt of the follow-up letter.
- ✓ If there are any critical/major findings – this shall be escalated using a spreadsheet/guidelines as specified by TRI.

2.6.3 Electronic Source data Verification

An electronic SDV tool was created and validated within the eCRF for this purpose. This SDV tool will allow the monitors to compare and verify locked data in the electronic Case Report Form with that in the source documentation. The electronic SDV allows the monitor to verify data, track missing data issue queries or to indicate where the source data is not available. If an event of interest is found in the source but not registered in the eCRF this can be added to the database by sending a request to the site to enter the data onto the eCRF. The findings should be reported in MVR.

2.6.4 EDC Database modifications

All data modifications to the database will be recorded electronically in an audit trail.

2.7 Review of protocol and regulatory compliance.

During the onsite monitoring visits the CRAs will be checking the investigator site files to ensure all necessary approvals have been received, the correct versions of consent forms and the latest amendments have been implemented. They will also be ensuring site staff are consenting patients correctly and managing their data entry workloads, completing the eCRF as per protocol and recruiting eligible patients. All protocol deviations and incidences of GCP violation will be reported in the visit reports.

3 Definition of Critical Variables

Through a program-level risk assessment the following data points were deemed to be critical to the results presented in the summary tables and listings.

Baseline:

- Date of diagnosis
- Inclusion/Exclusion Criteria
- Date of consent
- Gender
- Date of birth
- Demographics
    - Weight
    - Height
- Acute VTE Episode
    - Classification of VTE
    - Site of DVT
    - Confirmatory Test
- Laboratory Test
    - Haemoglobin
    - Platelets
    - Creatinine
    - INR
        - Date
        - Value
- Risk Factor Associated with VTE
    - Underlying Risk factors associated with VTE
        - Previous episode of DVT and /or PE
        - Complication of VTE
        - VTE Episodes Since Diagnosis
    - Provoking Risk Factor
    - Special Risk Factor associated with VTE
        - Active Cancer selected- check Cancer form in the Event folder
        - 'Recent Bleed' or 'Both' selected- check Bleeding Event form in the Event folder
- Medications
    - Prior Relevant Medications

  - Panned VTE Treatment Strategy
    - VTE treatment strategy at time of diagnosis
    - Anticoagulant therapy
- VTE episodes since Diagnosis
  - Recurrent VTE episodes
  - Site of DVT

Follow-up

- 3,6,12,24,36 months Date of event
  - Date of Follow up
  - Reason for Withdrawl
- Recurrent VTE episodes
- Complication of VTE
  - Signs/Symptoms of CTEPH
  - diagnosis of CTEPH

Events:

- Stroke/TIA
  - Date of event
  - Event type (TIA/Stroke)
- Bleeding event
  - Date of event
  - Cause of bleed
  - Site of bleed
  - Severity of bleed
  - Intervention required
  - Outcome of bleed
  - Date of Bleed Resolved
- Myocardial Infarction/Acute Coronary Syndrome Date
  - Date of Event
  - Therapy recieved
- Cancer
  - Site of Primary Cancer
  - Date of diagnosis
  - Treatment
- Death
  - Date
  - Primary cause of death
  - Cardiovacular cause of death
  - Non cardiovascular cause of death
- Hospitalization
  - Date of hospitalization
  - Reason for hospitalisation
  - Type of contact(planned/unplanned)
  - Date of discharge

**Note: This list may be expanded or reduced in light of feedback from Onsite Monitoring and centralized monitoring procedures. Greyed out fields will not be SDVd in Phase 1 schedule.

3.1 Reporting, summarising and analysing data

A detailed report of findings from monitoring visits will be electronically generated through Clinpal. The report will generate a summary statistics for the following variables;

- Total number of fields monitored.
- Number of % of Critical data fields verified
- Number of fields queried
- Number of fields missing from specific pages
- Number of patients monitored in each country, region or investigator site
- Number of patients undergoing critical data SDV
- % of data for which a source was not available
- Number of blank fields.
- Number and type of critical events of interest missing from the ECRF

In addition to summarising performance for individual cases the report will also permit comparisons to be made between sites, countries and regions while adjusting for variation in the number of cases monitored and/ or number of total events recorded. These data will be included in regular audit committee reports.

4 Audit strategy and oversight

4.1 Internal Site Audits

In order to establish if our proposed quality assurance processes are robust and effective, results from all monitoring activities will be summarised for independent review by the GARFIELD VTE Audit Committee. Monitoring visit reports will be reviewed for individual clinical sites that were selected for onsite SDV. The Audit Report will be generated from Monitoring visit report data including information provided in Section 4.3.

4.2 Audit Committee

An Audit Committee will assume overall responsibility for providing guidance and oversight on the quality control and quality assurance of the data held in the registry. At 6-monthly intervals the committee will meet to review clinical site audit reports (See Appendix 4). Site audit reports will summarise feedback from centralized and onsite monitoring visits. As specified in the Audit Committee Charter, after/ at the meeting, the Chair will propose and communicate preventive or corrective measures to the Steering Committee. Audit Committee: TBC

4.3 Audit reports

Prior to each audit committee meeting the audit committee will be provided with detailed site audit reports. These reports will be collated from all sites where data has been reviewed either remotely

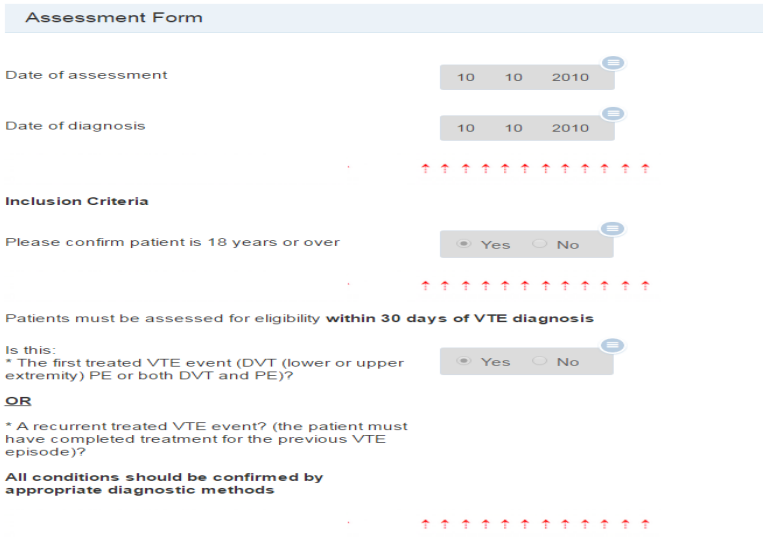
or during an onsite monitoring visit and the results summarised for each 6 month interval to include evidence and feedback on the following topics:

1. Regional and country level variation in measures of data quality and completeness.
2. Degree of accuracy observed in the reporting events of interest.
3. A description of all monitoring activities conducted during the observation period.
4. Summary statistics describing degree of concordance between CRF data and source docs.
5. Details of all protocol violations and deviations.
6. Incidence of non-compliance with ICH/GCP and any applicable local regulations
7. Accurate and complete information provided to the Sponsor.
8. Any other significant observations

Appendix 1 – Standard procedures for GARFIELD VTE Source Data Verification

Standard procedures for GARFIELD Source Data Verification:

1. Only patients with locked data will be SDV'd
    a. All locked data in the patients eCRF will be marked in the Clinpal system
    b. All data marked data fields should undergo source data verification.
    c. All death events, losses to followup or withdrawal of consent should be SDV'd regardless of whether or not the record is locked.
2. If a blank field exists in the CRF this will automatically be noted in the SDV checklist.
    a. The monitor is not required to search for the missing data in the source documentation.
    b. Missing data queries will be dealt with via Clinpal system and MVR.



3. Data from the first patient at each site will undergo 100% SDV.
4. Subsequent cases will undergo a limited scope of SDV on critical variables.

Appendix 2 – Source Document Checklist

- **To be used for 100% SDV only**
- To be captured in the Medical Records or other Source Notes. Please tick and use as guide only:

Signs and Symptoms of VTE	☐
Date of Diagnosis of VTE	☐
Confirmatory method of VTE	☐
Site of VTE	☐
Date of Informed Consent	☐
If Inclusion/Exclusion Criteria were met	☐
Care setting at diagnosis	☐
Height and Weight	☐
Smoking History	☐
Lab Tests (Haemoglobin, Creatinine, and Platelets if taken)	☐
Underlying Risk Factors associated with VTE	☐
History of Previous VTE events	☐
Initial Treatment Strategy (including procedures)	☐
Prior and Concomitant Relevant Medications	☐
Complications of VTE	☐
INR Tests (only the first three records to be checked)	☐
Recurrent VTE episode	☐
Current Bleeding Events (cause, site, severity, intervention required, transfusion required. only the first three events to be checked)	☐
Planned Hospitalisations (Additionally if patient is still currently in hospital)	☐
Cancer	☐
Signs and Symptoms of PTS	☐
Patients to complete baseline PROs following consent (SF-12, ACTS, and Villalta PTS Symptoms)	☐

Appendix 3 – Critical Variables and No. Of occurrence in the Data Base vs SDV Requirement

Critical Variables	No. of Occurrence in the Data base	SDV Requirement
Baseline:		
- Date of diagnosis	Once	Once
Inclusion/Exclusion Criteria	Once	Once
- Date of consent	Once	Once
- Gender	Once	Once
- Date of birth	Once	Once
- Demographics	Once	Once
○ Weight	Once	Once
○ Height	Once	Once
- Acute VTE Episode		
○ Classification of VTE	Once	Once
○ Site of DVT	Once	Once
○ Confirmatory Test	Once	Once
Laboratory Test		
○ Haemoglobin	Multiple	First Data value only
○ Platelets	Multiple	First Data value only
○ Creatinine	Multiple	First Data value only
○ INR	Multiple	First Data value only
▪ Date	Multiple	First Data value only
▪ Value	Multiple	First Data value only

Critical Variables	No. of Occurrence in the Data base	SDV Requirement
- Risk Factor Associated with VTE		
○ Underlying Risk factors associated with VTE	Once	Once
▪ Previous episode of DVT and /or PE	Multiple	First Data Value only
▪ Complication of VTE	Multiple	First Data Value only
▪ VTE Episodes Since Diagnosis	Multiple	First Data Value only
○ Provoking Risk Factor	Once	Once
○ Special Risk Factor associated with VTE	Once	Once
• Active Cancer selected- check Cancer form in the Event folder	Multiple	First Data value in the Baseline and Event folder
• 'Recent Bleed' or 'Both' selected- check Bleeding Event form in the Event folder	Multiple	First Data value in the Baseline and Event folder
- Medications		
○ Prior Relevant Medications	Once	Once
○ Planned VTE Treatment Strategy	Once	Once
▪ VTE treatment strategy at time of diagnosis	Once	Once
▪ Anticoagulants therapy	Once	Once
▪ Surgical/Mechanical Interventions	Once	Once
▪ Compression Therapy	Once	Once
- VTE episodes since Diagnosis	Once	Once
○ Recurrent VTE episodes	Multiple	First three Data value only
▪ Site of DVT	Multiple	First three Data value only

Critical Variables	No. of Occurrence in the Data base	SDV Requirement
Follow-up:		
3,6,12,24,36 months	Once	once
○ Date of Follow up	Once	once
○ Reason for Withdrawl	Once	once
○ Recurrent VTE episodes	Multiple	First three Data value only
○ Complication of VTE	Multiple	First three Data value only
▪ Signs/Symptoms of CTEPH	Multiple	First three Data value only
▪ diagnosis of CTEPH	Multiple	First three Data value only
Events:		
- Stroke/TIA	Multiple	First three Data value only
○ Date of event	Multiple	First three Data value only
○ Event type (TIA/Stroke)	Multiple	First three Data value only
- Bleeding event	Multiple	First three Data value only
○ Date of event	Multiple	First three Data value only
○ Cause of bleed	Multiple	First three Data value only
○ Site of bleed	Multiple	First three Data value only
○ Severity of bleed	Multiple	First three Data value only
○ Intervention required	Multiple	First three Data value only
○ Outcome of bleed	Multiple	First three Data value only
○ Date of Bleed Resolved	Multiple	First three Data value only

Critical Variables	No. of Occurrence in the Data base	SDV Requirement
- Myocardial Infarction/Acute Coronary Syndrome	Multiple	First three Data value only
○ Date of Event	Multiple	First three Data value only
○ Therapy recieved	Multiple	First three Data value only
- Cancer	Multiple	First three Data value only
○ Site of Primary Cancer	Multiple	First three Data value only
○ Date of diagnosis	Multiple	First three Data value only
○ Treatment	Multiple	First three Data value only
- Death	Once	Once
○ Date	Once	Once
○ Primary cause of death	Once	Once
○ Cardiovacular cause of death	Once	Once
○ Non cardiovascular cause of death	Once	Once
- Hospitalization	Multiple	First Data value only
○ Date of hospitalization	Multiple	First Data value only
○ Reason for hospitalisation	Multiple	First Data value only
○ Type of contact(planned/unplanned)	Multiple	First Data value only
○ Date of Discharge	Multiple	First Data value only

Appendix 4 - Clinical site audit summary report format

Global Anticoagulant Registry in the FIELD observing treatment and outcomes in patients with treated acute Venous Thromboembolic Events (GARFIELD – VTE) in the real world.

The clinical site audit commenced on *[Insert date*] and was completed *[Insert date].* The review included 100% remote central monitoring of all sites in addition to source data of X out of X enrolled patients.

Audit objectives were to:

1. Generate summary statistics for data quality to target best and worst performing sites.
2. Explore the distribution of data from the highest recruiting sites to identify unusual or abnormally distributed data.
3. Through onsite monitoring visits motivate sites to complete all pending CRFs and complete follow-up visits in a timely manner.
4. Identify potentially unreported events of interest.
5. Evaluate the quality of source documentation at sites.
6. Evaluate the degree of concordance between CRF and source data using onsite source data verification / monitoring.
7. Review the overall quality of study management at the investigator sites.
8. To determine key data points warranting SDV within phases of the strategic monitoring plan.

The following sections will summarise audit findings in relation to following audit objectives:

1. Evaluation of regional / country level variation in Alpha scores
2. Exploration of site level data for abnormally distributed or implausible data.
3. Estimate of the accuracy of reporting of events of interesting in the eCRF
4. Site Monitoring activities - appropriate SDV
5. Correct application of the protocol at all sites.
6. Provision of adequate training to the site study personnel with regards to the protocol and GCP for correct execution of the protocol
7. Issues with non-compliance with GCP and local regulations
8. Miscellaneous Observations