A Multi-center, Single Arm Post-market Clinical Study to Confirm Safety and Performance of PuraStat® Absorbable Haemostatic Material for the Management of Bleeding In Vascular Surgery

Statistical Analysis Plan

Versions	Date	Documents used	Author	Validation
Version 3.0	02DEC2019	- VASC-PMCF_Protocol_V6.0_19March2019_Final - CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	Jeanne GERVAIX	Marie-Christine REYMOND
Version 2.1	02DEC2019	- VASC-PMCF_Protocol_V6.0_19March2019_Final - CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	Jeanne GERVAIX	Marie-Christine REYMOND
Version 2.0	21JUN2019	- VASC-PMCF_Protocol_V5.0_24Sept2018_Final - CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	Jeanne GERVAIX	Marie-Christine REYMOND
Version 1.2	13JUN2019	- VASC-PMCF_Protocol_V5.0_24Sept2018_Final - CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	Jeanne GERVAIX	Marie-Christine REYMOND
Version 1.1	20MAY2019	- VASC-PMCF_Protocol_V5.0_24Sept2018_Final - CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	Jeanne GERVAIX	Marie-Christine REYMOND
Version 1.0	31JAN2019	- VASC-PMCF_Protocol_V5.0_24Sept2018_Final	Jeanne	Marie-

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		- CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	GERVAIX	Christine REYMOND
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Version 0.2	02OCT2018	- VASC-PMCF_Protocol_V4.0_06March2018_Final - CRF Version 1 – 15FEB2017CRF Version 2 – 27AUG2018	Jeanne GERVAIX	Marie-Christine REYMOND
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SIGNATURE PAGE

A Multi-center, Single Arm Post-market Clinical Study to Confirm Safety and Performance of PuraStat® Absorbable Haemostatic Material for the Management of Bleeding In Vascular Surgery

Version 3.0

3-D MATRIX EUROPE SAS

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

AE	Adverse Event
ADE	Adverse Device Effect
ASA	American Society of Anesthesiologists
BH	Bio-active Haemostatic
BMI	Body Mass Index
CA	Competent Authority
CABG	Coronary Artery Bypass Grafting
CBC	Complete Blood Count
CRO	Clinical Research Organization
DD	Device Deficiency
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
GI	Gastroinstestinal
HAS	Haute Autorité de Santé (French National Authority for Health)
hCG	Human Chorionic Gonadotropin
IFU	Instructions For Use
ITT	Intent-To-Treat
Min	Minute
mL	Millilitre
NBH	Non-Bioactive Haemostats
NCA	National Competent Authority
NSQIP	National Surgical Quality Improvement Program
PIC	Patient Informed consent
PI	Principal Investigator
PP	Per-Protocol
PMCF	Post-Market Clinical Follow-up
PTFE	Polytetrafluoroethylene
sec	Second
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SOP	Standard Operating Procedure
TTH	Total Time-to-Hemostasis
USADE	Unanticipated Serious Adverse Device Effect

1. OVERVIEW

This statistical analysis plan (SAP) describes the planned statistical analyses of the data collected in the course of the PuraStat-002-VASC clinical study.

This SAP provides additional details concerning the statistical analyses outlined in the protocol (version 5.0 dated 24 September 2018). The purpose of the SAP is to ensure the credibility of the study findings by pre-specifying the statistical approaches to the analysis of study data.

1.1. Study Objective

The objective of this study is to confirm the safety and the performance of PuraStat® in the management of bleeding in vascular surgery.

1.2. Study Design

This study is a prospective, multi-center, single arm post-marketing study to confirm safety and performance data on PuraStat® for the management of bleeding in vascular surgery.

Up to 10 clinical sites are expected to be involved in this post-market clinical study.

During 25 months, sixty-five (65) patients undergoing elective carotid endarterectomy either by direct closure (without the use of patch), or by patch reconstruction or eversion technique will be enrolled. The patients are followed at 1 month (± 15 days) after the operation.

1.3. Study Plan

1.3.1. Patient's Follow-up

5 visits are scheduled:

- Visit 1: Pre-operative consultation
- Visit 2: Surgery
- Visit 3: 24 hours post-procedure
- Visit 4: Discharge
- Visit 5: 1 month (± 15 days) post-operative follow-up

1.3.2. Study Device use

PuraStat® is a Class III medical device and is CE-marked since January 2014.

PuraStat® is a synthetic haemostatic material in the form of a prefilled syringe, filled with a clear, 2.5% concentration aqueous peptide solution, sterilized by aseptic filtration. The outer surface of the syringe and inner surface of the blister pack are sterilized by ethylene oxide (see current version of the IFU).

PuraStat® is indicated for haemostasis in the following situations encountered during surgery, when haemostasis by ligation or standard means is insufficient or impractical:

- Bleeding from small blood vessels and oozing from capillaries of the parenchyma of solid organs
- Oozing from vascular anastomoses
- Bleeding from small blood vessels and oozing from capillaries of the GI tract following surgical procedures

PuraStat is also indicated for the reduction of delayed bleeding following gastrointestinal endoscopic submucosal dissection (ESD) procedures in the colon.

1.3.3. Study Assessments

The following flowchart applies to the study:

Parameter/Examination	Prior to operation	Surgery	24 hours post-procedure	Discharge	Post-operative one month follow-up visit (+/- 15 days) (physical or phone call visit)
Signed Patient informed consent	X				
Demography, Medical history	X				
Physical exam	X				
Blood tests including CBC, Coagulation tests	X		X	When necessary	When necessary
β-hCG test	X				
Patient inclusion/exclusion criteria	X				
Intra-operative criteria		X			
Time-to-hemostasis*		X			
Blood loss (mL)		X			
Drainage volume (mL)			X	X	
Transfusion of blood products (if any) i.e blood loss by recording the blood product(s) and/or substitute(s) administered (mL)		X	X	X	
Information regarding the use of PuraStat® including ease of use of PuraStat®		X			
Other operative data		X			
Surgical revision for bleeding		X	X	X	X
Adverse Event, adverse device effect reaction		X	X	X	X
Concomitant medication related to coagulation disorder(s)	X	X	X	X	X
Length of hospital stay					X

* Time-to-haemostasis (min, seconds) will be measured from the first application of PuraStat® to a bleeding site after clamp release, until all bleeding at that site has ceased. In case of rebleeding of the treated sites and additional application of PuraStat®, the total time-to-haemostasis (TTH) will be calculated by the addition of TTH1+ $TTH_{(n+1)}$, where TTH1+ $TTH_{(n+1)}$ are the time to haemostasis after each application of PuraStat®.

2. STATISTICAL METHODS

2.1. General Statistical Considerations

2.1.1. Handling Missing Data

In order to provide unbiased and informative findings, no replacement of missing values is planned for any parameters.

2.1.2. Descriptive Statistics in Summary Tables

- *Continuous variables* will be summarized using standard quantitative statistics: number of non-missing observations, mean, standard deviation, median, quartiles and range (minimum and maximum observed values). The number of missing observations will also be specified.
- *Categorical variables* will be summarized using classical frequency statistics: number of non-missing observations and percentages by categories. Percentages will be calculated on the number of non-missing observations, and will be displayed using one decimal. The number of missing observations will also be specified.
- Confidence intervals:

The two-sided 95% confidence intervals (CI) will be presented for each primary and secondary endpoints.

For the primary endpoint, the 95% CI around the mean will be calculated.

For the categorical variables, 95% asymptotic CI will be presented if the theoretical assumptions are verified. If this is not the case, and the proportion is 0% or 100%, then the Agresti-Coull CI will be presented instead. In all other cases, the exact CI will be presented.

2.1.3. Interim Analysis

No interim analysis is planned.

2.1.4. Data Listings

Patient data listings will be selected data supportive of summary statistical tables, including derived/calculated data from statistical process. These key data listings will be performed on selected analysis sets according to the corresponding statistical tables.

2.2. Sample size calculation

The aim of this trial is to confirm the safety and the performance of PuraStat® in the management of bleeding in vascular surgery.
No formal statistical hypothesis has been conducted to derive the sample size since studies on peripheral vascular surgery selected in the French National Authority for Health (Haute Autorité de Santé) (HAS) report shows an extreme variability in Time-to-Hemostasis (reported results being between 25 s to 22 min). As a result, the establishment of an objective performance criterion is difficult and matter of discussion.

With a sample size of 65 treated subjects at the time of statistical reporting, an acceptable accuracy will be reached for all criteria, and in particular for the primary endpoint. Indeed, such a sample should ensure that all theoretical assumptions necessary to derive asymptotic 95% confidence intervals will be verified.

2.3. Analysis Sets

2.3.1. Definition of patient populations

2 populations will be defined:

- The Full Analysis Set (FAS) population will include all patients enrolled in the study who have signed their informed consent.
- The Intent-to-Treat (ITT) population will include all patients from the FAS population with at least one treated site with PuraStat®.
- The Per-Protocol (PP) population will include all patients from the ITT population excluding the subjects with at least one major deviation.

Assignment of patients to populations will be reviewed and approved by the sponsor before the database lock.

If less than 10% of the patients present at least one major deviation, primary endpoints will be analyzed on ITT and PP populations. Secondary endpoint will be analyzed only for ITT population.

2.3.2. Protocol deviations

On a case-by-case basis, all protocol deviations will be classified as “minor” or “major” according to the possible impact expected on primary results. All deviations will be reviewed and classified as major or minor by the sponsor with the data manager and the statistician from Medpass before the database lock. The list of major deviations (see below) will be updated in the SAP if needed.

Patients meeting at least one of the following major deviations will be excluded from the PP population:

- Non respect of Inclusion/Exclusion Criteria
- Non respect of Intra-operative Inclusion/Exclusion Criteria
- The site did not use the stopwatch to measure time to haemostasis

All protocol deviations other than those defined in this section will be considered as minor and will not lead to patient exclusion from the PP population.

2.4. Statistical Analyses

All statistical analysis will be presented on the ITT population except if specified otherwise.

Safety analysis will be done on the ITT population. If subjects excluded from the ITT population experimented adverse events, a specific summary will be provided (tables and/or listings). Performance analysis will be done on the ITT population.

The 95% 2-sided confidence intervals around the median and/or the mean will be presented for primary and secondary endpoints, when appropriate.

2.4.1. Patient Disposition and Follow-up

The number of patients included in each population and the reasons of exclusion from Full Analysis Set (FAS) population will be presented together with the end of participation reasons.

The number of patients present at each visit will be presented on the ITT population.

2.4.2. Preoperative Consultation Characteristics

Descriptive statistical data will be used to draw up a recapitulation of the characteristics of the patients at the time of enrolment.

- Demographics: age (at time of signature of the consent), sex/gender, height, weight and BMI.
- Medical history: smoking, status (current and former) and number of packs/year, diabetes, type and treatment, renal failure, Family history and specification, ASA score, Other vascular condition and description and Other and description.
- Physical exam: status, Systolic and diastolic blood pressures (mmHg), heart rate (BPM) and temperature (°C).
- Laboratory: Complete blood count (hematocrit (%), hemoglobin (g/dL), RBC, WBC (neutrophils, lymphocytes, monocytes, eosinophils, basophils) and blood platelet count) and blood coagulation tests (Quick Prothrombin time (PT) (sec)and Fibrinogen (g/L), Partial Thromboplastin time (PTT).
- Pregnancy test: β-hCG test and reason of non application (in a listing).

2.4.3. Operation Characteristics

Descriptive statistical data will be used to draw up a recapitulation of the characteristics of the patients and the site at time of surgery.

The following data will be presented:

- Operation general information: duration of vascular surgery procedure, type of technique, type of Patch and specification, type of clamp and time of clamp (min:sec) and type of haemostasis preferably used before PuraStat®,Quality of vessel (at suture/anastomosis site)
- Total-Time-to hemostasis: total time to hemostasis will be presented in the primary analysis section
- Blood loss during the surgery and Transfusion of blood products (if any):
  (Blood loss assessed during the operation (mL) and Transfusion of blood products (if any) i.e blood loss by recording the blood product(s) and/or substitute(s) administered (mL) necessary during surgery will be presented in the secondary analysis section)
- Condition before application of PuraStat®: severity of bleeding compared to “normal” (mild, moderate, severe)
- Application information:
  - per patient: total number of applications, total amount of product used (mL), total number of syringes used, any persistent bleeding or recurrent bleeding after haemostasis with PuraStat®, PuraStat® applied to the bleeding site after the vessel clamps have been removed, Stopwatch use to measure time to haemostasis
- Condition after application:
- per patient: status post application, severity compared to before application (identical, decreased, worse), action necessary to stop the bleeding (if yes, suture, electrocoagulation, clip, argon laser, other (if other, description) Assessment of product use: ease of preparation, Application system (syringe and/or nozzle), application of gel, Best properties of PuraStat® (Transparency, Use in narrow spaces, Ease of preparation, Other/specification, and If 1mL of PuraStat® used is sufficient

  (Overall ease of use of the product will be presented in the secondary analysis section)

The mean total and the corresponding 95% CI will be represented for: Duration of vascular surgery procedure, blood loss (mL) assessed during the operation (per patient), Total number of unit(s) of blood transfused during the operation (unit(s)), Number of unit(s) of blood transfused before first application.

2.4.4. 24 hours post-operation Characteristics

Descriptive statistical data will be used to draw up a recapitulation of the characteristics of the patients at 24 hours post-operation: The following data will be presented:

- Placement of a drain since last visit

- Drainage volume until drain removal (mL)
- Transfusion of blood products necessary since last visit
- Presence of haematoma
- Complete blood count and Blood coagulation

2.4.5. Discharge Characteristics

Descriptive statistical data will be used to draw up a recapitulation of the characteristics of the patients at discharge. The following data will be presented:

- Placement of a drain since last visit,
- Drainage volume until drain removal (mL),
- Transfusion of blood products necessary since last visit,
- Presence of haematoma.
- Complete blood count and Blood coagulation

2.4.6. 1 month post-operation Characteristics

Descriptive statistical data will be used to draw up a recapitulation of the characteristics of the patients at 1 month post-operation. The following data will be presented:

- Complete blood count and Blood coagulation

2.4.7. Concomitant Medications

Before the database frozen, a meeting will be organized with the data manager of Medpass International and the Clinical Affairs of 3-D Matrix to review and verify all the concomitant medications.
The concomitant medications will be homogenized during this meeting. Database will be corrected either by self evident corrections, or by issuing queries to investigators, as appropriate.
A listing will be provided to present all medications related to coagulation disorder(s).

2.4.8. Primary Endpoint Analysis

Primary endpoint analysis will be done on the ITT population.
Primary endpoint will be the Total Time-to-Haemostasis (min, seconds), measured from the first application of PuraStat® to a bleeding site after clamp release, until all bleeding at that site has ceased.
N.B: The area of bleeding to be studied will be identified after the vessel clamps are removed.
Counting the time-to-haemostasis begins when the surgeon starts applying PuraStat® on the area of bleeding. Several application of PuraStat® might be needed to obtain the initial haemostasis.
Haemostasis will be considered successful when there is no visible bleeding on the treated area.

In case of rebleeding of the treated sites and additional application of PuraStat®, the total time-to-haemostasis (TTH) will be calculated by the addition of TTH1+ $TTH_{(n+1)}$, where TTH1+ $TTH_{(n+1)}$ are the time to haemostasis after each application of PuraStat®.

The total Time of haemostasis will be measured thanks to a stopwatch.
The mean total TTH (in minutes, in seconds and in MM:SS) and the corresponding 95% bilateral CI will be presented.
The following analyzes will be also performed:

- Number of patients per range of TTH (according to the distribution of TTH, appropriate classes will be defined)
- TTH per severity of bleeding
- TTH per number of applications of PuraStat

2.4.9. Secondary Endpoints analysis

2.4.9.1. Performance endpoints

Performance endpoints will be done on the ITT population and will be presented together with the corresponding 95%CI:

- Blood Loss assessed during the operation (mL)
- Drainage volume (mL) (if any) at 24 hours post-operative visit, discharge visit and overall
- Rate of transfusion of blood products (if any) at surgery, 24 hours post-operative visit, discharge visit and overall
- Ease of use of PuraStat®

2.4.9.2. Safety endpoints

Safety endpoints will be done on the ITT population.

If subjects excluded from the ITT population experimented adverse events, a specific summary will be provided.

For all presence/absence endpoints, the 95% 2-sided exact binomial confidence intervals will be presented.

All safety data will be assessed by analysing the following adverse events occurring during the procedure, between the operation and the 24 hours post-operation, between the operation and the 15 days post-operation and between the operation and the 1 month post-operation and reported as follows:

- Rate of revision for bleeding
- Number of AEs/SAEs and corresponding number and percentage of patients
- Number of device related AEs/SAEs and corresponding number and percentage of patients
- Number of unanticipated device related SAEs and corresponding number and percentage of patients. An unanticipated AEs will be identified using the current IFU which documents the anticipated AE.
- The overall mortality rate

The adverse events at 1 month post-operation will be analysed according to the study window from the protocol, that is to say, all adverse events occurring between the date of the procedure and 1 month + 15 days following the implant will be included.

The total length of hospital stay during the study will be also analysed.

2.4.10. Other safety analysis

Other safety analysis will be done in the same way of the safety endpoint analysis. All other safety data will be presented and reported as follows:

- Number of PuraStat® application procedure related AEs/SAEs and corresponding number and percentage of patients
- Number of vascular procedure related AEs/SAEs and corresponding number and percentage of patients

2.4.11. Device deficiency

A listing will be provided to present all device deficiency.

2.5. Derived Criteria Calculation

Following section 2.1.1.Handling Missing Data, if at least one of the items needed to calculate a derived criteria is missing then the corresponding derived criteria will be considered as missing.

- Derived criterion “FAS” will be defined as follows:

  If the date of signature of the consent form is filled then “FAS” = “YES”, else “FAS” = “NO”.
- Derived criterion “ITT” will be defined as follows:

  If “FAS” = “YES” and “Was PuraStat used during the operation? “= “YES” then “ITT” = “YES”, else “ITT” = “NO”.
- Derived criterion “PP” will be defined as follows:

  If “ITT” = “YES” and the subject has no major deviation then “PP” = “YES”, else “PP” = “NO”.
- Derived criterion “Duration of vascular surgery” will be calculated as follows:

  “Duration of vascular surgery” = “end time of vascular surgery procedure” – “start time of vascular surgery procedure”.
- Dervied criterion “Quantity of blood product(s) and or substitute(s)” will be defined as follows:

  Sum of Blood product quantity 1 (mL), Blood product quantity 2 (mL) and Blood product quantity 3 (mL)
- Dervied criterion “Total number of application(s)” will be defined as follows:

  “Total number of application(s)” = 1,

  If “Other application needed at same site” = “Yes” then “Total number of application(s)” = “Total number of application(s)” + 1.
- Derived criterion “Adverse event” within the studied period will be defined as follows:

  If at least one AE occurred within the studied period then “Adverse event” = “YES”, else “Adverse event” = “NO”.
- Derived criterion “Device related” AE/SAE will be defined as follows:

  If “Relation to the PuraStat® medical device” = “Possible”, “Probable” or “Causal relationship ” then “Device related” = “YES”, else “Device related” = “NO”.
- Derived criterion “PuraStat® application procedure related” AE/SAE will be defined as follows:

  If “Relation to the PuraStat® application procedure” = “Possible”, “Probable” or “Causal relationship” then “PuraStat® application procedure related” = “YES”, else “PuraStat® application procedure related” = “NO”.
- Derived criterion “PuraStat® vascular procedure related” AE/SAE will be defined as follows:

  If “Relation to the vascular procedure” = “Possible”, “Probable” or “Causal relationship ” then “Vascular procedure related” = “YES”, else Vascular procedure related” = “NO”.

- Derived criterion “Unanticipated device related” AE/SAE will be defined as follows:
  If “Expected event (See Current IFU)” = “NO” and “Device related” = “YES” then “Unanticipated device related” = “YES”, else “Unanticipated device related” = “NO”.
- An event will be considered as having occurred
  - “during the procedure” if it occurs during the procedure,
  - “at 24 hours post-operation” if it occurs between the procedure (included) and 1 day after the procedure,
  - “at 15 days post-operation” if it occurs between the procedure (included) and 15 days after the procedure,
  - “at 1 month post-operation” if it occurs between the procedure (included) and 45 days (1 month + 15 days) after the procedure.
- Derived criterion “Death” will be defined as follows:
  If Serious Adverse Event “Led to death” is ticked in AE form or “Death” is ticked in the study termination form then “Death” = “YES”, else “Death” = “NO”.

3. STATISTICAL SOFTWARE

All statistical outputs (summary tables and data listings) will be generated using SAS® version 9.4.

4. STATISTICAL TABLES AND LISTINGS (TABLE OF CONTENTS)

4.1. Statistical Tables

Patient Disposition and follow-up

Table 1: Patient populations and reasons of end of participation (Type 1)
Table 2: ITT patients present at each visit and reasons of end of participation (Type 1)
Table 3: Visit out of window (type 1)

Preoperative consultation characteristics

Table 4: Age at time of signature of the consent (Type 2)
Table 5: Gender/Sex (Type 3)
Table 6: Height, weight and BMI (Type 2)
Table 7: Status of the physical exam (Type 2)
Table 8: Systolic and diastolic blood pressure (Type 2)
Table 9: Heart rate (Type 2)
Table 10: Temperature (Type 2)
Table 11: Medical history (Type 3)
Table 12: Complete blood count and Blood coagulation (Type 2)
Table 13: Pregnancy test (Type 2)

Operation characteristics

Operation general information

Table 14: Duration of vascular surgery (Type 2)

Condition before application of PuraStat®

Application information

Condition after application of PuraStat®

Assessment of product use

Follow-up characteristics

24 hours post-operation

Discharge

1 month post-operation

Primary analysis

Table 46: Total time-to-haemostasis (Type 2)
Table 47: Number of patients per range of TTH (Type 3b)
Table 48: TTH per severity of bleeding (Type 2b)
Table 49: TTH per number of applications of PuraStat (Type 2b)

Secondary analysis

Performance endpoints

Table 50: Blood Loss assessed during the operation (mL) (Type 2)
Table 51: Drainage volume (mL) at 24 hours post-operative and discharge (Type 2b)
Table 52: Total Drainage volume (mL) (overall) (Type 2)
Table 53: Rate of transfusion of blood products at surgery, 24 hours post-operative, discharge visit (Type 3b)
Table 54: Rate of transfusion of blood products (overall) (Type 3)
Table 55: Quantity of blood product(s) and or substitute(s) at operation, 1-day post-operative visit, 5-7 days post-operative visit (Type 2b)
Table 56: Quantity of blood product(s) and or substitute(s) (overall) (Type 2)
Table 57: Ease of use of PuraStat® during surgery (Type 3)

Safety endpoints

Table 58: Rate of revision for bleeding (Type 3)
Table 59: All AEs (Type 3)
Table 60: All SAEs (Type 3)
Table 61: All device related AEs (Type 3)
Table 62: All device related SAEs (Type 3)
Table 63: All Unanticipated device related SAEs (Type 3)
Table 64: All AEs (Type 4)
Table 65: All SAEs (Type 4)
Table 66: All device related AEs (Type 4)
Table 67: All device related SAEs (Type 4)
Table 68: All Unanticipated device related SAEs (Type 4)
Table 69: Mortality rate (Type 3)
Table 70: Length of hospital stay (Type 2)
The tables 58 to 69 will be done by visit as described in Part 2.4.8.2.

Other Safety analysis

Table 71: All PuraStat® application procedure related AEs (Type 3)
Table 72: All PuraStat® application procedure related SAEs (Type 3)
Table 73: All vascular procedure related AEs (Type 3)
Table 74: All vascular procedure related SAEs (Type 3)
Table 75: All PuraStat® application procedure related AEs (Type 4)
Table 76: All PuraStat® application procedure related SAEs (Type 4)
Table 77: All vascular procedure related AEs (Type 4)
Table 78: All vascular procedure related SAEs (Type 4)
The tables 71 to 78 will be done by visit as described in Part 2.4.8.2.

In case some subjects excluded from the ITT population experimented adverse events, Table 59, 60, 64, 65 and 69.

4.2. Listings

Patient Dispositions and Follow-up

Listing 1: Patients' dispositions

Preoperative Consultation Characteristics

Listing 2: Patients' characteristics at baseline (prior to operation)
Listing 3: Complete blood count and blood coagulation tests
Listing 4: Pregnancy test

Operation Characteristics

Listing 5: Procedure general information
Listing 6: Procedure characteristics
Listing 7: Assessment of product use

Post-operative bleeding

Listing 8: Assessment of post-operative bleeding

Follow-up characteristics

Listing 9: Patients' follow-up characteristics

Concomitant medication

Listing 10: Concomitant medication related to coagulations disorder(s)

Primary endpoint analysis

Listing 11: Primary endpoint

Secondary analysis

Listing 12: Patients' secondary endpoints
Listing 13: Revisions for bleeding

Safety analysis

Listing 14: Adverse events

Device deficiency

Listing 15: Device deficiency

5. LAYOUT OF THE STATISTICAL TABLES

5.1. Type 2: Quantitative variables

Variable	N	Missing	Mean	S.D.	Median	Min,Max	Q1-Q3	95% CI*
Variable Name	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	XX.X – XX.X	[XX.X ; XX.X]

* If needed

5.2. Type 2b: Quantitative variables by group/visit

Variable	Group	N	Missing	Mean	S.D.	Median	Min,Max	Q1-Q3	95% CI*
Variable Name	Group1 (visit 1)	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	XX.X – XX.X	[XX.X ; XX.X]
	Group 2 (visit 2)	XX	XX	XX.X	XX.X	XX.X	XX.X, XX.X	XX.X – XX.X	[XX.X ; XX.X]

* If needed

5.3. Type 3: Qualitative variables

		Population (N=XX)
Variable Name	N	XX
	Mod 1	XX (XX.X %)
	95% CI (Mod 1)*	[XX.X% - XX.X%]
	Mod 2	XX (XX.X %)
	95% CI (Mod 2)*	[XX.X% - XX.X%]
	Mod n	XX (XX.X %)
	95% CI (Mod n)*	[XX.X% - XX.X%]
	Missing	XX

* If needed

5.4. Type 3b: Qualitative variables by group/visit

		Group 1 (visiti1) (N=XX)	… (N=XX)	Group N (visit N) (N=XX)
Variable Name	N	XX	XX	XX
	Mod 1	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	95% CI (Mod 1)*	[XX.X% - XX.X%]	[XX.X% - XX.X%]	[XX.X% - XX.X%]
	Mod 2	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	95% CI (Mod 2)*	[XX.X% - XX.X%]	[XX.X% - XX.X%]	[XX.X% - XX.X%]
	Mod n	XX (XX.X %)	XX (XX.X %)	XX (XX.X %)
	95% CI (Mod n)*	[XX.X% - XX.X%]	[XX.X% - XX.X%]	[XX.X% - XX.X%]
	Missing	XX	XX	XX

* If needed

5.5. Other

5.5.1. Type 1: Conditional variable

Variable 1 / Variable 2	Population (N=XX)
Var 1 – Mod 1	XX (XX.X %)
Var 2 – Mod 1	XX (XX.X %)
Var 2 – Mod 2	XX (XX.X %)
Var 2 – Mod 3	XX (XX.X %)
Var 1 – Mod 2	XX (XX.X %)
Var 2 – Mod 1	XX (XX.X %)
Var 2 – Mod 2	XX (XX.X %)
Var 2 – Mod 3	XX (XX.X %)
Var 1 – Mod n	XX (XX.X %)
Var 2 – Mod 1	XX (XX.X %)
Var 2 – Mod 2	XX (XX.X %)
Var 2 – Mod 3	XX (XX.X %)

5.5.2. Type 4: Adverse events

	n (1)	% (2)	NAE (3)	% of events
ALL	8	53.3	16	16 (100.0%)
Adverse event 1	3	20.0	3	3 (18.8%)
Adverse event 2	3	20.0	3	3 (18.8%)
Adverse event n	2	13.3	2	2 (12.5%)

(1) number of patients with at least one event
(2) corresponding percentage of patients (N/total number of patient)
(3) number of events