SeraSeal®
4001

A Multi-center, Single Blinded, Parallel,
Randomized, Hemostatic Agent Clinical Study

Final Clinical Report

Victor Mendizabal, M.D.
Edgardo Rebagliati Martins National Hospital
Principal Investigator

Felipe Plaza, M.D.
Edgardo Rebagliati Martins National Hospital
Monitor

Jose Carlos Gutierrez, M.D.
Edgardo Rebagliati Martins National Hospital
Monitor

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Table of Contents

List of Tables

List of Figures

List of Graphs

List of Appendices

List of Abbreviations

1	a	artery
2	AC	anticoagulant
3	ad	adipose
4	ANOVA	Analysis of Variance
5	APTT	Activated Partial Thromboplastin Time
6	b	bone
7	BP	Blood Pressure
8	bpm	Beats per minute
9	CBC	Complete Blood Count
10	CT	clotting time
11	d	dermis
12	ECG	Electrocardio graph
13	ENT	Ear, nose, and throat
14	ep	epidermis
15	F	Female
16	gl	gland
17	HCT	Hematocrit
18	Hg	mercury
19	HGB	Hemoglobin
20	HIV	Human immunodeficiency virus
21	in	inches
22	IPO	investigational product
23	IU	International units
24	k	thousand
25	lbs	pounds
26	M	Male
27	m	muscle
28	me	mesentary
29	mg	miligram
30	min	minutes
31	ml	mililiter
32	mm	millimeter
33	mu	mucus membrane
34	n	number
35	NC	no change
36	ner	nerve
37	p	peritoneum
38	par	parenchymal
39	Pre-Op	Before Surgery
40	Post-Op	After Surgery
41	POB	post-operative bleeding
42	POI	post-operative infection
43	PT	Prothrombin Time
44	SD	Standard deviation
45	sec	seconds
46	skin-skin	First incision to surgical closure
47	sub	subcutaneous

48	U	units
49	v	vein
50	VS	vital sign
51	yrs	years

1. Report Synopsis

1.1 Title

A multi-center, single blinded, controlled study of the efficacy and safety of SeraSeal.

1.2 Investigators and Centers

Eighteen investigators from 5 centers in Lima, Peru, participated in this study. All had extensive experience in their respected surgical field.

1.3 Publications

None were submitted

1.4 Study Dates

The first patient received the study hemostatic agent on 6 July 2001, and the final patient was treated 3 February 2004.

1.5 Objectives

The primary objective was to compare the efficacy and safety of SeraSeal to cauterization to control bleeding. A secondary endpoint was to measure blood loss.

1.6 Study Design

This was a multi-center, single blinded, parallel, randomized, controlled study trial of the efficacy and safety of treatment with SeraSeal compared to cauterization to control bleeding. The study included both adult and pediatric patients. Surgical cases known for moderate (50-200 ml), heavy (200-500 ml), and severe (> 500 ml) blood loss were selected for this study. SeraSeal was applied to a specific wound site(s) and a stop watch was used to measure the time to hemostasis. To demonstrate efficacy, SeraSeal had to achieve hemostasis 25% faster than cauterization in 90% of all the surgical cases.

1.7 Study Population

All ages, both genders, and candidates on anticoagulant therapy, were eligible for this study.

1.8 Treatment and Administration

Test Product: SeraSeal lots 117401, 214001, 325301 were provided in 5 ml vials, containing 3000 IU/ml of activity. SeraSeal was applied topically to each created bleeding wound, usually 790-2000 IU/ml application, and removed through irrigation within 1-2 minutes after hemostasis was achieved.

1.9 Evaluation Criteria

Efficacy Parameters: The efficacy assessments in the trial measured the time to hemostasis for each treated wound. Hemostasis was defined as the complete cessation of blood flow with no oozing.

The protocol defined the primary efficacy parameters as individual measured times to hemostasis in each surgical case to be 25% faster than cauterization, and achieve an overall 90% success rate.

Safety Parameters: Adverse experiences, vital signs, laboratory evaluations.

1.10 Statistical Methods

All patients who received treatment of SeraSeal were included in the efficacy population. Statistical conclusions concerning the efficacy of the investigational product were made using data from the time to hemostasis from each surgical case. The hypothesis was two sided and tested at the alpha level of 0.05. Groups were compared using a one-way ANOVA, followed by pariwise multiple comparison using a tukey test.

1.11 Patient Disposition and Key Demographic Data

Two hundred thirty eight patients (238) were enrolled in this randomized hemostatic study. Twenty four (24) of them were pediatric patients. Both treatment groups were comparable at entry by having the same surgical procedure, known for moderate to severe blood loss, and the same surgical sites treated. Twenty percent (20%) of the study cases were challenged by having heparinized patients enrolled in the study. See Patient Disposition (Table 1) and Key Demographic Characteristics (Table 2).

Table 1 Patient Disposition

Enrollment	Number
evaluated for enrollment	350
did not meet inclusion criteria	49
met inclusion but denied	63
Randomization	
randomized	238
Treatment Allocation	
received treatment	119
Treatment Completion	
completed treatment	119
cross-over treatment	0
Follow-Up	
completed follow-up	119
did not complete follow-up	0
Analysis	
included in main analysis	238
excluded from main analysis	0

Table 2 Key Demographic Characteristics

	Adults	Pediatric
	(N=107)	(N=12)
	mean SD	mean SD
Age (yrs)	56.8 ± 19.0	6.4 ± 5.7
Weight (lbs)	148.1 ± 20.5	54.5 ± 36.5
Height (in)	64.3 ± 3.1	41.0 ± 15.4
Race		
Hispanic	107 (100%)	12 (100%)
Clotting		
Normal	70 (65.4%)	12 (100.0%)
Abnormal	37 (34.6%)	0 (0.0%)

1.12 Safety Results

Adverse Events:

There were no reported adverse event experiences

Vital Signs:

Sixty three (63) patients had baseline abnormal vital signs, due to dehydration 13 (20.6%), anxiety 11 (12.5%), history of hypertension 29 (44.4%) and hemorrhage 11 (17.5%). There were no adverse vital sign changes (blood pressure and pulse rate) following treatment. See Table 20 Flagged Abnormal Vital Signs, page 50.

Laboratory Test:

Thrity seven (37) patients had baseline abnormal laboratory results, where 12 (32.4%) were due purely to hemorrhage, 15 (40.5%) solely heparin, 7 (18.9%) both hemorrhage and heparin, and 3 (8.1%) prolong PTT assay, etiology unknown. There were no adverse laboratory changes following treatment. See Table 17 Flagged Abnormal Laboratory Results, page 45.

1.13 Conclusions

There were no therapeutic breaks with using SeraSeal to cauterization. The investigational product performed effectively to control both venous and arterial bleeds in moderate to severe forms of hemorrhages, even in patients on anticoagulant therapy.

As a result achieving hemostasis sooner, blood loss was significantly reduced, reducing the frequency of blood transfusions.

1.14 Efficacy Results

The protocol described two primary efficacy endpoints: achieve hemostasis 25% faster over cauterization in 90% of the patients studied. A secondary endpoint was the measurement of blood loss.

SeraSeal achieved clinical significance with a mean hemostatic time of 1.56 minutes compared to a mean 30.79 minutes for cauterization, more than 19 times shorter clotting time, and a 100% success rate in each surgical case. (Table 3)

Blood loss was significantly less for SeraSeal treated patients with a mean blood loss of 184.30 ml to 583.19 ml in the cauterized treatment group, a 300% reduction in blood loss. (Table 4)

Table 3 Mean Hemostatic Time of Normal Patients Treated with SeraSeal vs. Cauterization, and Heparin Patients Treated with SeraSeal vs. Cauterization

	Treatment Groups							
	Normal Patients				Heparin Patients			
Hemostasis (min)	**SeraSeal**	**n**	**Cauterization**	**n**	**SeraSeal**	**n**	**Cauterization**	**n**
mean	1.56	95	30.79	95	0.73	24	10.42	24
SD	2.30		21.55		0.29		8.13	
range	8.03-10.00		-90		0.03-1.00			

Ref: Efficacy Response Data Listing, section 12.2.6, page 110.

Table 4 Mean Blood Loss of Normal Patients Treated with SeraSeal vs. Cauterization, and Heparin Patients Treated with SeraSeal vs. Cauterization

	Treatment Groups							
	Normal Patients				Heparin Patients			
Blood Loss (ml)	**SeraSeal**	**n**	**Cauterization**	**n**	**Seraseal**	**n**	**Cauterization**	**n**
mean	184.30	95	583.19	95	0.73	24	10.42	24
SD	243.04		541.03		0.29		8.13	
range	1-3000		100-3000		0.03-1		2-35	

Ref: Efficacy Response Data Listing, section 12.2.6, page 110.

2. Ethics

2.1 Independent Ethics Committee (IEC)

This is to confirm that the study was reviewed by an IEC. A list of all IEC's consulted is provided in Appendix 12.1.3.

2.2 Ethical Conduct of the Study

This is to confirm that the study was conducted in accordance with the clinical principals that have their origins in the Declaration of Helsinki.

3. Introduction

Bleeding is still a major cause of morbidity and mortality in wounds. Thirteen percent (13%) of patients suffering acute trauma, die of bleeding.[1-9] In head and neck trauma, uncontrolled bleeding can cause airway compression and asphyxiation.[10,11] Inability to control bleeding leads to blood transfusions, increased complication ratio, immunosupression, inability to generate red blood cells, and prolonged time in the hospital.

A primary method to control bleeding utilizes standard surgical modalities, such as cauterization, a ligature, or direct pressure. Although they may be effective, each is limited in their benefit. Cauterization creates an inflammatory process from a 3rd degree burn. A ligature is limited to one blood vessel at a time, size of the vessel, and accessibility. Direct pressure is time consuming in normal patients, and inordinately long with coagulopathy patients.

Commercially available topical hemostatic agents, such as collagen sponges and fibrin sealants, are limited in their effectiveness as an adjunct to hemostasis. Impeding blood flow through direct pressure from blood soaked collagen sponges or a physical barrier over the wound from the fibrin sealant, will achieve hemostasis in 1-3 minutes for venous bleeds, and 5-10 minutes for capillary and small arterial hemorrhages.

The study that is summarized in this report was performed to examine the efficacy and safety of SeraSeal, a topical hemostatic agent, used to control bleeding from venous and arterial blood vessels. The study design was single-blinded, randomized, and compared to cauterization to control bleeding from venous and arterial blood vessels. The study was conducted at multiple sites to achieve a target enrollment that would provide sufficient statistical power to detect clinical significances. The inclusion and exclusion criteria for patient participation were rigorous so that the hemostatic properties of SeraSeal could be challenged. Only surgical procedure known to have moderate to severe blood loss were used in this study.

4. Study Objectives

4.1 Primary

- To determine the efficacy and safety of SeraSeal in the treatment of surgical procedures in five surgical departments.

4.2 Secondary

- Achieve a 25% faster hemostasis time over cauterization in 90% of the surgical cases.
- Measure the amount of blodd loss.

5. Investigational Plan

5.1 Overall Study Design and Plan: Description

This was a multi-center, single blinded, randomized, surgical study. Patients of all ages and both genders were eligible for inclusion if they agreed to using SeraSeal at specific surgical wound sites. The surgical procedures included tissues of the heart, vascular, liver, spleen, brains, vertebra, head and neck, bone, intestinal, uterus, lip, tongue, dental, skin.

The patients were randomized within each surgical department by drawing a SeraSeal or Cauterization slip. Whichever slip was drawn the next participating patient having the same surgical procedure would be given the opposite method to control bleeding at specific bleeding wound sites. One hundred nineteen (119) patients in both treatment groups, for a total of 238 patients, participated in this study.

SeraSeal was applied at specific wound sites. After hemostasis was achieved the excess SeraSeal was removed through irrigation and suction or absorption onto a surgical sponge. Blood loss was measured and recorded by reading the volume in the suction canister, or by weighing the blood soaked surgical sponges. The time to hemostasis was measured using a stop watch, from the time when the product or control was first applied to the wound, until no bleeding or oozing was observed for the entire wound. Any wound treated with the investigational product taking more than 10 minutes for hemostasis to occur would be considered a failure and would be abandoned for the intervention of standard surgical techniques to control the bleeding, and would be considered a failure.

The patients were monitored for post-operative bleeding, infection, or any other adverse event. Blood was drawn 24 hours, 48 hours, and 30 days post-operative for HGB, HCT, PT and PTT, and as often as needed if significant changes were observed. Any signs of infection from the wound blood cultures were to be collected.

Figure 1 Study Design and Schedule of Assessments

Assessment	**Screening**	**Surgery**	**24 Hrs Post-Op**	**48 Hrs Post-Op**	**30 Days Post-Op**
Medical history	X				
Physical examination	X				
Informed consent	X				
Designated Delivery system group		X			
HGB	X		X	X	X
HCT	X		X	X	X
PT	X		X	X	X
PTT	X		X	X	X
ECG	X				
Radiological work-up	X				
Wound care			X	X+	
Microbiological work-up			X*	X+	
Efficacy					
Primary variable		X	X	X	
Secondary variable		X	X	X	
Safety					
Adverse events		X	X	X+	

Ref. Protocol, Table 1 Schedule of Assessment, section 12.1.1, page 60.

+ Monitored beyond 48 hours as needed
* Measured as often as needed

A copy of the protocol and a sample case report are located in Appendix 12.1.1 (page 60) and 12.1.2 (page 62), respectively.

5.2 Discussion of Study Design, Including the Choice of Control Groups

The design of this study was to compare SeraSeal to cauterization to control bleeding in surgical cases known for moderate to severe blood loss. The patients were randomized in each surgical department by a drawn slip, and the same surgical procedure was given to the opposite method to control bleeding at the same specific bleeding wound sites.

Time to hemostasis was measured with a stop watch. Hemostasis was defined as complete cessation of blood flow with no oozing observed. Stopping criteria for treatment were if hemostasis failed to be achieved after 3 repeated applications at the point of origin of a given bleeding site, hemostasis failed to be achieved within 10 minutes for a particular wound, or at the discretion of the surgeon.

5.3 Selection of Study Population

5.3.1 Inclusion Criteria

- all ages and both genders
- wounds of a similar type, size, location and bleeding tendency
- currently on anticoagulant therapy with no dosage limitations
- diagnosed with a coagulation disorder
- participants must be able to participate for the 30 day duration of the study

A surgical procedure, known for moderate to severe blood loss, qualified the subjects for this study.

5.3.2 Exclusion Criteria

- any clinically infected wound, drawing pus, surrounding erythema or edema, or patients with systemic signs of infection
- subjects on antibiotic therapy prior to enrollment
- subjects with known allergy to bovine proteins, atopic reactions, history of anaphylaxis
- sensitivity to iodine
- inability to give informed consent
- inability to return for a 30 day follow-up visit
- HIV virus infection

5.3.3 Removal of Patients From Therapy or Assessment

Removing a patient from further assessment of SeraSeal in this study required either 3 failed SeraSeal application attempts to achieve hemostasis to any bleeding wound, or hemostasis taking longer than 10 minutes for a particular wound, or at the discretion of the surgeon.

5.4 Treatments

5.4.1 Treatments Administered

SeraSeal was applied topically to the surface of the bleeding wound with a syringe at 3000 IU/ml.

5.4.2 Identity of Investigational Product

SeraSeal contains the serine protease Factors II, VII, IX, X, Betadine bound to the proteins with no free iodine, and stabilizers, with an activity level of 3,000 IU/ml. Lots 117401, 214001, 325301 were used in this study. Patients receiving each batch are identified in Appendix 12.1.6.

5.4.3 Method of Assigning Patients to Treatment Groups

Patients were selected based on their surgical procedures. Only surgical procedures known for moderate to severe blood loss qualified for this study.

The patients were randomized within each surgical department and in each study center, by drawing a SeraSeal or Cauterization slip. A detailed description of the randomization method is given in Appendix 12.1.7.

5.4.4 Selection of Doses in the Study

The normal clotting time for the extrinsic coagulation pathway is 10-12 seconds and 22-35 seconds for the intrinsic system, when measured by the prothrombin time (PT) and activated partial thromboplastin time (APTT) assayed methods, respectively.

In-vitro studies, "Determining the Activity Level of SeraSeal In-Vitro" (Study XLW-14-23) determined the optimum SeraSeal activity level of 3,000 IU/ml achieved hemostasis in 2 seconds. Concentrations above 3,000 IU/ml did not increase the kinetic activity of the clotting cascade system. See Table 5.

Liver resection in the rabbit, Determining the Activity Level of SeraSeal in an Animal Model (XLW-14-47), confirmed the optimum SeraSeal activity level from the in-vitro studies, Study No. XLW-14-23, see Table 6, and affirmed this activity level of 3,000 IU/ml to effectively control hemostasis in the pig in such surgical procedures as an aorta resection, partial nephrectomy,

bowel resection, cholecystectomy, and urethra resection study 4327, The Effect of Single Dosage of SeraSeal in Swine Whole Blood, Table 7.

Table 5 Determining the Activity Level of SeraSeal In-Vitro

Hemostasis (sec)	1000 IU/ml	2000 IU/ml	3000 IU/ml	4000 IU/ml	5000 IU/ml
n	10	10	10	10	10
range	20.1-20.8	14.8-15.6	1.9-2.1	1.8-2.1	1.7-2.1
mean	20.39	15.12	2.00	1.97	1.97
SD	0.260	0.253	0.067	0.116	0.125

Ref. In-vitro Study XLW-14-23

Table 6 Determining the Activity Level of SeraSeal in an Animal Model

Clotting Time (sec)					
	Control	1000 IU/ml	2000 IU/ml	3000 IU/ml	4000 IU/ml
Male					
n	10	10	10	10	10
Range	290-312	19.9-20.5	13.9-15.3	1.7-2.3	1.7-2.2
Mean	300.3	20.3	14.7	1.9	2.1
SD	7.156	0.286	0.532	0.201	0.137
Female					
n	10	10	10	10	10
Range	291-308	19.6-20.4	14.3-15.9	1.6-2.4	1.7-2.2
Mean	298.8	20.0	14.9	2.0	2.0
SD	6.096	0.271	0.577	0.225	0.152
Total					
n	20	20	20	20	20
Range	290-312	19.6-20.5	13.6-15.9	1.6-2.4	1.7-2.2
Mean	299.6	20.2	14.9	2.0	2.0
SD	6.689	0.278	0.554	0.213	0.144

Blood Loss (ml)					
	Control	1000 IU/ml	2000 IU/ml	3000 IU/ml	4000 IU/ml
Male					
n	10	10	10	10	10
Range	18.6-20.6	7.6-8.8	5.0-5.9	1.9-2.3	1.9-2.4
Mean	19.4	8.1	5.2	2.2	2.1
SD	0.642	0.482	0.264	0.158	0.137
Female					
n	10	10	10	10	10
Range	18.4-20.2	7.4-8.8	4.9-5.4	2.0-2.5	1.9-2.5
Mean	19.1	8.1	5.1	2.0	2.2
SD	0.501	0.443	0.152	0.225	0.190
Total					
n	20	20	20	20	20
Range	18.4-20.6	7.4-8.8	4.9-5.9	1.9-2.5	1.9-2.5
Mean	19.2	8.1	5.2	2.1	2.2
SD	0.572	0.462	0.208	0.792	0.164

Ref. Activity Level in Animal Model XLW-14-47

Table 7 Affirmation of SeraSeal Activity in the Swine

Organ	Number	Hemostasis (sec)*	Mean	SD
aorta	3	60-80	68.33	10.41
kidney	5	20-35	25.20	5.97
bowel	2	25-30	27.50	3.54
gall bladder	7	20-40	29.14	7.08
urethra	4	15-25	15.25	9.18

* collective times to hemostasis for each surgical case
Ref. Animal Study 4327

5.4.5 Selection and Timing of Dose for Each Patient

The activity of SeraSeal was set at 3000 IU/ml, and applied at specific sites throughout the surgical procedure.

5.4.6 Blinding

This was a single-blinded study. Only the surgical team at the time of surgery knew which modality, SeraSeal or cauterization, would be used for that particular surgery to control bleeding at specific bleeding wound sites. As the patient was being prepped for surgery, a slip was drawn

in the operating room to reveal which hemostatic method would be used in that particular surgical case. The surgeon would automatically use the opposite modality for the next exact same surgical procedure.

The remaining medical staff was shielded from the study by having the surgical report kept in a locked cabinet in the surgeon's office. Since the investigational product was given only during surgery, and there was no access to the surgical report, interim analysis remained unblinded.

5.4.7 Prior and Concomitant Therapy

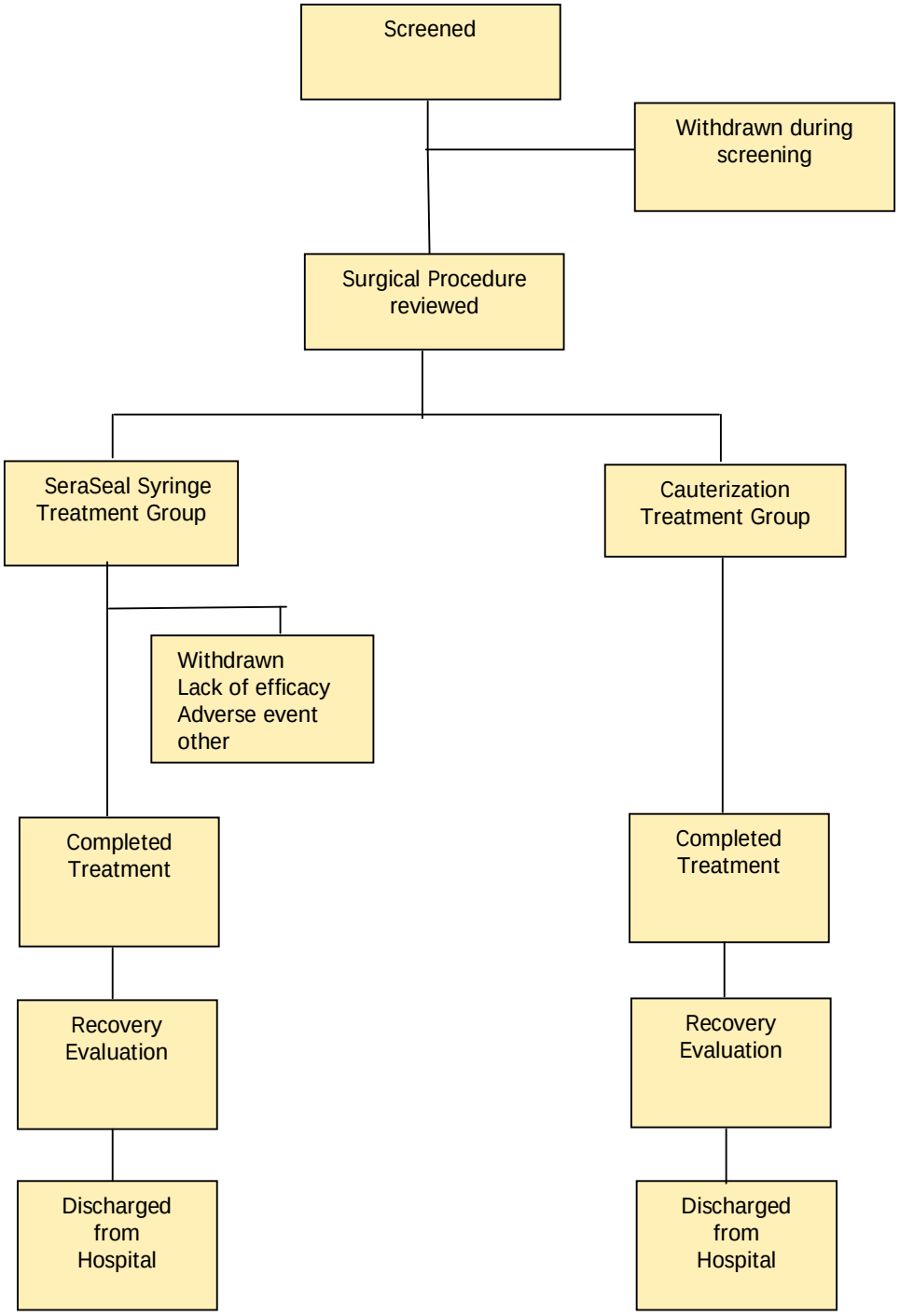
Patients on anticoagulant therapy, such as coumadin (warfarin), heparin or aspirin where allowed in the study and monitored at their prescribed dosage. It was believed the factors in SeraSeal would overcome the effects of the anticoagulant drug on the single factor in the patient's blood, and have no significant outcome on the study endpoints. This was confirmed by measuring their time to hemostasis.

5.5 Efficacy and Safety Variables

5.5.1 Efficacy and Safety measurement Assessed and Flow Chart

A flow chart displaying the frequency and timing of efficacy and safety measurements is provided in Figure 2.

Figure 2 Efficacy and Safety Measurement Flow Chart



The measurement of laboratory tests were standardized in this multicenter study by using the same laboratory instruments, controls, and reagents to assay all of the blood samples.

The means of obtaining adverse event data was through a checklist, Figure 3, with a rating scale of (-)[1] for negative; (+)[2] mild; (++)[3] moderate; (+++)[4] severe; (++++)[5] fatal adverse response. Any reported adverse response had to be followed up appropriately.

1. negative: no observed reaction or change
2. mild: slight changes
3. moderate: notable change but not life threatening
4. severe: significant change, life threatening
5. fatal: death

Figure 3 Adverse Event Checklist

Patient No. _____

Body System	Preferred Term	Rating	Comment
Body as a whole	Abdominal pain		
	Asthemia		
	Back pain		
	Chest pain		
	Headache		
	Infection		
	Trauma		
Cardiovascular System	Postural Hypotension		
	Tachycardia		
	Vasodilation		
Digestive System	Constipation		
	Decreased appetite		
	Diarrhea		
	Dry mouth		
	Dyspepsia		
	Nausea		
	Tooth disorder		
	Vomiting		
Nervous System	Dizziness		
	Emotional liability		
	Hostility		
	Insomnia		
	Nervousness		
	Somolence		
	Tremor		
Respiratory System	Cough increase		
	Pharyngitis		
	Respiratory disorder		
	Rhinitis		
	Sinusitis		
Other	Sweating		
	Abnormal vision		

(-) Negative: no observed reaction or change
(+) Mild: slight changes
(++) Moderate: notable change but not life threatening
(+++) Severe: significant change, life threatening
(++++) Fatal: death

5.5.2 Appropriateness of Measurements

All efficacy and safety assessments in this study were standard, generally recognized as reliable, accurate, and relevant.

5.5.3 Primary Efficacy Variable

SeraSeal was applied to specific bleeding wound sites in each surgical case, and the time to hemostasis was measured with a stop watch and recorded. Efficacy was determined by comparing the time for the SeraSeal surgical case to achieve hemostasis to the identical surgical case using Cauterization to control bleeding. Efficacy was achieved when SeraSeal reduced the clotting time by 25% in 90% of all surgical cases.

5.5.4 Drug Concentration Measurements

Drug concentration did not apply in this study, because SeraSeal was applied topically to the wound and removed within 1-2 minutes after hemostasis through irrigation. Further, SeraSeal does not enter the vascular system, nor is it absorbed at the cellular level.

5.6 Data Quality Assurance

Quality assurance and quality control systems were implemented in their multicenter center. Training sessions were conducted to ensure the proper use and application of SeraSeal, including the parameters of hemostasis.

The Monitoring Board was responsible for the collection of accurate, consistant, complete, and reliable data.

5.7 Statistical Methods Planned in the Protocol and Determination of Sample Size

5.7.1 Statistical and Analytical Plans

A comparison of continuous outcomes such as time to hemostasis (primary outcome), pre and post operative blood loss, surgery duration, (log) bacterial titer, and length of hospital stay with SeraSeal versus cauterization treatment, using factorial analysis of variance (ANOVA) methods.

For continous lab outcomes measured on four occasions (base, 24 hours, 48 hours, 30 days) repeated measure analysis of variance methods to compare mean lab values for cauterization versus SeraSeal overall was used.

For binary outcomes (including adverse event outcomes) that are not quantified or that may be dichotomized for clinical consequence and interpretability such as fever (yes or no) or pruritis (yes or no) the chi-square methods to compare cauterization versus SeraSeal treatment proportions overall was used.

Members of the monitoring board collected data daily from the five study centers. Since this was a single-blinded study, where SeraSeal was applied only during surgery and where the surgical reports were stored in locked cabinets, only the laboratory reports and daily physical status of the patient were monitored for adverse events. After the study had ended the effectiveness could be determined.

5.7.2 Determine of Sample Size

The sample size was based on the primary outcome, time to hemostasis. We considered at least a 25% mean reduction in time to hemostasis to be the smallest clinically important improvement as a primary hemostatic agent. Historically, liver surgeries in the multi-centers in this study showed that using cauterization, the mean time to hemostasis was about 30 minutes. To achieve a 25% reduction in the time to hemostasis the required mean clotting time was calculated to be $30 \times 0.75 = 22.5$ minutes.

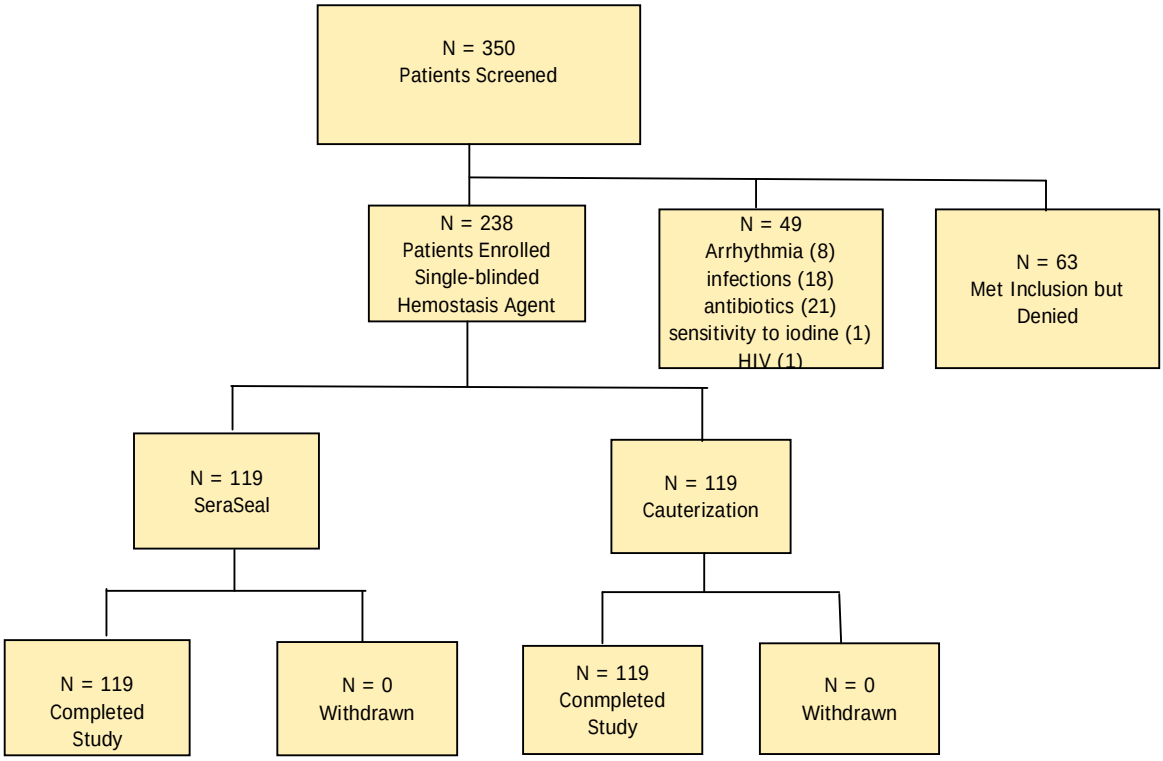
Based on this calculation, a sample size of 20 persons per group, would provide an 80% power for confirming this mean difference using the $p<0.05$ two sided significance criteria (alpha=0.05). Assuming that all of the surgical procedures could be collapsed within their respective departments, and assuming that the 25% mean difference or greater difference occurred in all 5 departments, the required total sample size was $20 \times 2 \times 5 = 200$.

5.8 Change in the Conduct of the Study or Planned Analysis

No change in the conduct of the study or planned analysis was made after the start of the study.

6. Study Patients

6.1 Disposition of Patients



6.2 Demographic Characteristics

Table 8 summarizes the demographic characteristics of all patients that were entered in the study. The study was composed of 107 adults (89.9%) and 12 pediatric (10.1%) SeraSeal treated patients, with an age range of 20 days to 92 years old and a mean of 52.12 years. The patients enrolled in the three surgical groups: cardiovascular, orthopedic and general surgery, no significant difference with gender (P=0.1096), significant difference in age between the 3 surgical groups (P=0.018), but no significant difference in age and gender in each surgical group (P=0.5842).

Table 8 Demographic Characteristics

	Treatment Group			
Demographic Characteristic	**Adult (n=107)**		**Pediatric (n=12)**	
Sex	**M**	**F**	**M**	**F**
	56 (52.3%)	51 (47.7%)	6 (50.0%)	6 (50.0%)
Age (yrs)				
0-2	-	-	2 (16.7%)	3 (25.0%)
2-10	-	-	3 (25.0%)	0 (0.0%)
11-17	-	-	1 (8.3%)	3 (25.0%)
18-20	3 (2.8%)	1 (0.9%)	-	-
21-30	3 (2.8%)	3 (2.8%)	-	-
31-40	9 (8.4%)	9 (8.2%)	-	-
41-50	8 (7.5%)	3 (2.8%)	-	-
51-60	12 (11.2%)	5 (4.6%)	-	-
61-70	8 (7.5%)	12 (11.0%)	-	-
71-80	5 (4.7%)	15 (13.8%)	-	-
81-90	7 (6.5%)	2 (1.8%)	-	-
91-92	1 (0.9%)	1 (0.9%)	-	-
Weight (lb)	(n=56)	(n=51)	(n=6)	(n=6)
mean ± SD	157.25 ± 20.73	138.20 ± 15.66	52.00 ± 34.76	72.00 ± 38.72
Range	110-202	112-172	4-99	15-110
Height (in)	(n=56)	(n=51)	(n=6)	(n=6)
mean ± SD	66.7 ± 2.47	62.35 ± 2.25	42.71 ± 13.30	47.00 ± 16.93
Range	67.71	58-67	16-54	23-63
Vital Signs	**Blood Pressure**		**Pulse Rate**	
Normal				
Male	42 (51.2%)		46 (52.3%)	
Female	40 (48.8%)		42 (47.7%)	
Abnormal				
Male	14 (56.0%)		10 (52.6%)	
Female	11 (44.0%)		9 (47.4%)	

Laboratory	Blood Level	Clotting Time
Normal		
Male	51 (57.3%)	40 (74.1%)
Female	38 (42.7%)	14 (25.9%)
Abnormal		
Male	5 (27.8%)	16 (30.2%)
Female	13 (72.2%)	37 (69.8%)

Ref: Demographic Data, section 12.2.3, page 100.

7. Efficacy Evaluation

7.1 Data Sets Analyzed

71.1 Number and Distribution of Patients

A total of 238 patients participated in this study at 5 centers. All of the centers were in Lima, Peru. There were no withdrawl of patients. The number of patients from each study center and by treatment group is shown in Table 9.

Table 9 Number in Each Enrolled (E) Group and Who Completed (C) Surgical Treatment at Each Center

		Treatment Group			
		SeraSeal		Cauterization	
Center No.	Site	E	C*	E	C
1	Edgardo Rebagliati Martins National Hospital	65	65	65	65
2	Guillermo Almenara National Hospital	13	13	13	13
3	Jose Casimiro Ulloa Emergency Hospital	6	6	6	6
4	FAP-Peruvian Air Force Hospital	20	20	20	20
5	Military Hospital of Peru	3	3	3	3

* Completed treatment is defined as no other surgical modality to control bleeding at the targeted surgical site(s).
Ref: Individual Patient Data Listing, section 12.4, page 119.

7.2 Demographic and Other Baseline Characteristics

Table 10 summarizes baseline characteristics regarding the treatment group.

Table 10 Baseline Characteristics

Baseline Characteristics	Treatment Group			
	Adult (N=107)		Pediatric (N=12)	
	M	F	M	F
	56 (52.3%)	51 (46.8%)	6 (50%)	6 (50%)
Pre-Op Mean (SD)				
HBG (g/dl)	13.90±1.56	12.43±1.02	15.02±1.83	14.62±0.46
HCT (%)	41.58±4.71	36.56±5.66	46.37±2.71	43.72±1.16
PT (sec)	11.58±0.22	11.68±0.26	11.68±0.19	11.42±0.17
PTT (sec)	34.56±12.91	32.26±12.54	32.26±12.54	23.67±0.82
Anticoagulant Therapy (Heparin) Number	16 (13.4%)	12 (10.1%)	0 (0.0%)	0 (0.0%)
Dose (U/Kg) Mean (SD)	303.1±112.1	248.9±110.8	0.00	0.0
Associated Illness				
Arterial Hypertension	16 (13.4%)	11 (9.2%)	0 (0.0%)	0 (0.0%)
Diabetes Mellitas	3 (2.5%)	2 (1.7%)	0 (0.0%)	0 (0.0%)
Depression	3 (2.5%)	8 (6.7%)	0 (0.0%)	0 (0.0%)
Targeted Organ				
heart	15 (5.9%)		0 (0.0%)	
arteries	22 (8.9%)		0 (0.0%)	
brain	4 (1.6%)		0 (0.0%)	
vertebra	8 (3.1%)		0 (0.0%)	
thyroid	2 (0.8%)		0 (0.0%)	
oral	3 (1.2%)		0 (0.0%)	
parotid	1 (0.4%)		0 (0.0%)	
sinuses	2 (0.8%)		0 (0.0%)	
radical neck	5 (2.0%)		3 (1.2%)	
leg amputation	1 (0.4%)		1 (0.4%)	
hip	2 (0.8%)		0 (0.0%)	
femur	2 (0.8%)		0 (0.0%)	
liver	16 (6.3%)		1 (0.4%)	
spleen	6 (2.4%)		0 (0.0%)	
gastro	22 (8.7%)		3 (1.2%)	
pancreas	3 (1.2%)		0 (0.0%)	
gall bladder	8 (3.1%)		0 (0.0%)	
breast	1 (0.4%)		0 (0.0%)	
ovary	1 (0.4%)		0 (0.0%)	
skin-muscle	85 (33.5%)		0 (0.0%)	
lung	1 (0.4%)		0 (0.0%)	
tongue	1 (0.4%)		0 (0.0%)	
bone	31 (12.2%)		4 (1.6%)	

Ref. Individual Patient Data Listing, section 12.4.

7.3 Efficacy Results and Tabulation of Individual Patient Data

7.3.1 Analysis of Efficacy

The primary efficacy measurement defined by the protocol stated that at specified bleeding sites, known for moderate to severe blood loss, SeraSeal would achieve hemostasis 25% faster than cauterization in 90% of the total surgical cases.

The time to hemostasis ranged from 0.03 – 10 minutes, with a mean of 1.59 minutes for SeraSeal, compared to a 2 -90 minute range for cauterization, with a mean of 31.22 minutes, statistical significance ($P<0.0001$) and nearly 20 times faster for clot formation over the control, Table 11. Children treated with SeraSeal significantly achieved hemostasis sooner than children in the control group, with a mean 1.77 minute clotting time compared to a mean 51.69 minutes ($P<0.0001$). Significant time to hemostasis was also observed in SeraSeal treated heparinized patients with a mean 0.72 min. (±0.29) compared to a mean 10.00 min (±8.10) in heparinized patients treated by cauterization ($P<0.0001$). In every SeraSeal surgical case, hemostasis occurred after only one application of the hemostatic agent.

A secondary efficacy measurement was blood loss. The mean blood loss for SeraSeal treated patients was 184.30 ml, with a range of 1-2,000 ml, compared to a mean of 583.19 ml and a 100-3,000 ml range in the cauterization treatment group with a statistical significance of ($P<0.001$). The mean blood loss in SeraSeal treated children was 42.92 ml (±70.60) significantly less compared to a mean 329.17 ml (±219.98) children treated in the control group ($P=0.0003$). There was significant less blood loss in SeraSeal treated heparinized patients, with a mean 347.20 ml (±141.38) to a mean 720.00 ml (±272.34) in heparinized subjects treated by standard surgical methods.

Twenty six patients (24.4%) were on Heparin, with 14 men having a mean dosage of 302.86 U/Kg and 248.91 U for 11 women. There was no significant difference between the two groups ($P=0.2320$). The mean Heparin dosage was 279.12 U/Kg (±110.21). Comparing normal treated patients to Heparin treated patients, the mean SeraSeal dosage was 4,039 IU and 5,076 IU, respectively, statistically significant between the two groups ($P=0.0156$).

There were no therapeutic breaks of SeraSeal to cauterization, achieving 100% success in obtaining hemostasis greater than 25% faster than the employment of cauterization.

Table 11 Efficacy of Seraseal vs. Cauterization

Primary Efficacy	**SeraSeal**				**Cauterization**			
Total Time to Hemostasis (min)								
n	119				119			
mean	1.59				31.22			
SD (±)	2.32				19.72			
range	0.03 – 10				2 – 90			
Blood Loss (ml)								
mean	199.66				595.63			
SD (±)	245.29				527.64			
range	0-2,000				50-30,000			
Time to Hemostasis of Adult and Pediatric and by Gender (min)	**SeraSeal**				**Cauterization**			
	Adult		**Pediatric**		**Adult**		**Pediatric**	
	M	**F**	**M**	**F**	**M**	**F**	**M**	**F**
n	56	51	6	7	56	51	6	6
mean	1.69	1.44	1.33	2.14	28.66	28.82	48.33	54.57
SD (±)	2.64	2.21	0.82	1.34	17.48	17.96	20.41	28.98
range	0.03-10	0.03-10	1-3	1-5	2-60	5-60	10-60	20-90
Total Time to Hemostasis of Heparin Patients (min)	**SeraSeal**				**Cauterization**			
n	24				24			
mean	0.73				10.42			
SD (±)	0.29				8.13			
range	0.03 – 1				2 – 35			
Time to Hemostasis of Heparin Patients by Gender (min)	**SeraSeal**				**Cauterization**			
	M		F		M		F	
n	14		10		14		10	
mean	0.75		0.70		10.36		10.50	
SD (±)	0.32		0.26		10.00		4.97	
range	0.03-1		0.5-1		2-35		5-20	
Secondary Efficacy Total Blood Loss (ml)	**SeraSeal**				**Cauterization**			
n	119				119			
mean	184.30				583.19			
SD (±)	243.04				541.63			
range	1 – 2,000				100 – 3,000			
Blood Loss of Normal Patients by Gender (ml)	**SeraSeal**				**Cauterization**			
	Adult		Pediatric		Adult		Pediatric	
	M	F	M	F	M	F	M	F
n	56	51	6	6	56	51	6	6
mean	216.23	184.96	75.00	70.83	653.57	546.60	375.00	283.33
SD (±)	299.61	183.85	92.03	4.92	635.24	472.30	311.05	68.31
range	1-2,000	1-500	10-250	5-50	50-3,000	50-2,000	250-400	200-400

Total Blood Loss of Heparin Patients (ml)	**SeraSeal**	**Cauterization**
n	24	24
mean	370.00	766.67
SD (±)	133.97	251.37
range	30 - 500	250 – 1,200

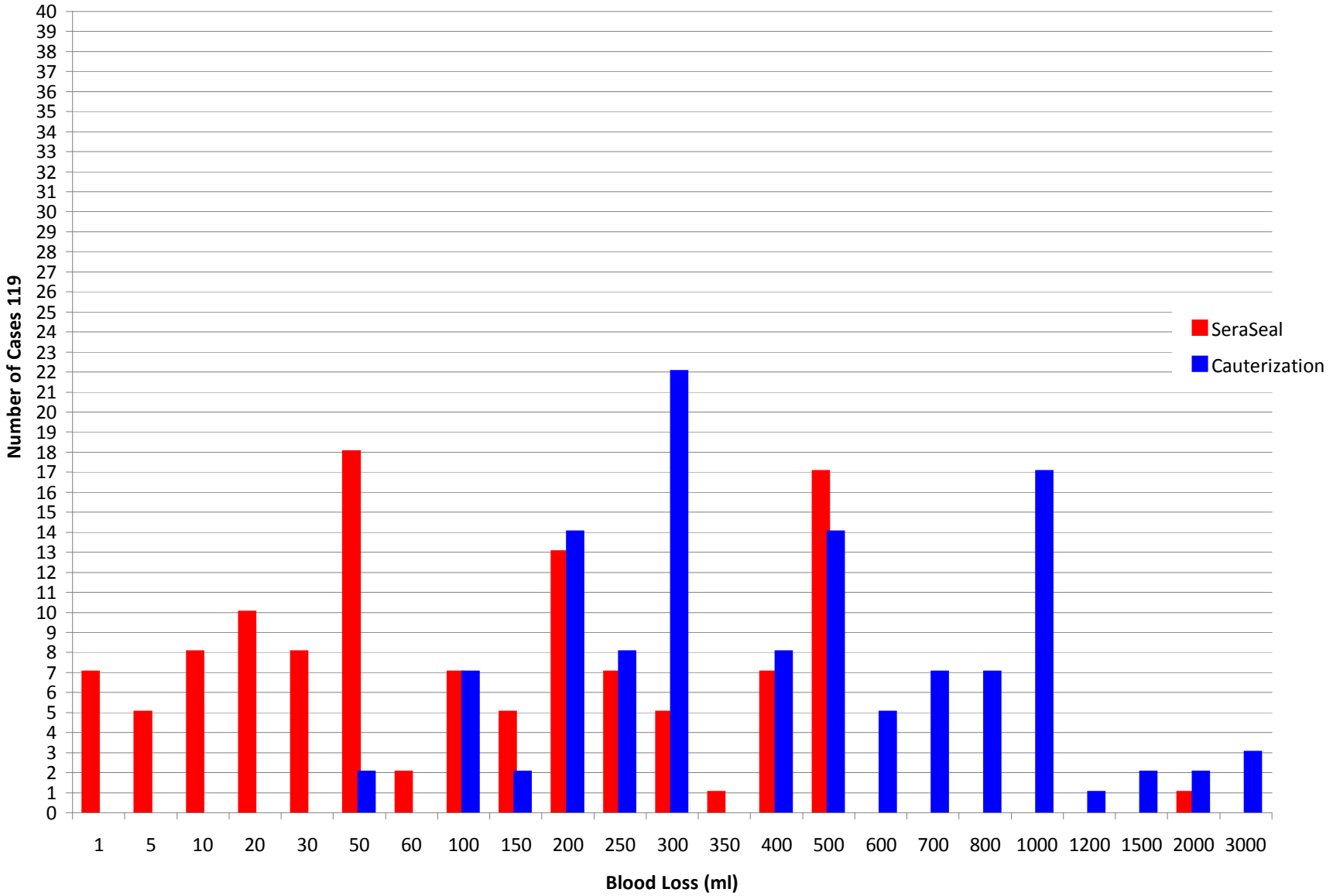
Blood Loss of Heparin Patients by Gender (ml)	**SeraSeal**		**Cauterization**	
	M	F	M	F
n	14	10	14	10
mean	378.57	358.00	771.43	760.00
SD (±)	110.44	167.25	249.39	267.50
range	200-500	30.-500	500-1,200	300-1,000

Number of SeraSeal Applications

No. Application/No. Case	**Adult**		**Pediatric**	
	M (n=56)	F (n=51)	M (n=6)	F (n=6)
1	2 (3.6%)	- (0.0%)	- (0.0%)	- (0.0%)
2	10 (17.9%)	13 (25.55)	2 (33.3%)	2 (33.3%)
3	22 (39.3%)	24 (47.0%)	2 (33.3%)	1 (16.7%)
4	9 (16.1%)	7 (13.7%)	2 (33.3%)	- (0.0%)
5	7 (12.5%)	6 (11.8%)	- (0.0%)	1 (16.7%)
6	2 (3.6%)	1 (2.0%)	- (0.0%)	2 (33.3%)
7	3 (5.4%)	- (0.0%)	- (0.0%)	- (0.0%)
8	- (0.0%)	- (0.0%)	- (0.0%)	- (0.0%)
9	- (0.0%)	- (0.0%)	- (0.0%)	- (0.0%)
10	1 (1.8%)	- (0.0%)	- (0.0%)	- (0.0%)
Attempts/Bleeds	1 (n=56)	1 (n=51)	1 (n=6)	1 (n=6)

Ref: Individual Response Data, appendix 12.2.4, page 103.

Graph 1 Efficacy: Blood Loss - SeraSeal vs. Cauterization



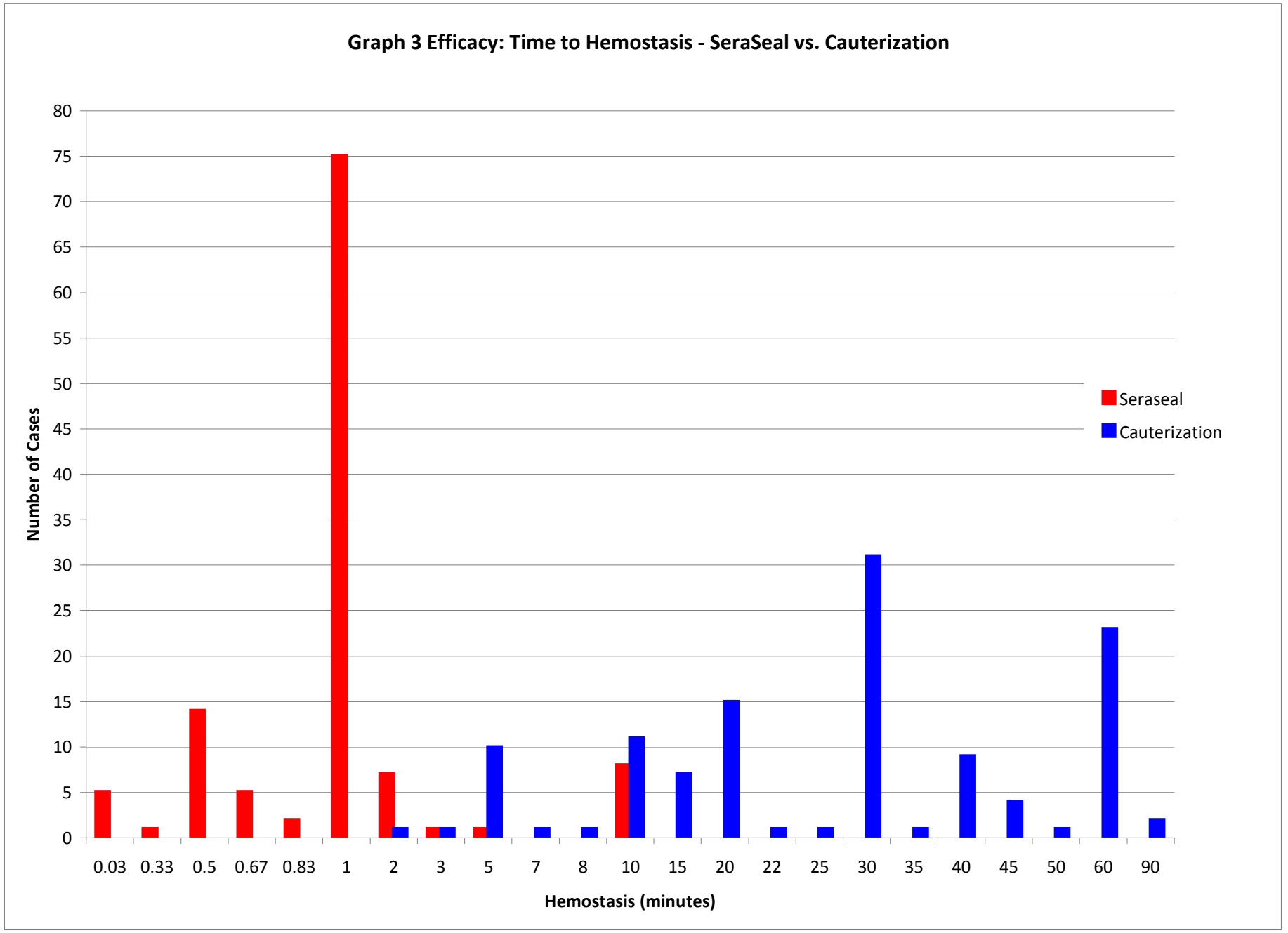

Graph 3 Efficacy: Time to Hemostasis - SeraSeal vs. Cauterization
Number of Cases
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
0.03
0.33
0.5
0.67
0.83
1
2
3
5
7
8
10
15
20
22
25
30
35
40
45
50
60
90
Hemostasis (minutes)
Seraseal
Cauterization

Table 12 Heparin Patients Treated by SeraSeal vs. Cauterization

	Treatment Group			
Hemostasis (min)	**SeraSeal**		**Cauterization**	
	n	**%**	**n**	**%**
0.03	1	4.17	0	0.00
0.5	11	45.83	0	0.00
1	12	50.00	0	0.00
2	0	0.00	1	4.17
3	0	0.00	1	4.17
5	0	0.00	8	33.33
7	0	0.00	1	4.17
8	0	0.00	1	4.17
10	0	0.00	6	25.00
15	0	0.00	3	12.5
20	0	0.00	1	4.17
30	0	0.00	1	4.17
35	0	0.00	1	4.17

Ref: Efficacy Response Data Listing by Dosage, section 12.2.7, page 114.

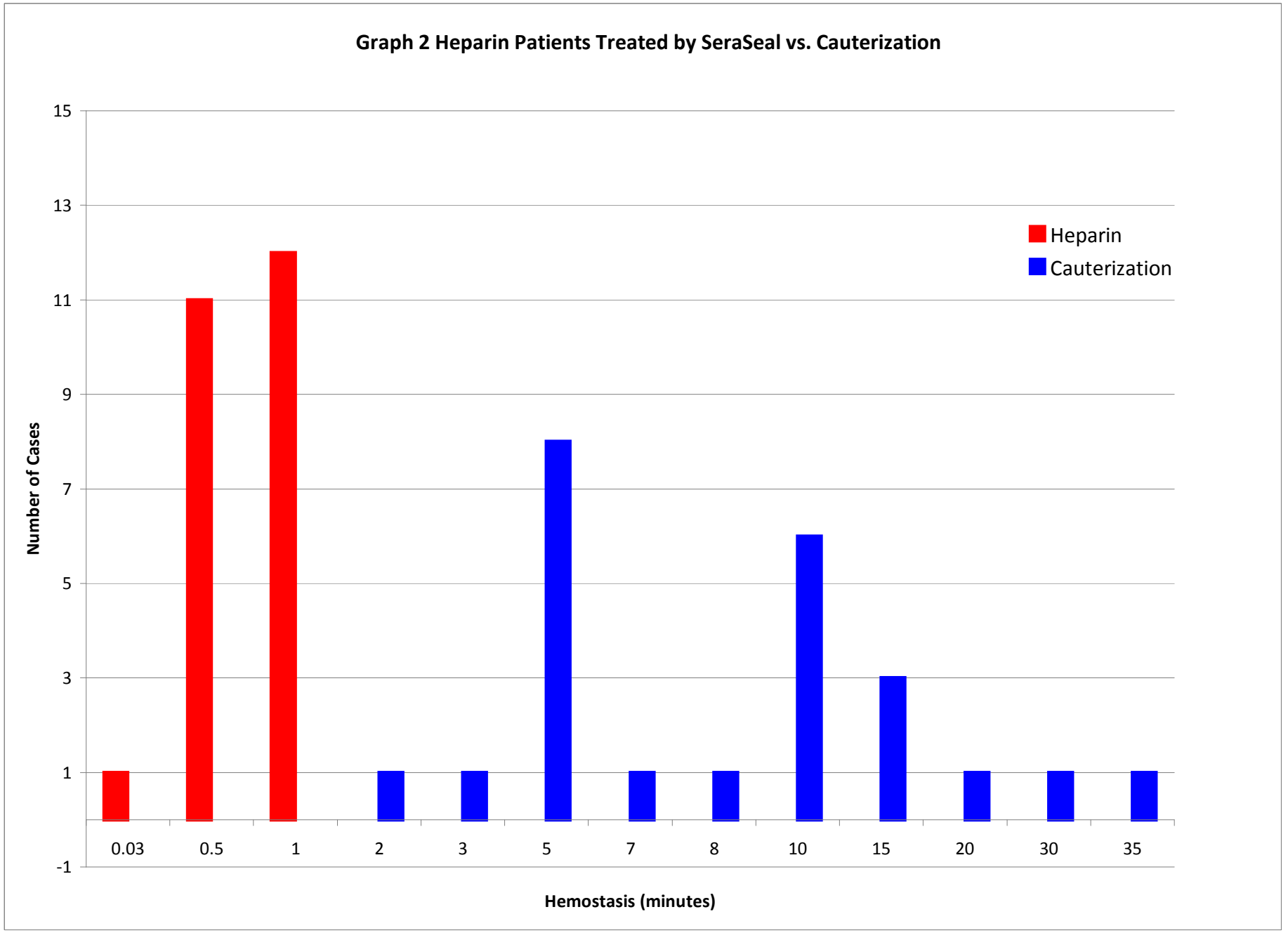
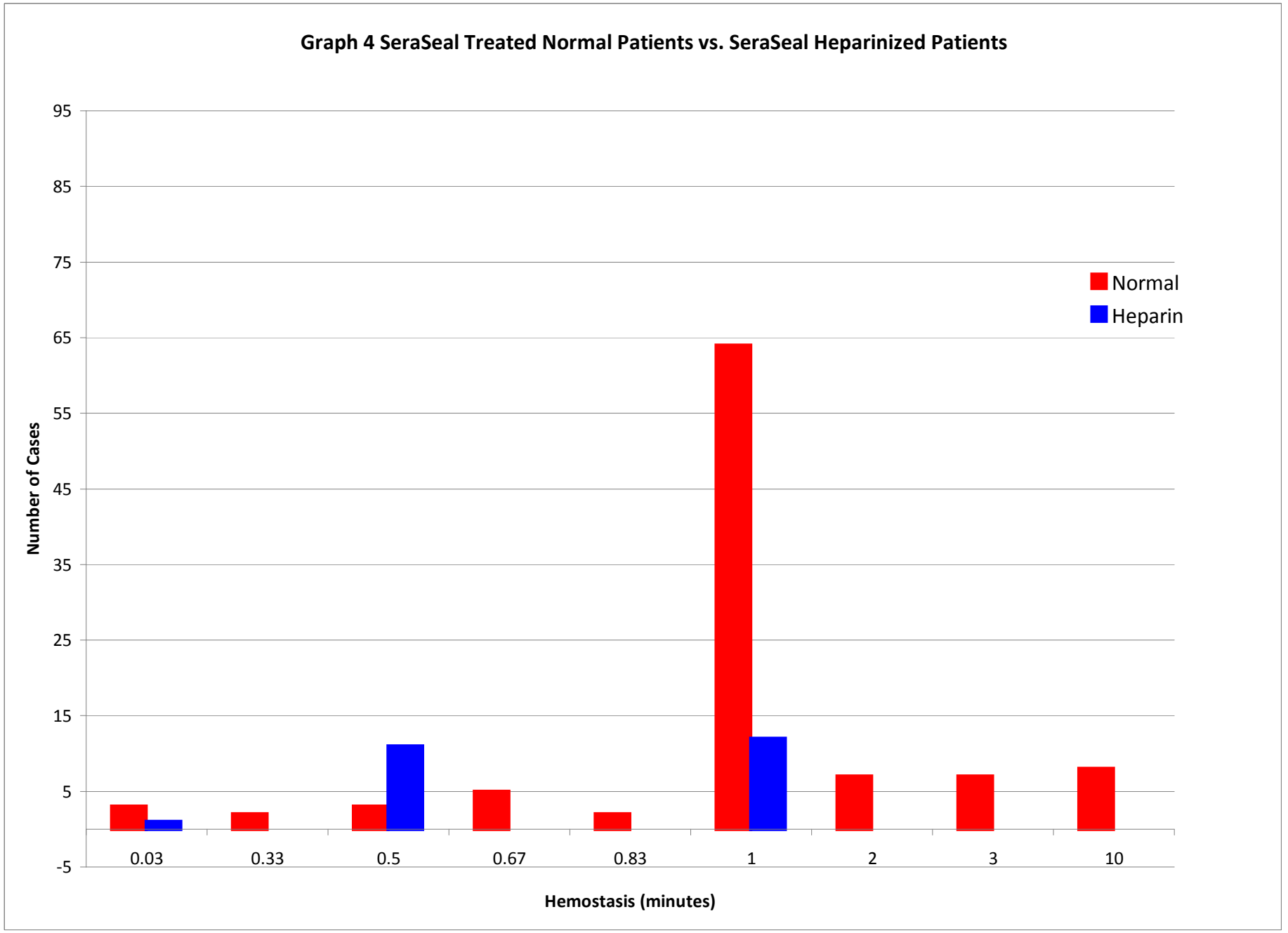

Graph 2 Heparin Patients Treated by SeraSeal vs. Cauterization
15
13
11
9
7
5
3
1
-1
Number of Cases
Heparin
Cauterization
0.03
0.5
1
2
3
5
7
8
10
15
20
30
35
Hemostasis (minutes)

Table 13 SeraSeal Treated Normal Patients vs. SeraSeal Treated Heparinized Patients

	Treatment Group			
Hemostasis (min)	**Normal (n=95)**		**Heparin (n=24)**	
	n	**%**	**n**	**%**
0.03	3	3.16	1	4.17
0.33	2	2.10	0	0.00
0.5	3	3.16	11	45.83
0.67	5	5.26	0	0.00
0.83	2	2.10	0	0.00
1	64	67.37	12	50.00
2	7	7.37	0	0.00
3	1	1.05	0	0.00
10	8	8.42	0	0.00

Ref: Efficacy Response Data Listing by Dosage, section 12.2.7, page 114.


Graph 4 SeraSeal Treated Normal Patients vs. SeraSeal Heparinized Patients
95
85
75
65
55
45
35
25
15
5
-5
Number of Cases
Normal
Heparin
0.03
0.33
0.5
0.67
0.83
1
2
3
10
Hemostasis (minutes)

7.3.2 Statistical/Analytical Issues

7.3.3 Tabulation of Individual Response Data

Tabulation of Individual Response lists the target organs, the type of tissue where SeraSeal was applied, the total dosage exposure, time to hemostasis, and blood loss, are listed in section 12.2.4, page 103.

The individual patient information sheet and the descriptive surgical procedure are listed in Appendix 12.4, page 119.

7.3.4 Dosage, Activity Level, and Relationship to Response

The activity level for the SeraSeal delivery system (syringe, general spray) were 3,000 IU/ml. The mean dosage applied to adults was 4074 IU (± 1767 IU) and 5000 IU (± 2335 IU) in the pediatric patients. As a result, the mean time to hemostasis was 1.57 minutes (± 2.43 minutes) and 1.77 minutes (± 1.16 minutes) for adults and pediatric, respectively, with a mean blood loss of 170.2 ml (± 248.1 ml) in adults and only 42.9 ml (± 70.6 ml) in children.

7.3.5 Efficacy Conclusion

SeraSeal demonstrated clinical significance over cauterization to control bleeding in a wide range of surgical applications and type of tissues by achieving hemostasis 19 times faster and half the blood loss.

It was believed the design of SeraSeal with its active agents Factors II, VII, IX, X, would be effective in every form of coagulopathy. Twenty percent of the subjects in this study were maintained on their heparin therapy and they also achieved hemostasis 19 times faster with 50% less blood loss than the study population in the control group.

8. Safety Evaluation

8.1 Extent of Exposure

All of the paitents were exposed to the hemostatic agent under 12 minutes with each application throughout the surgical procedure. Once hemostasis had occurred the investigational product was removed through irrigation and suction. The number of wounds treated by SeraSeal ranged from 1 – 10, with a mean of 6.10 applications in the adult surgical cases, and 3.5 applications in the pediatric cases (Table 11, Efficacy of SeraSeal vs Cautherization, page 31).

The mean dose/application for adults was 668 IU, while the pediatric patients received 1428 IU.

The drug concentration is directly linked to the dose level with each application and it does not accumulate on the surface of the wound, since it is removed a few minutes after each application, nor is it accumulated in the plasma, because SeraSeal does not enter the systemic system.

8.2 Adverse Events

8.2.1 Brief Summary of Adverse Events

There were no reported treatment-emergent adverse exposure for either SeraSeal treated adults or in children.

Table 14 details the emergent adverse exposure from the two SeraSeal treatment groups.

Table 14 Treatment-emergent Adverse Experience

Adverse Experience		Adult N = 107	Pediatric N = 12
Patients with Adverse Experience		0 (0.00%)	0 (0.00%)
Body system	Preferred Term	0 (0.00%)	0 (0.00%)
Body as a whole	Abdominal pain	0 (0.00%)	0 (0.00%)
	Asthenia	0 (0.00%)	0 (0.00%)
	Back pain	0 (0.00%)	0 (0.00%)
	Chest pain	0 (0.00%)	0 (0.00%)
	Headache	0 (0.00%)	0 (0.00%)
	Infection	0 (0.00%)	0 (0.00%)
	Trauma	0 (0.00%)	0 (0.00%)
Cardiovascular system	Postural Hypotension	0 (0.00%)	0 (0.00%)
	Tachycardia	0 (0.00%)	0 (0.00%)
	Vasodilatation	0 (0.00%)	0 (0.00%)
Digestive system	Constipation	0 (0.00%)	0 (0.00%)
	Decreased appetite	0 (0.00%)	0 (0.00%)
	Diarrhea	0 (0.00%)	0 (0.00%)
	Dry mouth	0 (0.00%)	0 (0.00%)
	Dyspepsia	0 (0.00%)	0 (0.00%)
	Nausea	0 (0.00%)	0 (0.00%)
	Tooth disorder	0 (0.00%)	0 (0.00%)
	Vomiting	0 (0.00%)	0 (0.00%)
Nervous system	Dizziness	0 (0.00%)	0 (0.00%)
	Emotional liability	0 (0.00%)	0 (0.00%)
	Hostility	0 (0.00%)	0 (0.00%)
	Insomnia	0 (0.00%)	0 (0.00%)
	Nervousness	0 (0.00%)	0 (0.00%)
	Somnolence	0 (0.00%)	0 (0.00%)
	Tremor	0 (0.00%)	0 (0.00%)
Respiratory system	Cough increased	0 (0.00%)	0 (0.00%)
	Pharyngitis	0 (0.00%)	0 (0.00%)
	Respiratory disorder	0 (0.00%)	0 (0.00%)
	Rhinitis	0 (0.00%)	0 (0.00%)
	Sinusitis	0 (0.00%)	0 (0.00%)
Other	Sweating	0 (0.00%)	0 (0.00%)
	Abnormal vision	0 (0.00%)	0 (0.00%)

Ref. Individual Patient Data Listing, section 12.4, page 119.

8.3 Death, Other Serious Adverse Events, and Other Significant Adverse Events

There were no deaths or other serious or significant events reported during the acute phase of this study or during the convalescent recovery period.

8.4 Clinical Laboratory Evaluation

Table 15 lists the mean laboratory results of HGB, HCT, PT, PTT at Baseline and at 24 hours, 48 hours, and 30 days post-operative endpoints. Eighty two of the patients (68.9%) baseline had normal laboratory results, while the remaining 37 subjects (31.1%) were outside the acceptable normal range. Table 16 Criteria for Flagging of Selected Laboratory Parameters, details each analyte abnormal level. The abnormal patients were equally divided between genders. Hemorrhage (15.1 %), and heparin (23.5 %), were the cause for the abnormal blood levels, which are listed in Table 17, Flagged Abnormal Laboratory Results.

Table 15 Laboratory Results at Baseline and at PostOperative Points (mean ± SD)

	Treatment Group			
Laboratory Test	**Adult**	**n**	**Pediatric**	**n**
Hemoglobin M (g/dl)				
Baseline	13.90 ± 1.56	56	15.02 ± 1.83	6
24h Post-Op	14.02 ± 1.12	56	15.23 ± 0.76	6
Change	0.09 ± 0.72	56	0.22 ± 1.23	6
48h Post-Op	14.15 ± 1.01	56	15.33 ± 0.84	6
Change	0.26 ± 0.74	56	0.32 ± 1.18	6
30d Post-Op	14.3 ± 0.86	56	15.56 ± 0.86	6
Change	0.50 ± 1.29	56	0.53 ± 1.22	6
Hemoglobin F (g/dl)				
Baseline	12.43 ± 1.02	51	14.62 ± 0.46	6
24h Post-Op	12.36 ± 1.01	51	14.53 ± 0.44	6
Change	-0.09 ± 0.29	51	-0.13 ± 0.14	6
48h Post-Op	12.49 ± 0.95	51	14.62 ± 0.55	6
Change	0.06 ± 0.34	51	0.02 ± 0.15	6
30d Post-Op	12.69 ± 0.88	51	14.77 ± 0.38	6
Change	0.19 ± 0.41	51	0.15 ± 0.12	6
Hematocrit M (%)				
Baseline	41.58 ± 4.71	56	46.37 ± 2.71	6
24h Post-Op	42.04 ± 3.43	56	46.03 ± 2.73	6
Change	0.47 ± 1.89	56	-0.33 ± 0.37	6
48h Post-Op	42.55 ± 2.94	56	46.27 ± 2.66	6
Change	0.99 ± 2.56	56	-0.10 ± 0.22	6
30d Post-Op	43.10 ± 2.57	56	46.33 ± 2.54	6
Change	1.54 ± 3.81	56	-0.03 ± 0.36	6
Hematocrit F (%)				
Baseline	36.56 ± 5.66	51	43.72 ± 1.16	6
24h Post-Op	36.83 ± 3.66	51	43.42 ± 1.14	6
Change	-0.13 ± 0.85	51	-0.33 ± 0.63	6
48h Post-Op	35.93 ± 7.64	51	43.73 ± 1.07	6
Change	0.18 ± 1.03	51	0.02 ± 0.56	6
30d Post-Op	37.23 ± 5.57	51	44.12 ± 1.10	6
Change	0.66 ± 1.43	51	0.40 ± 0.58	6
Prothrombin Time M (sec)				
Baseline	11.58 ± 0.22	56	11.23 ± 0.19	6
24h Post-Op	11.57 ± 0.19	56	11.27 ± 0.16	6
Change	-0.01 ± 0.09	56	0.03 ± 0.10	6
48h Post-Op	11.54 ± 0.22	56	11.32 ± 0.08	6
Change	-0.01 ± 0.08	56	0.05 ± 0.12	6
30d Post-Op	11.53 ± 0.25	56	11.30 ± 0.09	6
Change	-0.01 ± 0.10	56	0.07 ± 0.12	6
Prothrombin Time F (sec)				
Baseline	11.68 ± 0.26	51	11.42 ± 0.17	6
24h Post-Op	11.65 ± 0.24	51	11.35 ± 0.19	6
Change	-0.03 ± 0.11	51	-0.07 ± 0.12	6
48h Post-Op	11.64 ± 0.28	51	11.33 ± 0.12	6
Change	-0.01 ± 0.09	51	-0.08 ± 0.04	6
30d Post-Op	11.66 ± 0.26	51	11.37 ± 0.14	6
Change	-0.01 ± 0.11	51	-0.05 ± 0.05	6

Partial Thromboplastin Time M (sec)				
Baseline	34.56 ± 12.91	56	23.17 ± 1.60	6
24h Post-Op	34.61 ± 14.08	56	23.33 ± 1.51	6
Change	-0.04 ± 2.30	56	0.17 ± 0.98	6
48h Post-Op	34.10 ± 12.35	56	23.00 ± 1.10	6
Change	-0.67 ± 1.84	56	-0.17 ± 0.98	6
30d Post-Op	26.60 ± 3.52	56	22.83 ± 1.17	6
Change	-7.93 ± 13.49	56	-0.33 ± 0.82	6
Partial Thromboplastin Time F (sec)				
Baseline	32.26 ± 12.54	51	23.67 ± 0.82	6
24h Post-Op	32.96 ± 12.72	51	23.50 ± 1.05	6
Change	0.36 ± 1.78	51	-0.17 ± 0.75	6
48h Post-Op	32.84 ± 10.84	51	23.83 ± 0.75	6
Change	-0.32 ± 2.00	51	0.17 ± 0.41	6
30d Post-Op	27.64 ± 4.44	51	23.00 ± 0.89	6
Change	-5.20 ± 11.12	51	-0.67 ± 0.52	6

Ref: Listing of Individual Vital Sign by Patient, section 12.2.5, page 106.

Table 16 Criteria for Flagging of Selected Laboratory Parameters

Adults:	Laboratory Test	Normal Range
	Hemoglobin	11.8 – 16.2 g/dl
	Hematocrit	33 – 49 %
	Prothrombin Time	10.5 -12.5 sec
	Partial Thromboplastin Time	23 – 48 sec
Pediatric:	Laboratory Test	Normal Range
	Hemoglobin	10 – 13 g/dl
	Hematocrit	30 – 40 %
	Prothrombin Time	11 – 13 sec
	Partial Thromboplastin Time	20 – 30 sec

Ref: Listing of Individual Vital Sign by Patient, section 12.2.5, page 106.

Table 17 Flagged Abnormal Laboratory Results

.			HGB (g/dl)			HCT (%)			PT (sec)			PTT (sec)		
Patient No	**Age**	**Sex**	**Pre**	**24h PO**	**48h PO**	**Pre**	**24h PO**	**48h PO**	**Pre**	**24h PO**	**48h PO**	**Pre**	**24h PO**	**48h PO**
JM-01	68	M	14.0	13.8	14.1	42.9	42.6	42.2	11.6	11.5	11.5	54	56	51
JM-02	50	M	14.8	14.7	14.8	44.5	44.3	44.5	11.4	11.4	11.4	52	49	52
JM-03	74	M	137	13.9	13.9	41.0	40.6	41.2	11.9	11.9	11.8	58	61	54
JM-04	56	M	14.5	14.3	14.3	43.6	43.5	43.6	11.3	11.4	11.3	53	47	50
JS-002	40	F	11.2	11.2	11.3	35.4	33.6	33.8	12.2	12.1	12.3	40	40	41
JM-001	38	F	11.4	11.3	11.3	32.8	33.7	33.8	11.8	11.6	11.8	26	26	24
ML-006	54	M	9.4	11.6	12.1	28.1	34.9	36.3	11.9	11.5	11.5	30	26	25
ML-008	80	M	10.1	12.3	12.8	30.0	36.9	38.2	11.8	11.7	11.7	29	26	27
ML-009	30	F	10.5	12.0	12.6	31.5	35.9	37.6	11.9	11.6	11.6	30	27	27
ML-019	55	M	12.4	13.6	13.8	37.3	40.5	41.3	12.2	12.1	12.2	40	39	41
RG-001	63	F	10.8	10.4	10.9	32.0	31.1	32.6	12.5	12.6	12.5	43	46	41
RG-002	38	M	9.3	11.6	13.1	28.0	34.7	39.4	11.4	11.4	11.4	27	28	26
RG-003	65	F	10.5	10.2	10.9	31.3	30.4	32.6	11.6	11.5	11.7	30	29	31
RG-004	63	F	10.9	10.5	10.8	32.8	32.5	32.3	11.3	11.4	11.3	25	26	25
RG-005	50	M	10.7	10.3	11.0	31.9	30.7	32.9	11.6	11.5	11.6	30	30	31
EN-001	54	M	14.8	14.8	14.7	44.2	44.4	44.2	11.5	11.5	11.4	52	54	48
EN-014	53	M	14.9	14.7	14.9	44.5	44.3	44.7	11.5	11.3	11.3	50	50	50
AR-006	72	M	15.9	15.8	16.2	48.0	46.0	48.3	11.5	11.5	11.6	58	62	56
AR-017	48	F	11.4	11.0	11.2	33.3	32.7	33.0	11.8	11.7	11.7	52	56	49
AR-018	28	F	11.0	10.9	11.2	33.4	33.0	33.7	11.8	11.9	11.7	45	42	46
AR-022	92	F	10.5	10.2	10.9	31.2	31.0	32.7	12.0	11.9	12.0	52	48	45
AR-026	53	M	14.6	14.2	14.5	43.0	42.5	43.2	11.3	11.5	11.5	48	52	52
AR-030	57	F	11.7	11.4	11.9	34.2	33.8	35.5	11.5	11.4	11.5	50	54	48
AR-031	38	M	15.3	15.0	15.0	45.7	45.2	45.4	11.6	11.6	11.4	68	72	64
AR-032	61	M	14.8	14.4	14.7	44.1	43.8	44.0	11.3	11.3	11.2	46	52	45
AR-033	59	F	11.5	11.2	11.4	34.0	33.7	33.9	11.7	11.5	11.8	44	46	46
AR-034	59	M	15.2	15.0	15.3	45.6	45.2	45.5	11.2	11.3	11.2	48	45	42
VQ-01	76	F	11.5	11.4	11.6	34.2	34.2	34.3	11.8	11.7	11.7	63	65	62
VQ-02	76	F	12.0	11.7	11.8	35.8	35.0	35.7	11.8	11.5	11.7	64	65	67
VQ-03	82	M	14.3	14.0	14.1	37.3	42.1	42.5	11.5	12.1	11.4	68	72	64
VQ-04	75	M	13.9	13.7	14.0	40.2	40.0	40.4	11.2	11.3	11.2	64	70	64
ZC-01	55	F	12.2	11.9	12.1	36.5	36.1	36.3	11.4	11.4	11.3	45	48	40
ZC-02	67	M	14.6	14.2	14.5	43.6	43.0	44.0	11.8	11.7	11.7	51	53	50
ZC-03	32	F	11.0	11.2	11.3	33.2	33.4	33.7	11.9	11.7	11.9	46	50	45

ZC-04	37	M	15.2	14.9	15.2	45.3	45.0	45.5	11.3	11.4	11.2	48	45	49
ZC-05	72	F	14.0	13.7	14.0	42.2	41.3	42.4	11.4	11.5	11.5	68	72	64
CR-002	37	M	9.6	11.6	13.1	28.9	34.6	39.4	11.7	11.6	11.7	27	27	28

Ref: Laboratory Results Data Listing, section 12.2.6, page 110.

8.5 Vital Signs

The vital signs are tabulated in Table 18 Vital Signs at Baseline and Endpoint. All of the patients maintained normal vital signs throughout the study. The baseline of sixty three patients (52.9%) had abnormal vital signs, based on the Criteria of Flagged Vital Sign, Table 19. The contributing factors for the abnormal vital signs were history of hypertension (19.3%), dehydration (11.8%), hemorrhage (9.2%), and anxiety (9.2%), Table 20, Flagged Abnormal Vital signs.

Table 18 Vital Signs at Baseline and at PostOperative Points (mean ± SD)

	Treatment Group			
Vital Sign Parameter	**Adult**	**n**	**Pediatric**	**n**
Systolic BP (mmHg) M				
Baseline	115.43 ± 18.74	56	95.83 ± 21.78	6
24h Post-Op	120.46 ± 10.73	56	95.50 ± 21.03	6
Change	4.03 ± 12.68	56	0.33 ± 1.86	6
48h Post-Op	120.49 ± 9.91	56	95.17 ± 22.06	6
Change	5.51 ± 12.08	56	-0.67 ± 1.75	6
30d Post-Op	121.48 ± 9.85	56	96.83 ± 22.20	6
Change	5.74 ± 12.56	56	0.83 ± 1.47	6
Systolic BP (mmHg) F				
Baseline	115.12 ± 22.43	51	115.00 ± 5.48	6
24h Post-Op	120.00 ± 13.96	51	113.67 ± 6.38	6
Change	4.92 ± 9.69	51	-1.33 ± 1.63	6
48h Post-Op	121.36 ± 14.28	51	115.33 ± 5.32	6
Change	5.80 ± 10.77	51	0.33 ± 1.50	6
30d Post-Op	122.08 ± 14.59	51	115.00 ± 5.48	6
Change	6.72 ± 11.55	51	0.00 ± 0.00	6
Diastolic BP (mmHg) M				
Baseline	70.14 ± 12.22	56	55.00 ± 14.83	6
24h Post-Op	75.88 ± 10.81	56	55.33 ± 15.47	6
Change	6.90 ± 8.91	56	0.00 ± 1.67	6
48h Post-Op	80.52 ± 8.97	56	54.67 ± 14.90	6
Change	6.84 ± 9.62	56	-0.67 ± 1.51	6
30d Post-Op	77.76 ± 5.28	56	55.33 ± 14.73	6
Change	8.07 ± 11.11	56	-0.33 ± 1.03	6
Diastolic BP (mmHg) F				
Baseline	67.50 ± 12.76	51	66.67 ± 5.16	6
24h Post-Op	76.04 ± 5.41	51	67.67 ± 3.67	6
Change	8.72 ± 9.40	51	1.00 ± 1.67	6
48h Post-Op	76.12 ± 5.08	51	67.67 ± 5.28	6
Change	8.76 ± 10.24	51	1.00 ± 1.10	6
30d Post-Op	77.14 ± 6.06	51	67.67 ± 5.96	6
Change	10.18 ± 10.95	51	0.67 ± 1.03	6
Pulse (bpm) M				
Baseline	88.42 ± 10.42	56	103.00 ± 13.90	6
24h Post-Op	83.48 ± 3.12	56	101.00 ± 12.25	6
Change	-6.14 ± 10.33	56	-2.00 ± 2.53	6
48h Post-Op	83.38 ± 2.78	56	102.33 ± 12.48	6
Change	-6.11 ± 11.07	56	-1.33 ± 1.63	6
30d Post-Op	83.72 ± 3.29	56	102.33 ± 13.76	6
Change	-5.58 ± 11.02	56	-1.33 ± 1.63	6
Pulse (bpm) F				
Baseline	83.16 ± 22.79	51	99.67 ± 16.07	6
24h Post-Op	82.64 ± 3.29	51	100.33 ± 14.66	6
Change	-5.20 ± 9.81	51	0.00 ± 3.10	6
48h Post-Op	83.20 ± 3.54	51	102.33 ± 15.87	6
Change	-5.04 ± 9.93	51	2.67 ± 2.06	6
30d Post-Op	82.80 ± 3.33	51	101.67 ± 15.82	6
Change	-5.44 ± 10.60	51	2.00 ± 2.19	6

Ref: Listing of Individual Vital Sign by Patient, section 12.2.5, page 106.

Table 19 Criteria for Flagged Vital Signs

Adults:	Category	Systolic	Diastolic
	Normal	< 120	< 80
	Pre-hypertension	120 -139	80 -89
	Stage 1 Hypotensive	140 – 159	90 – 99
	Stage 2 Hypotensive	≥ 160	≥ 100
Pediatric:	Infancy	Normal = 80/45	
	Teenage	Normal = 110/70	
Heart Rate:	Tachycardia	bpm	
	1-2 days	123-159	
	3-6 days	129-166	
	1-3 week	107-182	
	1-2 mo.	121-179	
	3-5 mo.	106-186	
	6-11 mo.	109-169	
	1-2 year	89-151	
	3-4 year	73-137	
	5-7 year	65-133	
	8-11 year	62-130	
	12-15 year	60-119	

Table 20 Table Flagged Abnormal Vital Signs

Patient No.	Baseline			24h Post-Op			48h Post-Op			30d Post-Op			Cause
	S	D	P	S	D	P	S	D	P	S	D	P	
JM-01	140	90	84	140	88	82	142	88	86	142	90	82	Hx hypertension
JM-03	140	85	86	138	84	84	140	84	84	140	82	82	Hx hypertension
JM-04	140	90	82	142	88	84	140	88	82	140	86	80	Hx hypertension
PC-003	110	60	90	116	70	90	116	72	88	118	72	90	anxiety
GJ-001	130	75	82	124	78	78	126	76	80	128	78	82	Hx hypertension
GJ-002	110	55	78	112	68	80	112	70	76	114	70	76	dehydration
GJ-004	140	75	82	138	76	86	142	78	82	142	76	82	Hx hypertension
JS-002	90	60	100	108	70	84	110	76	86	110	76	80	dehydration
JM-002	140	90	92	140	88	84	140	88	88	142	88	82	Hx hypertension
JM-003	150	80	90	138	82	86	140	82	86	142	80	88	Hx hypertension
JM-004	150	80	94	150	82	90	152	80	88	154	82	86	Hx hypertension
JM-005	130	80	86	130	84	82	128	82	84	128	84	80	Hx hypertension
JM-007	130	70	84	128	72	82	130	70	84	130	74	82	Hx hypertension
JM-008	130	70	86	130	70	80	132	72	84	130	72	84	Hx hypertension
LC-003	110	60	86	118	72	84	116	72	84	114	74	88	dehydration
LC-004	110	60	86	120	74	80	122	74	82	118	72	84	dehydration
ML-001	90	70	104	110	80	86	114	82	82	114	80	84	dehydration
ML-002	80	50	112	108	76	80	116	80	84	118	82	82	dehydration
ML-004	100	50	98	118	76	86	118	74	88	116	84	82	anxiety
ML-005	110	60	80	112	70	84	116	72	80	116	76	80	anxiety
ML-006	90	60	106	120	82	82	120	80	80	118	82	82	hemorrhage
ML-007	80	50	118	114	78	88	116	80	84	116	80	84	dehydration
ML-008	70	40	122	108	70	86	114	74	82	118	78	86	hemorrhage
ML-009	70	40	116	104	68	84	110	72	84	114	80	80	hemorrhage
ML-010	90	60	108	112	78	82	114	76	80	114	76	80	dehydration
ML-012	100	70	80	108	74	82	110	72	80	110	74	80	anxiety
ML-014	130	85	82	128	86	84	126	86	80	128	84	82	Hx hypertension
ML-017	100	70	92	114	76	90	116	74	90	114	72	88	anxiety
RG-001	100	70	78	108	74	80	110	74	80	114	76	82	hemorrhage
RG-002	70	40	110	100	68	82	106	70	86	110	74	84	hemorrhage
RG-003	90	40	102	112	70	84	110	72	84	114	72	82	hemorrhage

RG-004	**60**	**40**	**114**	**102**	**74**	**82**	**108**	**76**	**82**	**112**	**80**	**86**	**hemorrhage**
RG-005	**80**	**50**	**120**	**106**	**70**	**88**	**108**	**72**	**84**	**110**	**76**	**86**	**hmeorrhage**
AM-002	**80**	**50**	**104**	**106**	**68**	**82**	**108**	**72**	**80**	**112**	**72**	**84**	**dehydration**
AM-003	**90**	**60**	**108**	**110**	**74**	**80**	**110**	**76**	**82**	**110**	**72**	**82**	**dehydration**
AM-004	**80**	**50**	**112**	**106**	**72**	**82**	**112**	**76**	**84**	**112**	**74**	**82**	**hemorrhage**
AM-007	**100**	**70**	**94**	**118**	**78**	**90**	**116**	**78**	**92**	**118**	**78**	**96**	**anxiety**
EN-014	**130**	**80**	**84**	**128**	**82**	**86**	**130**	**84**	**82**	**128**	**86**	**84**	**Hx hypertension**
AR-006	**140**	**80**	**84**	**140**	**82**	**80**	**142**	**82**	**78**	**140**	**84**	**80**	**Hx hypertension**
AR-018	**170**	**50**	**96**	**168**	**70**	**88**	**164**	**72**	**86**	**168**	**74**	**82**	**Hx hypertension**
AR-022	**100**	**70**	**84**	**108**	**74**	**80**	**110**	**72**	**82**	**110**	**74**	**80**	**hemorrhage**
AR-023	**100**	**70**	**82**	**114**	**76**	**86**	**112**	**72**	**84**	**114**	**74**	**86**	**anxiety**
AR-026	**135**	**75**	**82**	**130**	**78**	**80**	**132**	**76**	**86**	**130**	**78**	**84**	**Hx hypertension**
AR-030	**90**	**50**	**102**	**110**	**76**	**84**	**112**	**74**	**82**	**114**	**74**	**86**	**dehydration**
AR-031	**90**	**50**	**102**	**110**	**76**	**84**	**112**	**74**	**82**	**114**	**74**	**86**	**dehydration**
AR-032	**100**	**70**	**88**	**108**	**78**	**80**	**110**	**76**	**84**	**112**	**76**	**84**	**anxiety**
AR-033	**90**	**50**	**106**	**108**	**74**	**82**	**106**	**76**	**80**	**110**	**78**	**82**	**dehydration**
VQ-04	**140**	**80**	**84**	**136**	**82**	**82**	**138**	**80**	**86**	**136**	**82**	**88**	**Hx hypertension**
VQ-05	**120**	**60**	**78**	**118**	**74**	**80**	**120**	**72**	**78**	**120**	**76**	**76**	**anxiety**
ZC-01	**140**	**80**	**82**	**140**	**80**	**84**	**138**	**80**	**82**	**142**	**84**	**82**	**Hx**
ZC-02	**130**	**70**	**84**	**132**	**76**	**88**	**130**	**72**	**82**	**130**	**74**	**82**	**Hx**
ZC-03	**110**	**60**	**80**	**112**	**76**	**78**	**114**	**74**	**80**	**112**	**76**	**82**	**hemorrhage**
ZC-04	**140**	**0**	**98**	**142**	**72**	**88**	**140**	**74**	**84**	**142**	**76**	**84**	**Hx**
ZC-05	**150**	**80**	**82**	**146**	**82**	**80**	**148**	**84**	**86**	**148**	**84**	**82**	**Hx**
CR-005	**100**	**50**	**106**	**114**	**72**	**82**	**116**	**70**	**84**	**116**	**72**	**82**	**dehydration**
CR-007	**100**	**70**	**84**	**118**	**82**	**86**	**116**	**80**	**82**	**118**	**82**	**82**	**anxiety**
CZ-002	**130**	**70**	**80**	**126**	**76**	**88**	**128**	**74**	**84**	**128**	**76**	**86**	**Hx hypertension**
CZ-005	**160**	**90**	**82**	**158**	**90**	**80**	**160**	**88**	**78**	**160**	**92**	**80**	**Hx hypertension**
CZ-010	**160**	**90**	**82**	**158**	**90**	**80**	**160**	**92**	**84**	**162**	**92**	**80**	**Hx hypertension**
CZ-011	**140**	**90**	**86**	**140**	**92**	**82**	**138**	**90**	**82**	**140**	**90**	**84**	**Hx hypertension**
JR-001	**130**	**70**	**82**	**126**	**78**	**84**	**130**	**76**	**80**	**132**	**78**	**86**	**Hx**
JR-003	**130**	**70**	**78**	**132**	**76**	**80**	**128**	**74**	**80**	**130**	**76**	**84**	**Hx**
JR-004	**100**	**40**	**96**	**118**	**70**	**88**	**116**	**72**	**84**	**114**	**72**	**88**	**anxiety**

Ref: Listing of Individual Vital Sign by Patient, section 12.2.5, page 106.
Table 19, Criteria for Flagged Vital Signs, page 49.

8.6 Safety Conclusions

The 119 patients that were treated with SeraSeal were closely monitored during surgery, post operatively, and throughout their hospitalization for any adverse events: post-operative bleeding, anemia, atrial fibrillation, infection, hemorrhage, pneumonia, urinary tract infection, rash, edema, hypotension, respiratory distress, confusion, ventricular fibrillation, arrhythmia, heart failure, arterial thrombosis, fever, atelectasis, pleural effusion, and assessing adverse experiences by body system, none were reported.

9. Discussion and Overall Conclusions

The results of this single-blinded, parallel trial supports SeraSeal to be an effective hemostatic agent to control bleeding in a wide range of tissues, known for moderate to severe blood loss, both in adults and children, as well as in heparinized patients. SeraSeal, in both the primary and secondary efficacy study points overwhelmingly overshadowed cauterization to control bleeding by achieving hemostasis 1400% sooner, and reducing blood loss by 50%, far above the parameters established in the protocol.

This study also demonstrated SeraSeal to be safe for both genders and all age groups.

10. Tables, Figures, and Graphs Referred to but not Included

Table 21 Summary of Patient Distribution by Treatment Intent-to-Treat Population

	Treatment Group		
Study Center	**Adult**	**Pediatric**	**Total**
Edgardo Rebagliati Martins National Hospital	65	9	74
Guillermo Almenara National Hospital	13	0	13
Jose Casimiro Ulloa Emergency Hospital	6	0	6
FAP-Peruvian Air Force Hospital	20	2	22
Military Hospital of Peru	3	1	4
Total	107	12	119

Ref: Individual Patient Data Listing, appendix 12.4, page 119.

Table 22 Summary of Demographic Data Intent-to-Treat Population

		Treatment Group					
		Adult		Pediatric		Total Patients	
		N	%	N	%	N	%
Race	Hispanic	107	89.9	12	10.1	119	100
Sex	Male	56	52.3	6	50	62	52.1
	Female	51	47.7	6	50	57	47.9
Age	0-2	0	0.0	5	41.7	5	4.2
	3-10	0	0.0	3	25.0	3	2.5
	11-17	0	0.0	4	33.3	4	3.4
	18-20	4	3.7	0	0.0	4	3.4
	21-30	6	5.6	0	0.0	6	5.0
	31-40	18	16.8	0	0.0	18	15.1
	41-50	12	11.2	0	0.0	12	10.1
	51-60	16	15.0	0	0.0	16	13.4
	61-70	20	18.7	0	0.0	20	16.8
	71-80	20	18.7	0	0.0	20	16.8
	81-90	9	8.4	0	0.0	9	7.6
	91-92	2	1.9	0	0.0	2	1.7
Total Patients		107	100	12	100	119	100

Ref: Demographic Data Listing, appendix 12.2.3, page 100.

Table 23 Summary of Demographic Mean (+/-) Data Intent-to-Treat Population

		Treatment Group		
		Adult	Pediatric	Total Patients
Age (yrs)	mean	56.82	9.25	52.12
	minimum	18	20 days	20 days
	maximum	92	16	92
	Std Dev	10.39	5.84	23.83

Ref: Demographic Data Listing, appendix 12.2.3, page ___.

Table 24 Summary of Height and Weight at Baseline Intent-to-Treat Population

	Treatment Group									
	Adult					Pediatric				
	n	mean	SD	min	max	n	mean	SD	min	max
Height (in)	107	64.29	3.07	58	70	12	41.75	14.84	16	63
Weight (lbs)	107	148.47	20.49	110	202	12	54.50	36.52	4	110

Ref: Demographic Data Listing, appendix 12.2.3, page 100.

Table 25 Summary Total Time to Hemostasis of Seraseal Treated Heparinized Patients vs. Cauterized Heparin Patients

	Treatment Group	
Hemostasis (min)	**SeraSeal (n=24)**	**Cauterization (n=24)**
mean	0.73	10.42
minimum (min)	0.03	2.00
maximum (max)	1.00	35.00
Std Dev	0.29	8.13

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 26 Summary Time to Hemostasis of Total SeraSeal Patients vs. Cauterization Patients

	Treatment Group	
Hemostasis (sec)	**SeraSeal (n=120)**	**Cauterization (n=120)**
mean	1.59	31.225
minimum (min)	0.03	2.00
maximum (max)	10.00	90.00
Std Dev	2.32	19.72

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 27 Summary Time to Hemostasis of Normal SeraSeal Patients vs. Cauterization Patients by Gender

	Treatment Group							
	SeraSeal				Cauterization			
	Adult		Pediatric		Adult		Pediatric	
Hemostasis (min)	**M (n=42)**	**F (n=41)**	**M (n=6)**	**F (n=7)**	**M (n=42)**	**F (n=41)**	**M (n=6)**	**F (n=7)**
mean	2.00	1.16	1.33	2.14	34.76	33.29	31.67	50.28
minimum (min)	0.03	0.03	1.00	1.00	5.00	5.00	10.00	10.00
maximum (max)	10.00	10.00	3.00	5.00	60.00	60.00	60.00	90.00
Std Dev	2.99	2.41	0.82	1.34	15.02	17.12	24.83	33.38

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 28 Summary Time to Hemostasis of Heparinized SeraSeal Patients vs. Cauterization Patients by Gender

	Treatment Group			
Hemostasis (min)	**SeraSeal**		**Cauterization**	
	M (n=14)	F (n=10)	M (n=14)	F (n=10)
mean	0.75	0.70	10.36	10.50
minimum (min)	0.03	0.50	2.00	5.00
maximum (max)	1.00	1.00	35.00	20.00
Std Dev	0.32	0.26	10.00	4.97

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 29 Summary of Time to Hemostasis Between Total Normal and Heparin Patients Treated with SeraSeal

Hemostasis (min)	Normal Patients (n=96)	Heparin Patients (n=24)
mean	1.80	0.73
minimum (min)	0.03	0.03
maximum (max)	10.00	1.00
Std Dev	2.55	0.29

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 30 Summary of Comparing Time to Hemostasis Between Normal to Heparin Patients with SeraSeal by Gender

	Treatment Groups							
	SeraSeal Normal Patients				SeraSeal Heparin Patients			
Hemostasis (min)	**Male**	**n**	**Female**	**n**	**Male**	**n**	**Female**	**n**
mean	1.69	56	1.44	51	0.75	14	0.70	10
minimum (min)	0.03	56	0.03	51	0.03		0.50	
maximum (max)	10	56	10.00	51	1.00		1.00	
Std Dev	2.64	56	2.21	51	0.32		0.26	

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 31 Summary Total Time to Hemostasis of SeraSeal Treated Heparinized Patients vs. Cauterized Heparin Patients

	Treatment Group	
Hemostasis (min)	SeraSeal (n=24)	Cauterization (n=24)
mean	0.73	10.42
minimum (min)	0.03	2.00
maximum (max)	1.00	35.00
Std Dev	0.29	8.13

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 32 Summary of the Number of SeraSeal Applications Between Normal and Heparin Patients

	Normal Patients				Heparin Patients			
Hemostasis (sec)	**Male**	**n**	**Female**	**n**	**Male**	**n**	**Female**	**n**
mean	3.41	48	3.23	40	3.64	14	3.70	10
minimum (min)	1		2		2		2	
maximum (max)	10		6		7		6	
Std Dev	1.54		1.12		1.39		1.49	

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 33 Summary of Blood Loss of Total SeraSeal Patients vs. Cauterization Patients

	Treatment Group	
Blood Loss (ml)	**SeraSeal (n=119)**	**Cauterization (n=119)**
mean	184.30	583.19
minimum (min)	1.00	100.00
maximum (max)	2000.00	3000.00
Std Dev	243.04	541.63

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 34 Summary of Blood Loss of Normal SeraSeal Patients vs. Cauterization Patients by Gender

	Treatment Group							
	SeraSeal				Cauterization			
	Adult		Pediatric		Adult		Pediatric	
Blood Loss (ml)	**M (n=56)**	**F (n=51)**	**M (n=6)**	**F (n=6)**	**M (n=56)**	**F (n=51)**	**M (n=6)**	**F (n=6)**
mean	216.23	184.96	75.00	10.83	653.57	546.60	375.00	283.33
minimum (min)	1.00	1.00	10.00	5.00	50.00	50.00	250.00	200.00
maximum (max)	2000.00	500.00	250.00	50.00	3000.00	2000.00	400.00	400.00
Std Dev	299.61	183.85	92.03	4.92	635.24	472.30	311.05	68.31

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 35 Summary Blood Loss of Heparinized SeraSeal Patients vs. Cauterization Patients by Gender

	Treatment Group			
	SeraSeal		Cauterization	
Blood Loss (ml)	**M (n=14)**	**F (n=10)**	**M (n=14)**	**F (n=10)**
mean	378.57	358.00	771.43	760.00
minimum (min)	200.00	30.00	500.00	300.00
maximum (max)	500.00	500.00	1200.00	1000.00
Std Dev	110.44	167.25	249.39	267.50

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 36 Summary of Blood Loss Between Total Normal and Heparinized Patients Treated with SeraSeal

	Treatment Group	
Blood Loss (ml)	**Normal Patients (n=95)**	**Heparin Patients (n=24)**
mean	138.15	370.00
minimum (min)	1.00	30.00
maximum (max)	2000.00	500.00
Std Dev	242.11	133.97

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 37 Summary of Comparing Blood Loss Between Normal to Heparin Patients Treated with SeraSeal by Gender

	Treatment Group			
	SeraSeal Normal Patients		SeraSeal Heparin Patients	
Blood Loss (ml)	M (n=48)	F (n=47)	M (n=14)	F (n=10)
mean	148.24	125.17	378.57	358.00
minimum (min)	1.00	1.00	200.00	30.00
maximum (max)	2000.00	500.00	500.00	500.00
Std Dev	302.42	156.06	110.44	167.25

Ref: Individual Response Data, appendix 12.2.4, page 103.

Table 38 Summary of Adverse Events

Adverse Event						
Body System:	Body or a whole	Cardio-vasc system	Digestive system	Nervous system [1]	Respiratory system	Other
n	0	0	0	0	0	0
%	0.00	0.00	0.00	0.00	0.00	0.00

Ref: Adverse Event Listing, appendix 12.2.8, page 117.

10. Tables, Figures, and Graphs Referred to But Not Included In the Text

10.1 Table 21 Summary of Patient Distribution by Treatment Intent-to-Treat Population
10.2 Table 22 Summary of Demographic Data Intent-to-Treat Population
10.3 Table 23 Summary of Demographic Mean (+/-) Data Intent-to-Treat Population
10.4 Table 24 Summary of Height and Weight at Baseline Intent-to-Treat Population
10.5 Table 25 Summary Total Time to Hemostasis of Seraseal Treated Heparinized Patients vs. Cauterization Heparin Patients
10.6 Table 26 Summary Time to Hemostasis of Total SeraSeal Patients vs. Cauterization Patients
10.7 Table 27 Summary Time to Hemostasis of Normal SeraSeal Patients vs. Cauterization Patients by Gender
10.8 Table 28 Summary Time to Hemostasis of Heparinized SeraSeal Patients vs. Cauterization Patients by Gender
10.9 Table 29 Summary of Time to Hemostasis Between Total Normal and Heparin Patients Treated with SeraSeal
10.10 Table 30 Summary of Comparing Time to Hemostasis Between Normal to Heparin Patients with SeraSeal by Gender
10.11 Table 31 Summary of Time to Hemostasis of SeraSeal Heparinized Patients vs. Cauterization Heparinized Patients

11. REFERENCE LIST

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12. Appendices

12.1 Study Information
- 12.1.1 Protocol
- 12.1.2 Sample case report form
- 12.1.3 List of regulatory members, patient information, and sample consent form
- 12.1.4 List of investigators, training and experience
- 12.1.5 Signatures of principal investigators
- 12.1.6 Listing of patients receiving investigational product
- 12.1.7 Statistical methods
- 12.1.8 Inter-laboratory standardization methods
- 12.1.9 Referenced publications

12.2 Patient Data Listings
- 12.2.1 Discontinued patients
- 12.2.2 Patients excluded from the efficacy analysis
- 12.2.3 Demographic data
- 12.2.4 Individual response data
- 12.2.5 Listing of Individual Vital Sign by Patient
- 12.2.6 Laboratory Results Data Listing
- 12.2.7 Efficacy Response Data Listing by Dosage
- 12.2.8 Adverse event listing

12.3 Case Report Forms (CRF's)
- 12.3.1 CRF's for deaths, other serious adverse events, and withdrawn for adverse events

12.4 Individual Patient Data Listing

12.1 STUDY INFORMATION

12.1.1 Protocol

Study No.: WLI-1196-PER

Clinical Investigation - Lima Peru

1. **Title:** Efficacy and Safety Investigation of SeraSeal

2. **Principal Investigator: Thoracic & Cardiovascular:** Victor Mendizabal, MD
Alfonso Rivasplata, MD
Zoe Diaz Chavez, MD
Eduardo Nieto, MD
Julio Moron, MD

General Surgery: Gilberto Jayme, MD
Luis Castro, MD
Marco Lanatta, MD
Juan Santillana, MD
Rafael Garatea, MD
Arnaldo Munoz, MD
Ceasar Rotta, MD
Jamie Rocafuerte, MD
Luis Borda, MD

Head & Neck: Julio Moron, MD
Fernando Huerta, MD

Orthopedics: Pedro Cayetano, MD

Neurosurgery: Carlos Zapater, MD

3. **Monitors:** Felipe Plaza, MD
Edgardo Rebagliati Martins National Hospital

Jose Carlos Gutierrez, MD
Edgardo Rebagliati Martins National Hospital

4. **This protocol focuses on treatment**

5. **Location:** Edgardo Rebagliati Martins National Hospital, Lima, Peru
Guillermo Almenara I. EsSalud National Hospital, Lima, Peru
Jose Casimiro Ulloa Emergency Hospital
FAP- Peruvian Air Force Hospital, Lima, Peru
Military Hospital of Peru, Lima

6. **Research Plan:**

6.1 Purpose: The purpose of this study is to investigate the safety and effectiveness of SeraSeal on clotting time in surgical or trauma wounds. This study is designed to determine whether it is safe and effective in achieving hemostasis in different types of wounds.

6.2 Hypothesis or Research Questions or Objectives: The null hypothesis is that cauterization is more effective than SeraSeal in achieving hemostasis. The alternative hypothesis is SeraSeal will achieve hemostasis sooner than cauterization. A secondary endpoint is the measurement of blood loss.

6.3 Significance: SeraSeal shows promise of being an effective hemostatic agent applicable to wounds, surgical operations in which hemostasis is difficult (hepatic, renal and splenic trauma, debridement, burns, skin grafting, endoscopic procedures), control of epistaxis, esophageal variceal bleeding, bleeding peptic ulcers, and bleeding associated with proctitis and cystitis. For some of these conditions, there is no entirely satisfactory treatment.

6.4 Relevance: The availability of an easy to use, stable, safe, effective hemostatic agent, would be a tremendous advantage to the trauma patient (surgical or accidental), possibly reducing morbidity and mortality significantly, and conserving surgical and blood resources.

6.5 Background and Review of Literature:

Problem with Bleeding Wounds

Bleeding is still a major cause of morbidity and mortality in wounds. Thirteen percent of patients suffering acute trauma, die of bleeding[1]. Of the total deaths occurring on the battlefield, eight-five percent are due to blood loss[2]. Particularly vulnerable areas are the face, groin, pelvis and extremities, areas not protected by body armor. In head and neck trauma, uncontrolled bleeding can cause airway compromise and asphxiation[3]. In trauma survivors, inability to control bleeding leads to blood transfusion, increased complication rates, immunosuppression, inability to generate red blood cells, and prolonged time in the hospital. The ideal solution to these problems is to control the bleeding in the first place. The limiting factor in performing burn debridement of chronic wounds results in bleeding, which is essentially an end point for debridement, because there is no satisfactory way of controlling bleeding in granulation tissue. This results in repeated debridement. Bleeding is a major cause of skin graft loss and flap necrosis. Outside of the hospital, the paramedic has only compresses to control bleeding. A quick, effective, and safe device to control bleeding, would be extremely beneficial.

Hemostatic agents in wounds

Commercially available topical thrombogenic agents include microfibillar collagen (Avitene®), collagen sponges (Gelfoam®, Instat®), and fibrin sealants (Tisseel®, AFTA®, ViGuard®). Topical collagen preparations have been available for more than 25 years and have a limited ability to facilitate clotting. When hemorrhage is excessive or the patient's clotting factors are inhibited, they are less effective.

Fibrin Sealants

These are prepared from homolgous, pooled human or bovine fibrinogen, Factor XII, and thrombin that must be combined to make the fibrin. Other components include calcium to provide activation of Factor XIII, fibronectin to aid in adhesion, and an inhibitor of fibrinolysis to prolong fibrin clot life. Fibrin sealants have shown great promise in controlling wound hemorrhage. Fibrin sealants have been shown to reduce operating time, blood loss, and do not appear to interfere with healing[4]. When applied to a ballistic wound as a dry dressing, the sealant reduced blood loss by 64%[5].

Problems with current tissue sealants

Several problems exist with the commercially available fibrin sealants: They are a two part system of fibrin and thrombin, which must be mixed at operation or trauma setting, adding to the operative time and delaying transportation to a stable operative setting. Previously, the FDA withheld approval from European products because they used pooled human plasma as a product source[6]. The fibrin sealants are somewhat difficult to use, as they must be mixed from four components, a process which takes approximately 15 minutes, and then must be used within four hours. If they are to be used endoscopically, they must be placed through a dual luman catheter and mixed in situ[7]. Their viscosity makes application difficult via catheters and in small areas, and limits methods of application such as sprays, or foams, which would be useful for large wounds. The time between mixing and hemostasis can be

several minutes, typically 3-5 minutes, further slowing operation repair[8]. The incorporation of fibrin sealants into a dry dressing has reduced some of these problems. The strength of the clot formation, when utilizing a dry dressing, can be sub-optimal. These shortcomings limit the utility of fibrin sealants for hemostasis in the battlefield, emergency response teams such as paramedics, and in the surgical arena.

Bovine topical thrombin in most cases, is a heterolgous plasma thrombin concentrate that has been used for hemostasis since the 1940's. Some commercial bovine thrombin preparations are highly immunogenic, and appear to be associated with an increased risk for adverse clinical outcomes during subsequent surgical procedures[9]. Antibody formation and anaphylaxis (rates 0.5 to 5.8%) have also been seen with Factor V and aprotinin, a polyvalent proteinase inhibitor isolated from bovine lungs, and used alone to enhance clot stability, or in combination with fibrin sealants[10, 11, 13]. These antibodies may interfere with the heparin anti-Xa assay, thereby complicating the monitoring of anticoagulant therapy[12]. The commercially available product, Tisseel VH fibrin sealant, contains bovine aprotinin, resulting in the risk of hypersensitivity.

What this study will determine

This study is designed to determine whether SeraSeal is safe, effective, and will improve the quality of care, in achieving hemostasis in surgical wounds or other emergent hemorrhagic episodes. The effectiveness will be determined by achieving hemostasis after application of the product. The safety will be determined by monitoring outcomes from application: recurrence of bleeding, infection, lack of healing, and presence of hypersensitivity reactions, e.g. pruritus, fever, rash, anaphylaxis. An improved quality of care will be achieved by reducing or eliminating the hospital length of stay.

Characteristics of SeraSeal

SeraSeal is a bovine protein-derived accelerator of hemostasis interacting with the intrinsic and extrinsic pathways. It is obtained from pathogen and prion free cows. SeraSeal can be provided as a solution, spray, foam, incorporated into an absorbable dressing or a non-absorbable removable dressing. Its active ingredients are the bovine proteins Factors II, VII, IX, and X.

Toxicity of SeraSeal

A total dosage level of SeraSeal over 13,000 IU/Kg (2.4 mg protein) in leporids and canines had no adverse effects[14]. The total expected treatment levels to be used in this study is less than 1,000 IU/Kg, a 130 fold lower level than the no toxic effect. Cell culture studies reveal that SeraSeal is not directly toxic for any cells tested. Thus, drug related toxicity is not expected to be seen in this clinical study.

6.6 Research Design and Methods: This clinical trail will be a difference study where SeraSeal will be used as a liquid, administered by a syringe (300 IU/0.1ml), and compared to standard surgical technique as the control. Patients receiving treatment at Edgardo Rebagliati Martins Hospital, the National Guillermo Hospital, Peruvian Air Force Hospital, and the Military Hospital of Peru will serve as study volunteers. Prior to enrollment in the study, an initial screening test and subsequent studies will take place, including: informed consent, collection and recording of subject demographic information, medical history, current medications, assessment of inclusion/exclusion criteria, physical examination, with blood draws for hematological assessment and coagulation studies for bleeding and time to hemostasis. The location of the study wounds will be invasive. The study wound sites will involve bone and soft tissue.

This is a single-blinded, parallel, randomized clinical trial, where the primary endpoint is hemostasis. Secondary endpoints will include reduction of blood loss, fewer blood transfusions. There are 18 designated surgical faculty members from Head & Neck, Vascular, Thoracic Cardiovascular, Neurosurgery, Orthopedics, and General Surgery participating in this study, with a minimum of 10 surgical procedures being studied. All of the participating surgeons are highly skilled and have extensive expertise in their surgical specialty.

Randomization: The patients will be randomized within each surgical department by drawing a SeraSeal or Cauterization slip. Which ever slip is drawn the next participating patient having the same surgical procedure will

be given the opposite method to control bleeding at same specific bleeding wound sites.

In this trial, the dosage level of SeraSeal is 3,000 IU/ml, with a maximum expected dosage of 10,000 IU, 50 times less than the pre-clinical toxicity studies[14]. After hemostasis is achieved the excess SeraSeal will either be removed through irrigation and suction or absorption onto a surgical sponge. Blood loss will be measured and recorded by reading the volume in the suction canister, or by weighing the blood soaked surgical sponges (1 ml whole blood = 1.04 g). A time to hemostasis is measured from the time when the product or the control is first applied to the wound, until no bleeding or oozying is observed for the entire wound. A nurse will use a stopwatch to record the time to hemostasis. SeraSeal is expected to achieve hemostasis 25% faster than the control. Stopping criteria for treatment in the investigational group will be when hemostasis fails to be achieved within 10 minutes for a particular wound, or at the discretion of the surgeon. If this should happen, the patient will be switched over to standard surgical practices. There are no stopping criteria for the control, since the control employ standard surgical procedures.
The patients will be monitored for 30 days, and will be measured by the amount of post-operative bleeding and overall wound healing for those wounds that can be observed. A base line hemoglobin (HGB) and hematocrit (HCT) blood count, prothrombin time (PT), partial thromboplastin time (PTT), will be drawn and measured 24 hours, and also at 48 hours after surgery. The HGB, HCT, PT and PTT will be drawn 30 days after surgery (Table 1). The patients will be observed and assessed for a minimum of 60 minutes after application of SeraSeal for signs of hypersensitivity to the investigational product, and throughout the 30 days. They will be assessed for, but not limited to, skin rash; wheezing; anaphylaxis; pruritus; prolong coagulation tests; delayed healing or infection through quantitative cultures. In the event there is progression of edema leading to respiratory distress, anaphylaxis, or shock due to blood loss, a crash cart and/or any additional standard and customary treatment(s), will be available. This study will not limit the standard of care performed at both investigational hospitals. The following components of wound care are “standard practice” at each of the hospitals: daily dressing changes; quantitative cultures when infection may be present; routine blood tests. All enrolled study subjects may request to be withdrawn from the study at any time, and will be terminated from the study and provided standard of care. All adverse events will be recorded according to whether the event was unrelated, unlikely, possibly or probably related to the study treatment.

Table 1: Schedule of Assessments

Test	Pre-Op	Surgery	24 Hrs Post Op	48 Hrs Post Op	30 Days
Medical History	X				
Physical Examination	X				
Informed Consent	X				
Designated Delivery System		X			
HGB	X		X*	X+	X
HCT	X		X*	X+	X
PT	X		X*	X+	X
PTT	X		X*	X+	X
ECG	X				
X-Ray Work-UP	X				
Wound care			X	X+	
Microbiological work-up			X*	X+	
Adverse Events			X	X	
Primary Variable		X	X	X	
Secondary Variable		X	X	X	
Safety					
Adverse Events		X	X	X+	X

* measured as often as needed
+ monitored beyond 48 hours as needed

6.7 Inclusion/Exclusion Criteria

Inclusion criteria:

1. All ages and both genders
2. Wounds of a similar type, size, location and bleeding tendency listed in Table 1.
3. Currently on anticoagulation therapy with no dosage limitations.
4. Diagnosed with a coagulation disorder.
5. Participants must be able to participate for the 30 day duration of the study.

Exclusion criteria:

1. Any clinically infected wound, draining pus, surrounding erythema or edema, or patients with systemic signs of infections.
2. Subjects on antibiotic therapy prior to enrollment.
3. Subjects with known allergy to bovine proteins, atopic reactions, history of anaphylaxis.
4. HIV virus infection
5. Sensitivity to idodine
6. Inability to give informed consent.
7. Inability to return for a 30 day follow-up visit.

6.8 Source of Research Material

6.9 Number of Subjects: A total of 200 subjects, are to participate in this study.

7.0 Recruitment: Subjects will be randomly selected from within each participating surgical department at Edgardo Rebagliati Martins National Hospital, Guillermo Almenara I. EsSalud National Hospital, Peruvian Air Force Hospital, and the Military Hospital of Peru. The faculty from all of the hospitals will obtain an informed consent, prior to their participation in the study. No promotional fliers are planned. The consent form will be provided by the hospitals in Spanish. Subjects will not be paid for participation in this study.

7.1 Benefits: The possible benefit of the patient's participation in this study is a faster time to clotting, less blood loss, faster wound healing, and less loss of tissue. However, the participant should understand there is no guarantee or promise that they will receive any benefit from this study, other than knowing that the information may help future patients.

7.2 Risks: The risks of application of SeraSeal are theoretical. These risks may be bleeding, infection, and allergic reaction[14]. Anaphylaxis is a possible risk, but the incidence is not clearly known. In clinical case studies, SeraSeal was used in Greece on 39 dialysis patients[15]. These patients received SeraSeal 3-4 times each over a period of two weeks, and no reactions or adverse sequeal were noted[16]. Aprotinin, a bovine protein derived from the bovine lung, is used in cardiac surgery and is the component of some fibrin sealants. It has an anaphylaxis rate of 2.5% on second exposure, with a mean interval of 1,654 days (range, 16-7,136 days)[16,17]. SeraSeal contains no aprotinin. Bovine gelatin is a component of some vaccines and anaphylaxis has been reported with this protein[18]. Other bovine proteins for which anaphylaxis and hypersensitivity reactions have been reported, are bovine serum albumin[19], thrombin[20,21], recombinant Factor VIII[22], insulin[23], and tissue sealants[24]. The risk of anaphylaxis appears to be lower for topical devices than injected ones, and repeated administration with a break, as proposed in this study, also appears to have a lower incidence of anaphylaxis[25]. We surmise that anaphylaxis may be a risk of application of SeraSeal. Measures to reduce and treat anaphylaxis are to exclude those patients who are sensitive to bovine proteins from the study, and to provide a crash cart, and/or any additional standard and customary treatment(s). One of the purposes of this study is to determine that risk. Reports of an autoimmune reaction to fibrin sealants containing bovine Factor V mimicking hemophilia have been reported. SeraSeal does not contain Factor V.

7.3 Safeguards for Protecting Subjects: The risks of SeraSeal treatment are minimized by the patient selection

process. Should an allergic reaction occur, the participant will be withdrawn from the study and standard of care will be administered. Physicians, nurses, and technicians, will be on hand for all procedures. Patients will be monitored through routine post-operative care. Should any adverse event occur during treatment, immediate intervention will be taken. A crash cart is kept in the treatment room and on the hospital floor. Patient records will be kept confidential.

7.4 Alternatives: Alternatives to SeraSeal are the application of no hemostatic agents, electric cauterization, ligature, pressure dressings, collagen dressings, and the use of fibrin sealants.

8.0 Data Analysis:

8.1 Data Collection: There will be one study form for each patient. The surgery form will have all of the outcome data, including blood loss and complications. Once a patient is placed on the surgery schedule, the patient will be asked to participate in the clinical trial by the participating investigator surgeon. The only patients that will require special action are the SeraSeal patients. For those patients the need for SeraSeal will be made known only to the attending surgeon and/or fellows, and made available to the OR room. At the time of the pre-op exam, the inclusion/exclusion of participation in the study will be filled out. The research nurse will collect all data forms and will be responsible for evaluating them for completeness and accuracy, except for time to hemostasis supplied by the surgeon.

8.2 Statistical Analysis: We will compare continuous outcomes such as time to hemostasis (primary outcome), pre and post operative blood loss, surgery duration, (log) bacterial titer, and length of hospital stay in SeraSeal versus conventional treatment, using factorial analysis of variance (ANOVA) methods.

For continuous lab outcomes measured on four occasions (base, 24 hours, 48 hours, 30 days), we will use repeated measure analysis of variance methods to compare mean lab values for conventional versus SeraSeal overall.

For binary outcomes, (including adverse event outcomes) that are not quantified or that may be dichotomized for clinical convenience and interpretability such as fever (yes or no) or pruritus (yes or no) we will use chi-square methods to compare conventional versus SeraSeal treatment proportions overall. Since the total follow up times may differ between groups, we will also compare rates per person-time of binary outcomes under conventional versus SeraSeal treatment overall.

Sample size: The sample size is based on the primary outcome, time to hemostasis. We consider at least a 25% mean reduction in time to hemostasis to be the smallest clinically important average improvement. Historically, the mean time to hemostasis for liver surgery is 30 minutes. A 25% reduction from 30 minutes corresponds to a mean time to hemostasis of 30 x 0.75 = 22.5 minutes under SeraSeal. Based on this calculation, a sample size of 20 persons per group provides 80% power for confirming this mean difference using the $p<0.05$ two sided significance criterion (alpha =0.05). Assuming that all of the surgical procedures can be collapsed within their respective departments, and assuming that the 25% mean difference or greater difference occurs in all 5 departments, the required total sample size is 20 x 2 x 5 = 200.

9. Duration of Study: Subject participation is 30 days post study procedure. Expected enrollment time is 12 months.

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12.1.2 Sample Case Report Form

The Effect of SeraSeal on Clotting in Bleeding Wounds

DEMOGRAPHIC FORM

Patient Name*:

Hospital Number*:

Date of Surgery*:

Department:

Patient Study Number:**

Gender:

Age:

Sex:

Weight:

Height:

Pre-Op Blood Pressure:

Prolong Bleeding (Anticoagulants, Factor Deficiency, Cirrhosis):

Blood Assay Results:

Randomization Result:

*** This item will not be entered into the computer and will not be given to the statistician in order that the data set will be non identifiable.**
**** Assigned at the time of randomization.**

The Effect of SeraSeal on Clotting in Bleeding Wounds

SURGERY FORM

Name:

Patient Study Number:

Department:

Diagnosis:

Surgery Type:

Type of Wound (Degree of Invasive):

Treatment Received (Product or Control):

Length of Surgery:

Blood Assay Results (please indicate if within normal limits, or any abnormal coagulation):

Any Treatment (Such as Warfarin) for the Possibility of PE'S:

Time of Hemostasis for the Entire Wound with SeraSeal Compared to Standard Treatment:

Need for Further Control of Bleeding or Uncontrolled Bleeding:

Any Post OP Bleeding:

Wound Infection:

Total Blood Loss (Compare SeraSeal to Standard Treatment):

Adverse Effects:

Surgeon

Adverse Event Checklist

Patient No. _____

Body System	Preferred Term	Rating	Comment
Body as a whole	Abdominal pain		
	Asthemia		
	Back pain		
	Chest pain		
	Headache		
	Infection		
	Trauma		
Cardiovascular System	Postural Hypotension		
	Tachycardia		
	Vasodilation		
Digestive System	Constipation		
	Decreased appetite		
	Diarrhea		
	Dry mouth		
	Dyspepsia		
	Nausea		
	Tooth disorder		
	Vomiting		
Nervous System	Dizziness		
	Emotional liability		
	Hostility		
	Insomnia		
	Nervousness		
	Somolence		
	Tremor		
Respiratory System	Cough increase		
	Pharyngitis		
	Respiratory disorder		
	Rhinitis		
	Sinusitis		
Other	Sweating		
	Abnormal vision		

(-) Negative: no observed reaction or change
(+) Mild: slight changes
(++) Moderate: notable change but not life threatening
(+++) Severe: significant change, life threatening
(++++) Fatal: death

12.1.3 Monitor Board, Patient Information Sheet, Sample Consent Form

Monitor Board

The Scientific and Ethics Committee
Edgardo Rebagliati Martins National Hospital
Lima, Peru

Chairman: Raul German Mederos, MD

Panel: Jose A. Perez Correa, MD
Esther Lilia Toledo Rodriguez, MD
Calixto Valdes Perez, MD
Orestes Jose Ponce Gonzales, MD

Wortham Laboratories, Inc.

Clinical Study

Patient Information

1. What is SeraSeal?

   SeraSeal is a hemostatic agent, made from bovine proteins, designed to stop bleeding within seconds.

2. How is SeraSeal applied?

   SeraSeal can be applied to any type of bleed and to any bleeding site. It is applied to the surface of the bleed.

3. What advantages does SeraSeal have over cauterization?

   There are several advantages such as no lost of tissue, faster recovery period due to no edema or inflammation, and SeraSeal reduces surgical time by blanketing all the severed blood vessels at one time.

4. Is SeraSeal active in the presence of anticoagulants ("blood thinners")?

   Yes, SeraSeal is reactive in patients taking coumadine, heparin, and aspirin. Further, the hemostatic agent overcomes factor deficiencies.

5. Is SeraSeal safe?

   SeraSeal is still an investigated product; however, in both animal and other human clinical studies the hemostatic agent had proven to be effective and safe.

   Patients sensitive to bovine products may be advised not to participate in this investigation study.

6. Is there financial compensation for participating in this study?

No

7. Why should I participate in this study?

There are several reasons why you should participate in this study:

SeraSeal does not destroy tissue.

No loss of tissue results in a faster healing process.

Shorter surgical time.

Some surgical procedures may reduce the need for blood transfusions.

Your participation will contribute to the quality of health care.

Patient Consent Form

WORTHAM LABORATORIES, INC.

SeraSeal
Efficacy and Safety Study

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with friends, relatives, and your physician if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Purpose of this Study

Hemorrhages (bleeds) require an immediate response to stop the bleeding. There are two means to treat hemorrhages: pressure and cauterization. Direct pressure or the use of a tourniquet is commonly used, while chemical, electrical or laser cauterization, gives a more immediate response to bleeds. Each method has its own limits and effectiveness.

A biological, called SeraSeal, developed by Wortham Laboratories, Inc. is designed to stop bleeding, even in the face of challenging situations, such as anticoagulant therapy, and factor deficiencies. Unlike current methods to treat hemorrhages, SeraSeal requires no pressure, and does not burn or cause tissue damage.

This clinical research study will evaluate the safety and efficacy of SeraSeal, in the treatment of hemorrhages, for both surgical and non-surgical procedures.

Enrollment

Subjects selected for this study are those who are having a hemorrhagic episode, or those who will incur bleeding as a result of an incision, debreedment insertion or any other method that may induce bleeding.

This study is open to all patients experiencing blood loss, however, those subjects diagnosed with Lupus or those who are allergic to bovine products, should consult with their physician.

To test the safety and efficacy of SeraSeal, a total of 120 patients will be tested.

Participation

This study is intended to be a one-time treatment. Blood is drawn before the procedure, and again 24 hours after treatment. Each patient undergoing surgery will have a repeat blood test 48 hours after the operation.

Disadvantages and Risks

There is a risk of developing Factor V antibodies, which may produce prolong bleeding.

Subjects sensitive to bovine products may experience a rash, edema, fever, changes in blood pressure, or shortness of breath.

Benefits

There are three significant advantages in participating in this study: no burning of the tissue, possibly less blood lost, and no discontinuation of anticoagulant therapy.

If Something Goes Wrong

If the product should fail, conventional surgical techniques will be applied. If you are harmed, by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for legal action, but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, you may file a complaint with the Ministry of Health.

Confidentiality

All information collected about you during the course of the research will be kept strictly confidential. Any information about you, which leaves the hospital/surgery will have your name and address removed so that you cannot be recognized from it.

Your personal physician and other medical practitioners treating you will be informed of the results.

Results of the Research Study

The results of the research study will be used for the Ministry of Health approval of the product, and may also be published in the medical journals. Any publication would occur within one year of the study. The identity of the subject will not be published. A copy of the published results can be obtained from the sponsor.

Sponsor

Wortham Laboratories, Inc.
6340 Bonny Oaks Drive
Chattanooga, TN 37416
Telephone: 1-423-296-0090
E-mail: lwortham@worthamlabs.com
Contact: Leon Wortham

The sponsor of this study will pay the laboratory fees for those tests used in this research.

12.1.4 Investigators CV's

Alfonso Rivasplata, M.D.
Lima, Peru

Current Position
Professor
Surgeon in Chief
Thoracic & Cadiovascular Surgery
Edgardo Rebagliati Martins National Hospital

Licensure
Peru CMP 7422

Education
Doctor of Medicine, San Marin of Porres University, College of Human Medicine
Lima, Peru, May 1975

Postdoctoral Training
Chief Resident, General Surgery, Edgardo Rebagliati Martins National Hospital,
July 1977 – June 1978
General Surgery Residency, Edgardo Rebagliati Martins National Hospital,
July 1976 – Junr 1977
General Surgery Internship, Edgardo Rebagliati Martins National Hospital,
July 1975 – June 1976

Work Experience
Surgeon in Chief, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, November 1993 – Present
Associate Director, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, May 1987 – November 1993
Staff Surgeon, Edgardo Rebagliati Martins National Hospital, August 1978 – May 1987

Julio Moron, M.D.
Lima, Peru

Current Position
Professor
Surgeon in Chief
Head and Neck Surgery
Edgardo Rebagliati Martins National Hospital

Licensure
Peru CMP 7422

Education
Doctor of Medicine, Piura National University, College of Human Medicine
Piura, Peru, May 1976

Postdoctoral Training
Chief Resident, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1978 – June 1979
General Surgery Residency, Edgardo Rebagliati Martins National Hospital, July 1977 – June 1978
General Surgery Internship, Edgardo Rebagliati Martins National Hospital, July 1976 – June 1977

Work Experience
Surgeon in Chief, Head and Neck Surgery, Edgardo Rebagliati Martins National Hospital, February 1997 – Present
Associate Director, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, September 1990 – February 1997
Staff Surgeon, Head and Neck Surgery, Edgardo Rebagliati Martins National Hospital July 1979 – September 1990

Juan Santillana, M.D.
Lima, Peru

Current Position
Associate Professor
General Surgery
Edgardo Rebagliati Martins National Hospital

Licensure
Peru CMP 11616

Education
Doctor of Medicine, Pedro Ruiz Gallo of Lambayeque National University, College of Human Medicine, May 1976

Postdoctoral Training
Chief Resident, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1981 – June 1982
General Surgery Residency, Edgardo Rebagliati Martins National Hospital, July 1980 – June 1981
General Surgery Internship, Edgardo Rebagliati Martins National Hospital, July 1979 – June 1980

Work Experience
Staff Surgeon, Edgardo Rebagliati Martins National Hospital, July 1982 - Present

Victor Mendizabal, M.D.
Lima, Peru

Current Position

Associate Professor
Thoracic & Cardiovascular Surgery
Edgardo Rebagliati Martins National Hospital

Licensure

Peru CMP 12327

Education

San Agustin National University, College of Human Medicine
Arequipa, Peru May 1980

Postdoctoral Training

Chief Resident, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, July 1982 – June 1983
Residency, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, July 1981 – June 1982
Internship, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1980 – June 1981

Work Experience

Staff Surgeon, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital August 1983 - Present

Jaime Rocafuente, M.D.
Lima, Peru

Current Position
Associate Professor
General Surgery
Edgardo Rebagliati Martins National Hospital

Licensure
Peru CMP 12746

Education
Doctor of Medicine, Private University of Tacna, College of Human Medicine
Tacna, Peru, May 1980

Postdoctoral Training
Chief Resident, General Surgery, Edgardo Rebagliati Martins National Hospital,
July 1983 – June 1984
Residency, General Surgery, Edgardo Rebagliati Martins National Hospital,
July 1982 – June 1983
Internship, General Surgery, Edgardo Rebagliati Martins National Hospital,
July 1981 – June 1982

Work Experience
Staff Surgeon, Edgardo Rebagliati Martins National Hospital
August 1984 – Present

Luis Castro, M.D.
Lima, Peru

Current Position
Associate Professor
Jose Casimio Ulloa Emergency Hospital

Licensure
Peru CMP 12835

Education
Doctor of Medicine, Catholic University of Santa Maria, College of Human Medicine
May 1980

Postdoctoral Training
Chief Resident, General Surgery, Jose Casimio Ulloa Emergency Hospital,
July 1982 – June 1983
Residency, General Surgery, Jose Casimio Ulloa Emergency Hospital,
July 1981 – June 1982
Internship, General Surgery, Jose Casimio Ulloa Emergency Hospital,
July 1980 – June 1981

Work Experience
Staff Surgeon, Jose Casimio Ulloa Emergency Hospital,
August 1983 – Present

Arnaldo Muñoz, M.D.
Lima, Peru

Current Position
Associate Professor
FAP – Peruvian Air Force Hospital

Licensure
Peru CMP 13104

Education
Doctor of Medicine, San Martin of Porres University, College of Human Medicine, Lima, Peru May 1981

Postdoctoral Training
Chief Resident, General Surgery, FAP – Peruvian Air Force Hospital,
July 1983 – June 1984
Residency, General Surgery, FAP – Peruvian Air Force Hospital,
July 1982 – June 1983
Internship, General Surgery, FAP – Peruvian Air Force Hospital,
July 1981 – June 1982

Work Experience
Staff Surgeon, FAP – Peruvian Air Force Hospital,
August 1984 – Present

Marco Lanatta, M.D.
Lima, Peru

Current Position
Associate Professor
General Surgery
Edgardo Rebagliati Martins National Hospital

Licensure
Peru CMP 13725

Education
Doctor of Medicine, Jose Faustino Sanchez Corron of Huacho National University, College of Human Medicine, May 1981

Postdoctoral Training
Chief Resident, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1983 – June 1984
Residency, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1982 – June 1983
Internship, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1981 – June 1982

Work Experience
Staff Surgeon, Edgardo Rebagliati Martins National Hospital, August 1984 – Present

Eduardo Nieto, M.D.
Lima, Peru

Current Position

Associate Professor
Thoracic & Cardiovascular Surgery
Edgardo Rebagliati Martins National Hospital

Licensure

Peru CMP 13882

Education

Doctor of Medicine, Catholic University of Santa Maria, College of Human Medicine, Arequipa, Peru May 1981

Postdoctoral Training

Chief Resident, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, July 1983 – June 1984

Residency, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, July 1982 – June 1983

Internship, Thoracic & Cardiovascular Surgery, Edgardo Rebagliati Martins National Hospital, July 1981 – June 1982

Work Experience

Staff Surgeon, Edgardo Rebagliati Martins National Hospital,
August 1984 – Present

Cesar Rotta, M.D.
Lima, Peru

Current Position

Associate Professor
General Surgery
Edgardo Rebagliati Martins National Hospital

Licensure

Peru CMP 14314

Education

Doctor of Medicine, Pedro Ruiz Gallo of Lambayeque National University, College of Human Medicine, Lambayeque, Peru May 1982

Postdoctoral Training

Chief Resident, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1984 – June 1985
Residency, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1983 – June 1984
Internship, General Surgery, Edgardo Rebagliati Martins National Hospital, July 1982 – June 1983

Work Experience

Staff Surgeon, Edgardo Rebagliati Martins National Hospital, August 1985 – Present

Zoe Diaz Chavez, M.D.
Lima, Peru

Current Position

Associate Professor
Thoracic & Cardiovascular Surgery
Guillermo Almenara I. EsSalud National Hospital

Licensure

Peru CMP 15297

Education

Doctor of Medicine, Private University San Pedro, College of Human Medicine, May 1983

Postdoctoral Training

Chief Resident, Thoracic & Cardiovascular Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1985 – June 1986
Residency, Thoracic & Cardiovascular Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1984 – June 1985
Internship, Thoracic & Cardiovascular Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1983 – June 1984

Work Experience

Staff Surgeon, Guillermo Almenara I. EsSalud National Hospital, August 1986 – Present

Julio Moron, M.D.
Lima, Peru

Current Position

Associate Professor
Thoracic & Cardiovascular Surgery
Guillermo Almenara I. EsSalud National Hospital

Licensure

Peru CMP 19098

Education

Doctor of Medicine, San Martins of Porres University, College of Human Medicine, Lima, Peru May 1987

Postdoctoral Training

Chief Resident, Thoracic & Cardiovascular Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1989 – June 1990
Residency, Thoracic & Cardiovascular Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1988 – June 1989
Internship, Thoracic & Cardiovascular Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1987 – June 1988

Work Experience

Staff Surgeon, Guillermo Almenara I. EsSalud National Hospital, August 1990 – Present

Fernando Huerta, M.D.
Lima, Peru

Current Position
Associate Professor
Head and Neck Surgery
Guillermo Almenara I. EsSalud National Hospital

Licensure
Peru CMP 21377

Education
Doctor of Medicine, San Martin of Porres University, College of Human Medicine, Lima, Peru May 1990

Postdoctoral Training
Chief Resident, General Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1991 – June 1992
Residency, Head and Neck Surgery, Edgardo Rebagliati Martins National Hospital, July 1990 – June 1991
Internship, Head and Neck Surgery, Edgardo Rebagliati Martins National Hospital, July 1989 – June 1990

Work Experience
Staff Surgeon, Edgardo Rebagliati Martins National Hospital,
August 1992 – Present

Luis Borda, M.D.
Lima, Peru

Current Position
Associate Professor
General Surgery
Guillermo Almenara I. EsSalud National Hospital

Licensure
Peru CMP 21377

Education
Doctor of Medicine, San Martin of Porres University, College of Human Medicine, Lima, Peru May 1990

Postdoctoral Training
Chief Resident, General Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1992 – June 1993
Residency, General Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1991 – June 1992
Internship, General Surgery, Guillermo Almenara I. EsSalud National Hospital, July 1990 – June 1991

Work Experience
Staff Surgeon, Guillermo Almenara I. EsSalud National Hospital, August 1993 – Present

Gilberto Jayme, M.D.
Lima, Peru

Current Position
Associate Professor
General Surgery
FAP – Peruvian Air Force Hospital

Licensure
Peru CMP 26882

Education
Doctor of Medicine, Piura National University, College of Human Medicine, May 1995

Postdoctoral Training
Chief Resident, General Surgery, FAP – Peruvian Air Force Hospital, July 1997 – June 1998
Residency, General Surgery, FAP – Peruvian Air Force Hospital, July 1996 – June 1997
Internship, General Surgery, FAP – Peruvian Air Force Hospital, July 1995 – June 1996

Work Experience
Staff Surgeon, FAP – Peruvian Air Force Hospital, August 1998 – Present

Pedro Cayetano, M.D.
Lima, Peru

Current Position
Associate Professor
Orthopedic Surgery
Military Hospital of Peru

Licensure
Peru CMP 16058

Education
Doctor of Medicine, Catholic University of San Maria, College of Human Medicine, Arequipa, Peru May 1984

Postdoctoral Training
Chief Resident, Orthopedic Surgery, Military Hospital of Peru,
July 1986 – June 1987
Residency, Orthopedic Surgery, Milirary Hospital of Peru,
July 1985 – June 1986
Internship, Orthopedicl Surgery, Military Hospital of Peru,
July 1984 – June 1985

Work Experience
Staff Surgeon, Military Hospital of Peru,
August 1987 – Present

Carlos Zapater, M.D.
Lima, Peru

Current Position
Associate Professor
Neurosurgery
Military Hospital of Peru

Licensure
Peru CMP 16413

Education
Doctor of Medicine, San Martin of Porres University, College of Human Medicine, Lima, Peru May 1984

Postdoctoral Training
Chief Resident, Neurosurgery, Military Hospital of Peru,
July 1986 – June 1987
Residency, Neurosurgery, Milirary Hospital of Peru,
July 1985 – June 1986
Internship, Neurosurgery, Military Hospital of Peru,
July 1984 – June 1985

Work Experience
Staff Surgeon, Military Hospital of Peru,
August 1987 – Present

12.1.5 Signature Page

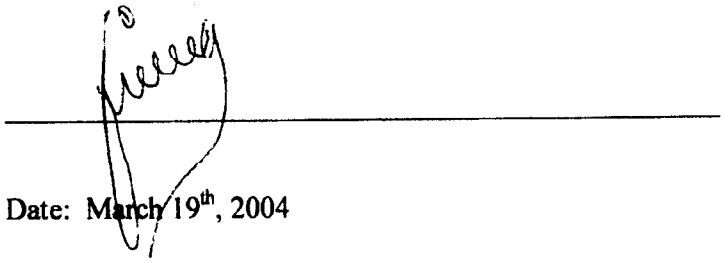
Document No.: WLI- I 196-PER

Title: Efficacy and Safety Investigation of SeraSeal

Name of Report Author: Victor Mendizabal, M.D.

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Position: Principal Investigator



Date: March 19th, 2004

MINISTERIO DE SALUD

DIRECCIÓN GENERAL DE MEDICAMENTOS, INSUMOS Y DROGAS

April 6, 2005

Dear Dr. Wortham,

A broad range of surgical applications of SeraSeal were conducted in this clinical study. The hemostatic agent was evaluated to cauterization with great success in achieving hemostasis in surgical procedures known for substantial blood loss. Over a third of the patients studied were on heparin at the time of their surgery, and their bleeding was completely controlled by SeraSeal.

Notably, pain management was better controlled in the investigational group than in the control group, by avoiding the creation of a third degree burn, as seen in cauterization. No adverse events were associated with SeraSeal making the hemostatic agent safe for both adults and pediatrics.

The Review Committee recommends the approval of SeraSeal as a topical hemostatic agent.

12.1.6 Statistical Methods

All of the 119 patients who received the study hemostatic agent were included in the efficacy population. Statistical conclusions covering the efficacy of SeraSeal was made using data obtained from total hemostasis time and blood loss. The hypothesis was two-sided. The comparison of interest was SeraSeal vs. Cauterization. Hypothesis concerning this comparison was tested at the alpha level of 0.05. Test of significance involving the sample mean and using the two-tailed t-test, the time to hemostasis for SeraSeal, had high statistical significance with a p-value of <0.01, and achieving $>25\%$ faster over cauterization.

12.1.7 Inter-Laboratory Standardization Methods and Quality Assurance Procedures

All investigational blood samples collected were processed and brought to Edgardo Rebagliati Martins National Hospital for testing. The hematology test samples were collected in 7 ml EDTA test tubes and stored at 2-4°C. The coagulation study samples were collected in 3.8% sodium citrate 5 ml vacuum tubes, centrifuged, and the plasma frozen within 2 hours from collection.

The investigation samples were all tested at the same time each day on the Coulter cell counter with its control and reagents, and on the fibrometer, using Dade controls and reagents.

12.2 PATIENT DATA LISTINGS

12.2.1 Discontinued Patients

There were no patiens discontinued from this study.

12.2.2 Patient Excluded from the Efficacy Analysis

No patients were excluded from the efficacy analysis.

12.2.3 Demographic Data Listing

Demographic Data Listings					
Patient No.	**Sex**	**Age**	**Wt (lbs)**	**Ht (in)**	**AC (U/Kg)**
JM-01	M	68	150	66	Hep 400
JM-02	M	50	136	65	Hep 400
JM-03	M	74	154	64	Hep 400
JM-04	M	56	191	62	Hep 400
PC-001	M	11	99	54	N
PC-002	M	29	136	64	N
PC-003	M	31	163	66	N
PC-004	M	20	132	66	N
GJ-001	F	55	132	62	N
GJ-002	M	69	134	66	N
GJ-003	M	3	24	45	N
GJ-004	M	48	143	62	N
JS-001	F	16	110	63	N
JS-002	F	40	154	67	N
JS-003	M	10	77	51	N
JS-004	F	14	99	60	N
JM-001	F	38	150	62	N
JM-002	M	63	176	67	N
JM-003	F	61	128	60	N
JM-004	F	68	123	58	N
JM-005	M	69	128	62	N
JM-006	M	68	150	66	N
JM-007	F	60	145	64	N
JM-008	F	64	132	62	N
LB-001	F	79	121	59	N
LB-002	M	84	110	63	N
LB-003	M	91	143	71	N
LB-004	F	42	127	62	N
LC-001	M	25	158	67	N
LC-002	M	35	172	69	N
LC-003	F	18	112	63	N
LC-004	M	20	163	67	N
LC-005	F	38	144	63	N
LC-006	M	45	180	68	N
ML-001	M	49	172	67	N
ML-002	M	43	158	64	N
ML-003	F	64	139	58	N
ML-004	F	43	128	64	N
ML-005	F	35	119	62	N
ML-006	M	54	167	67	N
ML-007	M	53	117	64	N
ML-008	M	80	143	65	N
ML-009	F	30	150	62	N
ML-010	M	34	154	65	N
ML-011	M	46	117	60	N
ML-012	F	66	123	59	N
ML-013	M	84	128	62	N
ML-014	F	84	134	64	N
ML-015	F	78	130	62	N
ML-016	F	73	161	64	N

ML-017	F	64	139	60	N
ML-018	F	57	158	62	N
ML-019	M	55	165	64	N
RG-001	F	63	134	64	N
RG-002	M	38	150	64	N
RG-003	F	65	143	66	N
RG-004	F	63	154	62	N
RG-005	M	50	165	66	N
AM-001	F	76	132	62	N
AM-002	M	40	165	66	N
AM-003	F	35	132	64	N
AM-004	F	25	121	62	N
AM-005	F	72	143	58	N
AM-006	F	72	121	62	N
AM-007	F	62	143	62	N
EN-001	M	54	165	69	Hep 300
EN-014	M	53	167	70	Hep 300
AR-006	M	72	194	68	Hep 300
AR-017	F	48	150	62	Hep 300
AR-018	F	28	10	64	Hep 300
AR-022	F	92	172	62	Hep 300
AR-023	F	87	128	59	Hep 300
AR-026	M	53	163	69	Hep 300
AR-030	F	57	154	63	Hep 300
AR-031	M	38	141	69	Hep 78
AR-032	M	61	165	69	Hep 300
AR-033	F	59	141	64	Hep 300
AR-034	M	59	167	69	Hep 300
VQ-01	F	76	132	62	Hep 83
VQ-02	F	76	121	58	Hep 91
VQ-03	M	82	176	68	N
VQ-04	M	75	176	68	Hep 62
VQ-05	M	73	187	70	N
ZC-01	F	35	121	60	Hep 350
ZC-02	M	67	180	67	Hep 350
ZC-03	F	32	158	63	Hep 350
ZC-04	M	37	167	69	Hep 350
ZC-05	F	72	172	62	Hep 64
FH-001	F	2	35	31	N
FH-002	M	20 day	4	16	N
FH-003	M	6	57	47	N
FH-004	F	2	33	29	N
FH-005	F	11	75	47	N
FH-006	F	7 mo.	15	23	N
CR-001	M	54	198	66	N
CR-002	M	37	176	70	N
CR-003	F	73	121	62	N
CR-004	F	73	121	62	N
CR-005	F	82	110	62	N
CR-006	M	86	202	68	N
CR-007	F	39	143	60	N
CR-008	M	42	147	66	N
CR-009	F	33	123	62	N

CZ-001	M	48	176	69	N
CZ-002	M	39	165	67	N
CZ-003	M	18 mo.	26	35	N
CZ-004	M	21	136	66	N
CZ-005	F	68	172	62	N
CZ-006	M	84	143	66	N
CZ-007	M	51	136	63	N
CZ-008	M	20	150	66	N
CZ-009	M	86	154	67	N
CZ-010	F	76	143	66	N
CZ-011	M	58	154	66	N
JR-001	M	68	156	67	N
JR-002	F	75	154	65	N
JR-003	F	70	154	66	N
JR-004	F	72	143	63	N
JR-005	F	78	150	62	N

12.2.4 Individual Response Data

Case No.	Target Organ	Tissue	Dosage	Hemostasis (min)	Blood Loss (ml)
AR-006	heart	b,a	12K	0.5	500
AR-017	heart	b,a,v	6K	0.5	500
AR-018	heart	b,a	6K	0.5	500
AR-022	heart	b,a,v	3K	0.5	250
AR-023	heart	b,a,v	3K	0.5	150
AR-026	heart	b,a,m	3K	0.5	500
AR-030	heart	b,a,m	9K	1	500
AR-031	heart	a	6K	0.5	200
AR-032	heart	b,a	6K	1	500
AR-033	heart	b,a	6K	1	500
AR-034	heart	b,a	6K	1	500
ZC-01	heart	b,a	6K	1	500
ZC-02	heart	b,v,a	6K	1	300
ZC-03	heart	b,a	3K	1	200
ZC-04	heart	b,a	6K	1	500
ZC-05	heart	b,a	3K	0.5	300
JM-01	heart	v,a	3K	1	300
JM-02	heart	b,a,m	3K	1	400
JM-03	heart	b,a,v	3K	1	300
JM-04	heart	v,a	3K	1	400
EN-001	heart	b,a,v	6K	1	250
EN-014	heart	b,a,v	3K	0.5	250
VQ-01	carotid	m,v	3K	0.5	30
VQ-02	femo-popliteal	m,a,v	3K	0.5	300
VQ-03	lung	par,v	3K	0.5	200
VQ-04	arterial aneurism	a	3K	0.5	400
VQ-05	lymph node	a,gl	3K	2	50
CZ-001	vertebra	b,m	6K	1	400
CZ-002	vertebra	b,m	3K	1	350
CZ-003	vertebra	b,m	3K	1	250
CZ-004	brain	ep, ner	3K	1	250
CZ-005	vertebra	b,m	6K	1	500
CZ-006	vertebra	b,m	6K	1	30
CZ-007	brain	ep,d,ner	3K	1	50
CZ-008	brain	ep,d,ner	3K	1	50
CZ-009	vertebra	b,m	3K	1	100
CZ-010	vertebra	b,m	3K	1	400
CZ-011	vertebra	b,m	3K	1	200
LC-001	oral mucosa	mu	9K	1	5
LC-002	oral mucosa	mu	1.5K	10	5
LC-003	knee	ep,d,m	3K	10	50

LC-004	oral mucosa	mu	3K	1	50
LC-005	appendix	m,ep	3K	1	200
LC-006	gall bladder	par,a	3K	1	20
JM-001	thyroid	gl,a,v,m	6K	2	10
JM-002	parotid	gl,m,a	3K	1	20
JM-003	cervical	gl,v,m	6K	1	500
JM-004	carotid	m,v	6K	1	100
JM-005	orbit sinus	ep,d,m	3K	1	10
JM-006	larynx	m,a,v	6K	1	10
JM-007	thyroid	gl,a,v,m	3K	1	5
JM-008	maxillary sinus	mu,m,b	3K	1	15
FH-001	cervical	v.m	3K	2	
FH-002	cervical	ep,gl,m	6K	1	
FH-003	cervical	b,m	6K	3	
FH-004	cervical	m,v	6K	2	
FH-005	mandible, hip	mu,b,m	9K	jaw 2 hip 5	60 200
FH-006	parieto-ocipital	ep,d,ner	9K	2	5
PC-001	leg	ep,d,m,b	9K	3	250
PC-002	leg	b	2.2K5	10	150
PC-003	leg	ep,d,m,b	7.5K	10	80
PC-004	leg	m,b	7.5K	1	100
LB-001	colon	m,ep	3K	1	50
LB-002	hip	m	3K	1	150
LB-003	stomach	a	9K	2	150
LB-004	liver	par,v	3K	1	30
GJ-001	breast	m,a,v	3K	1	150
GJ-002	intestine	v	3K	2	500
GJ-003	liver,spleen	par	3K	0.5	20
GJ-004	liver	par,v	6K	1	50
ML-001	liver	par,v	3K	0.67	50
ML-002	intestine	m,a,v	3K	0.67	30
ML-003	gall bladder	par,m	3K	0.83	30
ML-004	ovary	ep,m	3K	0.33	20
ML-005	liver	par,v	6K	1	30
ML-006	intestine	m,a,v	6K	0.67	30
ML-007	liver	par,v,m	3K	0.67	50
ML-008	liver	par,v	6K	1	60
ML-009	liver,spleen	par	3K	0.5	20
ML-010	liver,mesenteric vein	par,v	3K	1	50
ML-011	pancreas	par,v	3K	1	20
ML-012	stomach	v,a	3K	0.67	200
ML-013	stomach	a,v	6K	0.83	20
ML-014	stomach	a,v	3K	1	20

ML-015	stomach	a,v	3K	1	20
ML-016	gall bladder	par,m	3K	1	20
ML-017	spleen	par	3K	1	20
ML-018	gall bladder	m,a	3K	1	20
ML-019	liver	par,v	6K	1	2000
AM-001	liver	par,v	3K	1	50
AM-002	liver	par,v	6K	1	50
AM-003	spleen	a,v	3K	1	50
AM-004	spleen	par	3K	1	60
AM-005	pancreas	par,v	3K	1	200
AM-006	spleen,pancreas	par,a	6K	1	100
AM-007	liver	par,v	3K	2	50
JS-001	intestinal	v	3K	2	100
JS-002	intestinal	m,v	3K	5	50
JS-003	intestinal	v	3K	1	30
JS-004	intestinal	v,m	3K	1.5	20
RG-001	intestinal	m,a	3K	0.33	500
RG-002	liver	par,v	3K	1	500
RG-003	pancreas	par,v	3K	1	400
RG-004	intestinal	ep,v	3K	1	500
RG-005	intestinal	ep,v	3K	1	500
CR-001	gall bladder	a	6K	1	100
CR-002	gall bladder	par,m	3K	10	500
CR-003	intestine	a	3K	10	200
CR-004	gall bladder	a,m	3K	1	200
CR-005	appendix	ner,m	3K	1	200
CR-006	appendix	ner,m	3K	1	100
CR-007	gall bladder	par,m	3K	1	100
CR-008	colon	ep,ner,m	3K	1	200
CR-009	stomach	ep,m	3K	1	50
JR-001	liver	par,v	3K	10	200
JR-002	sacrum	a,m	6K	10	500
JR-003	stomach	ep,m	6K	10	100
JR-004	spleen	a,v	6K	1	200
JR-005	intestine	a	6K	1	400

Tissue key: epithelial (ep), derma (d), artery (a), vein (v), muscle (m), gland (gl), mucus membrane (mu), bone marrow (b), parenchymal (par), nerve (ner)

12.2.5 Listing of Individual Vital Signs by Patient

Patient No.	Baseline			24h Post-Op			48h Post-Op			30d Post-Op		
	S	D	P	S	D	P	S	D	P	S	D	P
JM-01	140	90	84	140	88	82	142	88	86	142	90	82
JM-02	120	70	90	120	74	84	118	74	86	120	72	84
JM-03	140	85	86	138	84	84	140	84	84	140	82	82
JM-04	140	90	82	142	88	84	140	88	82	140	86	80
PC-001	115	65	92	112	66	92	114	68	94	114	66	92
PC-002	120	80	88	114	82	82	116	84	86	114	84	86
PC-003	110	60	90	116	70	90	116	72	88	118	72	90
PC-004	110	70	84	114	72	82	112	68	84	112	70	84
GJ-001	130	75	82	124	78	78	126	76	80	128	78	82
GJ-002	110	55	78	112	68	80	112	70	76	114	70	76
GJ-003	75	45	98	75	42	94	72	44	96	74	44	96
GJ-004	140	75	82	138	76	86	142	78	82	142	76	82
JS-001	120	60	82	120	64	84	120	62	82	120	60	84
JS-002	90	60	100	108	70	84	110	76	86	110	76	80
JS-003	110	70	96	112	70	94	112	72	96	112	70	96
JS-004	120	60	88	118	62	90	122	60	92	120	60	90
JM-001	130	80	84	132	80	80	130	82	90	130	84	86
JM-002	140	90	92	140	88	84	140	88	88	142	88	82
JM-003	150	80	90	138	82	86	140	82	86	142	80	88
JM-004	10	80	94	150	82	90	152	80	88	154	82	86
JM-005	130	80	86	130	84	82	128	82	84	128	84	80
JM-006	110	70	78	112	70	80	110	70	78	110	72	78
JM-007	130	70	84	128	72	82	130	70	84	130	74	82
JM-008	130	70	86	130	70	80	132	72	84	130	72	84
LB-001	110	70	84	114	70	86	116	72	88	114	72	86
LB-002	120	80	86	122	78	82	118	76	82	118	78	86
LB-003	120	80	80	116	82	84	120	80	86	118	80	92
LB-004	112	78	80	114	80	78	114	80	80	116	80	84
LC-001	120	70	80	116	74	82	112	72	84	120	74	80
LC-002	110	70	78	112	70	80	116	74	84	112	70	86
LC-003	110	60	82	118	72	84	116	72	84	114	74	88
LC-004	110	60	86	120	74	80	122	74	82	118	72	80

LC-005	**114**	**72**	**86**	**114**	**74**	**82**	**116**	**72**	**88**	**112**	**72**	**84**
LC-006	**110**	**70**	**90**	**108**	**72**	**86**	**112**	**74**	**84**	**112**	**72**	**92**
ML-001	**90**	**70**	**104**	**110**	**80**	**86**	**114**	**82**	**82**	**114**	**80**	**84**
ML-002	**80**	**50**	**112**	**108**	**76**	**80**	**116**	**80**	**84**	**118**	**82**	**82**
ML-003	**120**	**70**	**82**	**120**	**74**	**86**	**120**	**72**	**82**	**120**	**74**	**84**
ML-004	**120**	**50**	**98**	**118**	**76**	**86**	**118**	**74**	**88**	**116**	**84**	**82**
ML-005	**110**	**60**	**80**	**112**	**70**	**84**	**116**	**72**	**80**	**116**	**76**	**80**
ML-006	**90**	**60**	**106**	**120**	**82**	**82**	**120**	**80**	**80**	**118**	**82**	**82**
ML-007	**80**	**50**	**118**	**114**	**78**	**88**	**116**	**80**	**84**	**116**	**80**	**84**
ML-008	**70**	**40**	**122**	**108**	**70**	**86**	**114**	**74**	**82**	**118**	**78**	**86**
ML-009	**70**	**40**	**116**	**104**	**68**	**84**	**110**	**72**	**84**	**114**	**80**	**80**
ML-010	**90**	**60**	**108**	**112**	**78**	**82**	**114**	**76**	**80**	**114**	**76**	**80**
ML-011	**110**	**70**	**84**	**110**	**72**	**84**	**112**	**70**	**82**	**110**	**70**	**84**
ML-012	**100**	**70**	**80**	**108**	**74**	**82**	**110**	**72**	**80**	**110**	**74**	**80**
ML-013	**120**	**70**	**86**	**122**	**72**	**84**	**120**	**72**	**82**	**120**	**70**	**84**
ML-014	**130**	**85**	**82**	**128**	**86**	**84**	**126**	**86**	**80**	**128**	**84**	**82**
ML-015	**110**	**70**	**82**	**108**	**70**	**80**	**110**	**72**	**82**	**110**	**72**	**82**
ML-016	**120**	**80**	**80**	**120**	**80**	**84**	**122**	**78**	**82**	**120**	**82**	**82**
ML-017	**100**	**70**	**92**	**114**	**76**	**90**	**116**	**74**	**90**	**114**	**72**	**88**
ML-018	**110**	**60**	**84**	**112**	**68**	**82**	**114**	**70**	**82**	**112**	**70**	**84**
ML-019	**110**	**60**	**88**	**110**	**74**	**86**	**110**	**72**	**88**	**112**	**74**	**88**
RG-001	**110**	**70**	**78**	**108**	**74**	**80**	**110**	**74**	**80**	**114**	**76**	**82**
RG-002	**70**	**40**	**110**	**100**	**68**	**82**	**106**	**70**	**86**	**110**	**74**	**84**
RG-003	**90**	**40**	**102**	**112**	**70**	**84**	**110**	**72**	**84**	**114**	**72**	**82**
RG-004	**60**	**40**	**114**	**102**	**74**	**82**	**108**	**76**	**82**	**112**	**80**	**86**
RG-005	**80**	**50**	**120**	**106**	**70**	**88**	**108**	**72**	**84**	**110**	**76**	**86**
AM-001	**120**	**80**	**82**	**116**	**82**	**84**	**120**	**82**	**82**	**118**	**80**	**80**
AM-002	**80**	**50**	**104**	**106**	**68**	**82**	**108**	**72**	**80**	**112**	**72**	**84**
AM-003	**90**	**60**	**108**	**110**	**74**	**80**	**110**	**76**	**82**	**110**	**70**	**82**
AM-004	**80**	**50**	**112**	**106**	**72**	**82**	**112**	**76**	**84**	**112**	**74**	**82**
AM-005	**120**	**80**	**104**	**120**	**78**	**86**	**118**	**80**	**88**	**120**	**80**	**82**
AM-006	**120**	**80**	**82**	**120**	**84**	**80**	**122**	**82**	**82**	**120**	**82**	**82**
AM-007	**100**	**70**	**94**	**118**	**76**	**90**	**116**	**78**	**92**	**118**	**78**	**96**
EN-001	**110**	**70**	**84**	**112**	**74**	**82**	**110**	**74**	**84**	**112**	**76**	**80**
EN-014	**130**	**80**	**84**	**128**	**82**	**86**	**130**	**84**	**82**	**128**	**86**	**84**
AR-006	**140**	**80**	**84**	**140**	**82**	**80**	**142**	**82**	**78**	**140**	**84**	**80**
AR-017	**110**	**70**	**84**	**114**	**76**	**86**	**110**	**74**	**82**	**112**	**72**	**86**
AR-018	**170**	**50**	**96**	**168**	**70**	**88**	**164**	**72**	**86**	**168**	**74**	**82**
AR-022	**100**	**70**	**84**	**108**	**74**	**80**	**110**	**72**	**82**	**110**	**74**	**80**

AR-023	**100**	**70**	**84**	**110**	**82**	**80**	**108**	**80**	**80**	**110**	**82**	**82**
AR-026	**135**	**75**	**82**	**130**	**78**	**80**	**132**	**76**	**86**	**130**	**78**	**84**
AR-030	**130**	**80**	**90**	**128**	**82**	**82**	**130**	**80**	**84**	**132**	**84**	**84**
AR-031	**90**	**50**	**102**	**110**	**76**	**84**	**112**	**78**	**82**	**114**	**74**	**86**
AR-032	**100**	**70**	**88**	**108**	**78**	**80**	**110**	**76**	**84**	**112**	**76**	**84**
AR-033	**90**	**50**	**106**	**108**	**74**	**82**	**106**	**76**	**80**	**110**	**78**	**82**
AR-034	**110**	**70**	**82**	**114**	**76**	**86**	**112**	**72**	**84**	**114**	**74**	**86**
VQ-01	**120**	**80**	**80**	**120**	**84**	**78**	**122**	**80**	**80**	**120**	**82**	**80**
VQ-02	**110**	**70**	**84**	**114**	**72**	**82**	**110**	**72**	**80**	**112**	**70**	**82**
VQ-03	**120**	**70**	**86**	**116**	**74**	**84**	**118**	**72**	**84**	**118**	**76**	**80**
VQ-04	**140**	**80**	**84**	**136**	**82**	**82**	**138**	**80**	**86**	**136**	**82**	**88**
VQ-05	**120**	**60**	**78**	**118**	**74**	**80**	**120**	**72**	**78**	**120**	**76**	**76**
ZC-01	**140**	**80**	**82**	**140**	**80**	**84**	**138**	**80**	**82**	**142**	**84**	**82**
ZC-02	**130**	**70**	**84**	**132**	**76**	**88**	**130**	**72**	**82**	**130**	**74**	**82**
ZC-03	**110**	**60**	**80**	**112**	**76**	**78**	**114**	**74**	**80**	**112**	**76**	**82**
ZC-04	**140**	**50**	**98**	**142**	**72**	**88**	**140**	**74**	**84**	**142**	**76**	**84**
ZC-05	**150**	**80**	**82**	**146**	**82**	**80**	**148**	**84**	**86**	**148**	**84**	**82**
FH-001	**110**	**70**	**100**	**106**	**70**	**98**	**110**	**72**	**102**	**110**	**70**	**104**
FH-002	**70**	**40**	**114**	**70**	**42**	**110**	**70**	**40**	**114**	**72**	**40**	**112**
FH-003	**120**	**70**	**92**	**118**	**72**	**94**	**118**	**68**	**92**	**122**	**70**	**92**
FH-004	**110**	**70**	**118**	**110**	**70**	**114**	**112**	**72**	**120**	**110**	**72**	**116**
FH-005	**120**	**70**	**90**	**120**	**70**	**94**	**118**	**70**	**96**	**120**	**70**	**92**
FH-006	**110**	**70**	**120**	**108**	**70**	**122**	**110**	**70**	**122**	**110**	**72**	**124**
CR-001	**120**	**70**	**80**	**120**	**74**	**82**	**118**	**72**	**86**	**118**	**74**	**84**
CR-002	**120**	**70**	**86**	**116**	**74**	**84**	**116**	**72**	**88**	**118**	**74**	**82**
CR-003	**110**	**60**	**80**	**118**	**68**	**82**	**116**	**70**	**78**	**118**	**70**	**80**
CR-004	**110**	**60**	**78**	**116**	**70**	**78**	**116**	**68**	**80**	**116**	**70**	**76**
CR-005	**100**	**50**	**106**	**114**	**72**	**82**	**116**	**70**	**84**	**116**	**72**	**82**
CR-006	**110**	**70**	**92**	**112**	**70**	**94**	**112**	**74**	**90**	**114**	**72**	**92**
CR-007	**100**	**70**	**84**	**118**	**82**	**86**	**116**	**80**	**82**	**118**	**82**	**82**
CR-008	**120**	**80**	**82**	**122**	**80**	**80**	**120**	**78**	**84**	**120**	**80**	**80**
CR-009	**120**	**70**	**76**	**118**	**74**	**78**	**118**	**70**	**74**	**116**	**70**	**76**
CZ-001	**120**	**80**	**84**	**124**	**80**	**82**	**120**	**82**	**84**	**120**	**82**	**84**
CZ-002	**130**	**70**	**80**	**126**	**76**	**88**	**128**	**74**	**84**	**128**	**76**	**86**
CZ-003	**85**	**40**	**126**	**86**	**40**	**122**	**85**	**40**	**122**	**86**	**42**	**126**
CZ-004	**120**	**75**	**90**	**120**	**72**	**88**	**120**	**74**	**86**	**122**	**74**	**86**
CZ-005	**160**	**90**	**82**	**158**	**90**	**80**	**160**	**88**	**78**	**160**	**92**	**88**
CZ-006	**120**	**80**	**88**	**122**	**82**	**88**	**120**	**80**	**86**	**120**	**80**	**88**
CZ-007	**120**	**80**	**86**	**120**	**78**	**82**	**120**	**78**	**84**	**120**	**82**	**84**

CZ-008	**120**	**80**	**80**	**118**	**84**	**78**	**116**	**80**	**82**	**118**	**82**	**84**
CZ-009	**120**	**80**	**82**	**120**	**80**	**80**	**120**	**82**	**80**	**118**	**82**	**84**
CZ-010	**160**	**90**	**82**	**158**	**90**	**80**	**160**	**92**	**84**	**162**	**92**	**80**
CZ-011	**140**	**90**	**76**	**140**	**92**	**82**	**138**	**90**	**82**	**140**	**90**	**84**
JR-001	**130**	**70**	**82**	**126**	**78**	**84**	**130**	**76**	**80**	**132**	**78**	**86**
JR-002	**110**	**70**	**84**	**114**	**80**	**82**	**112**	**78**	**86**	**116**	**82**	**80**
JR-003	**130**	**70**	**78**	**132**	**76**	**80**	**128**	**74**	**80**	**130**	**76**	**84**
JR-004	**100**	**40**	**96**	**118**	**70**	**88**	**116**	**72**	**84**	**114**	**72**	**88**
JR-005	**120**	**70**	**80**	**118**	**74**	**82**	**120**	**84**	**86**	**122**	**84**	**86**

12.2.6 Laboratory Results Data Listings

Patient No.	Baseline				24h Post-Op				48h Post-Op				30d Post-Op			
	HGB	HCT	PT	PTT	HGB	HCT	PT	PTT	HGB	HCT	PT	PTT	HGB	HCT	PT	PTT
JM-01	14.0	42.9	11.6	54	13.8	42.6	11.5	56	14.1	42.2	11.5	51	14.1	43.2	11.6	27
JM-02	14.8	44.5	11.4	52	14.7	44.3	11.4	49	14.8	44.5	11.4	52	14.7	44.4	11.3	23
JM-03	13.7	41.0	11.9	58	13.9	40.6	11.9	61	13.9	41.2	11.8	54	14.0	41.7	11.9	26
JM-04	14.5	43.6	11.3	53	14.3	43.5	11.4	47	14.3	43.6	11.3	50	14.6	43.4	11.3	27
PC-001	11.5	33.5	11.0	22	14.2	43.0	11.0	22	14.2	43.2	11.2	23	14.5	43.2	11.2	22
PC-002	14.8	44.3	11.7	24	14.7	44.1	11.8	23	14.8	44.4	11.8	23	14.8	44.5	11.8	23
PC-003	15.1	45.4	11.5	26	15.1	45.3	11.6	25	15.1	45.2	11.5	25	15.0	45.0	11.6	25
PC-004	15.3	45.8	11.3	24	15.2	45.6	11.3	24	15.3	45.9	11.3	23	15.2	45.5	11.3	24
GJ-001	13.7	41.0	11.7	28	13.6	40.7	11.7	29	13.7	41.1	11.6	28	13.7	41.0	11.7	28
GJ-002	14.2	42.5	11.4	25	14.2	42.6	11.5	24	14.2	42.6	11.4	25	14.1	42.2	11.4	24
GJ-003	15.9	47.6	11.4	26	15.9	47.8	11.4	26	15.9	47.6	11.4	25	15.8	47.4	11.4	25
GJ-004	14.8	44.3	11.9	27	14.8	44.3	11.8	27	14.7	44.0	11.9	27	14.8	44.2	11.9	28
JS-001	14.2	42.7	11.3	23	14.2	43.0	11.0	22	14.2	43.2	11.2	23	14.5	43.2	11.2	22
JS-002	11.2	35.4	12.2	40	11.2	33.6	12.1	40	11.3	33.8	12.3	41	12.2	33.5	12.1	40
JS-003	16.0	48.2	11.4	24	15.7	47.9	11.4	23	15.9	48.0	11.4	23	16.3	48.3	11.3	23
JS-004	14.2	42.5	11.5	25	14.2	42.3	11.5	24	14.3	43.2	11.4	25	14.5	43.9	11.5	24
JM-001	11.4	33.8	11.8	26	11.3	33.7	11.6	26	11.3	33.8	11.8	24	11.5	39.0	11.8	25
JM-002	14.8	44.2	11.5	30	14.6	44.0	11.5	30	14.8	44.3	11.5	29	14.7	44.2	11.4	30
JM-003	12.8	38.5	11.9	28	12.8	38.2	11.8	27	12.9	38.5	11.9	28	12.8	38.4	11.8	28
JM-004	13.3	39.7	11.3	24	13.2	39.6	11.3	24	13.4	40.0	11.4	23	13.3	39.8	11.3	24
JM-005	14.2	43.4	11.8	29	14.2	43.2	11.7	29	14.2	43.4	11.8	28	14.0	43.1	11.8	29
JM-006	15.0	45.1	11.5	32	15.0	44.9	11.4	31	15.0	45.0	11.5	30	15.2	45.3	11.3	31
JM-007	13.5	40.2	11.4	28	13.4	40.4	11.4	29	13.5	40.4	11.2	27	13.5	40.4	11.3	28
JM-008	14.2	42.7	11.5	29	14.3	42.8	11.5	28	14.4	43.0	11.5	27	14.3	42.7	11.4	28
LB-001	13.3	39.7	11.5	30	13.2	39.7	11.5	29	13.3	39.8	11.5	27	13.3	40.0	11.5	30
LB-002	13.8	41.1	11.9	32	14.2	42.6	11.7	30	14.2	42.4	11.7	30	14.1	42.2	11.6	29
LB-003	12.9	38.5	11.5	26	13.4	40.0	11.6	28	13.4	40.3	11.5	28	13.2	39.5	11.5	27
LB-004	13.4	40.2	11.8	27	13.3	39.8	11.8	26	13.5	40.6	11.8	27	13.5	40.4	11.7	28
LC-001	14.8	44.5	11.4	25	14.8	44.3	11.4	24	14.7	44.1	11.4	25	14.8	44.4	11.4	25
LC-002	14.9	44.6	11.7	25	14.8	44.3	11.7	25	14.8	44.4	11.6	24	14.8	44.4	11.7	24
LC-003	12.5	37.5	11.9	25	12.4	37.1	11.9	26	12.5	37.5	11.9	26	12.6	37.6	11.8	26
LC-004	15.3	45.8	11.5	23	15.3	45.9	11.5	22	15.3	45.9	11.5	22	15.3	45.8	11.5	22

LC-005	**13.3**	**39.7**	**11.4**	**25**	**13.1**	**39.2**	**11.4**	**25**	**13.3**	**39.8**	**11.4**	**25**	**14.5**	**43.6**	**11.7**	**28**
LC-006	**14.5**	**43.5**	**11.7**	**29**	**14.4**	**43.2**	**11.7**	**28**	**14.4**	**43.2**	**11.6**	**29**	**14.5**	**43.6**	**11.7**	**28**
ML-001	**12.5**	**37.4**	**12.0**	**31**	**12.9**	**38.5**	**11.9**	**29**	**12.9**	**38.6**	**11.9**	**29**	**13.2**	**39.5**	**11.9**	**29**
ML-002	**14.0**	**42.1**	**11.6**	**25**	**14.2**	**42.5**	**11.6**	**25**	**14.2**	**42.6**	**11.6**	**26**	**14.4**	**43.2**	**11.6**	**24**
ML-003	**12.4**	**37.0**	**11.7**	**27**	**12.6**	**37.7**	**11.7**	**26**	**12.7**	**38.0**	**11.7**	**28**	**12.9**	**38.6**	**11.8**	**27**
ML-004	**12.8**	**38.3**	**11.5**	**29**	**12.9**	**38.7**	**11.4**	**29**	**12.9**	**38.6**	**11.5**	**28**	**12.9**	**38.7**	**11.5**	**28**
ML-005	**11.9**	**35.6**	**11.6**	**27**	**12.1**	**36.3**	**11.5**	**26**	**12.1**	**36.2**	**11.6**	**27**	**12.2**	**36.7**	**11.6**	**27**
ML-006	**9.4**	**28.1**	**11.9**	**30**	**11.6**	**34.9**	**11.5**	**26**	**12.1**	**36.3**	**11.5**	**25**	**14.4**	**43.0**	**11.5**	**26**
ML-007	**14.0**	**41.9**	**11.8**	**25**	**14.3**	**42.9**	**11.8**	**25**	**14.4**	**43.1**	**11.9**	**25**	**14.6**	**43.9**	**11.8**	**25**
ML-008	**10.1**	**30.0**	**11.8**	**29**	**12.3**	**36.9**	**11.7**	**26**	**12.8**	**38.2**	**11.7**	**27**	**13.0**	**38.8**	**11.8**	**27**
ML-009	**10.5**	**31.5**	**11.9**	**30**	**12.0**	**35.9**	**11.6**	**27**	**12.6**	**37.6**	**11.6**	**27**	**12.4**	**37.2**	**11.6**	**28**
ML-010	**12.5**	**37.6**	**11.5**	**24**	**13.7**	**41.0**	**11.5**	**24**	**14.0**	**41.8**	**11.4**	**25**	**14.4**	**43.2**	**11.4**	**23**
ML-011	**12.7**	**38.2**	**11.7**	**25**	**12.7**	**38.0**	**11.6**	**25**	**12.6**	**38.0**	**11.7**	**27**	**12.7**	**38.2**	**11.6**	**27**
ML-012	**12.3**	**36.8**	**11.4**	**25**	**12.1**	**36.3**	**11.6**	**28**	**12.2**	**36.5**	**11.5**	**27**	**12.4**	**37.0**	**11.5**	**26**
ML-013	**14.5**	**43.2**	**11.6**	**24**	**14.5**	**43.5**	**11.6**	**24**	**14.5**	**43.5**	**11.6**	**25**	**14.4**	**43.3**	**11.6**	**24**
ML-014	**13.9**	**41.5**	**11.7**	**28**	**14.0**	**42.0**	**11.6**	**28**	**14.0**	**42.2**	**11.7**	**29**	**14.1**	**42.3**	**11.6**	**28**
ML-015	**12.7**	**38.2**	**11.4**	**25**	**12.8**	**38.4**	**11.4**	**23**	**12.8**	**38.3**	**11.5**	**23**	**12.9**	**38.5**	**11.4**	**24**
ML-016	**12.5**	**37.5**	**11.5**	**26**	**12.7**	**38.2**	**11.5**	**27**	**12.8**	**38.4**	**11.6**	**26**	**12.8**	**38.4**	**11.5**	**25**
ML-017	**13.1**	**39.0**	**12.0**	**33**	**13.2**	**39.5**	**11.9**	**34**	**13.3**	**39.8**	**12.0**	**33**	**13.3**	**39.7**	**12.0**	**33**
ML-018	**12.8**	**38.2**	**11.4**	**29**	**13.0**	**38.8**	**11.5**	**29**	**13.0**	**39.0**	**11.5**	**27**	**13.0**	**39.0**	**11.4**	**28**
ML-019	**12.4**	**37.3**	**12.2**	**40**	**13.6**	**40.5**	**12.1**	**39**	**13.8**	**41.3**	**12.2**	**41**	**14.2**	**46.5**	**12.2**	**41**
RG-001	**10.8**	**32.0**	**12.5**	**43**	**10.4**	**31.1**	**12.6**	**46**	**10.9**	**32.6**	**12.5**	**41**	**11.5**	**34.2**	**12.7**	**42**
RG-002	**9.3**	**28.0**	**11.4**	**27**	**11.6**	**34.7**	**11.4**	**28**	**13.1**	**39.4**	**11.4**	**26**	**14.2**	**42.5**	**11.5**	**26**
RG-003	**10.5**	**31.3**	**11.6**	**30**	**10.2**	**30.4**	**11.5**	**29**	**10.9**	**32.6**	**11.7**	**31**	**11.5**	**34.2**	**11.6**	**29**
RG-004	**10.9**	**32.8**	**11.3**	**25**	**10.5**	**32.5**	**11.4**	**26**	**10.8**	**32.3**	**11.3**	**25**	**12.1**	**36.1**	**11.3**	**25**
RG-005	**10.7**	**31.9**	**11.6**	**30**	**10.3**	**30.7**	**11.5**	**30**	**11.0**	**32.9**	**11.6**	**31**	**13.2**	**39.4**	**11.6**	**30**
AM-001	**12.3**	**36.8**	**11.6**	**28**	**12.2**	**36.5**	**11.6**	**29**	**12.2**	**36.4**	**11.5**	**28**	**12.0**	**35.9**	**11.6**	**27**
AM-002	**14.7**	**44.0**	**11.4**	**28**	**14.6**	**43.9**	**11.5**	**27**	**14.8**	**44.3**	**11.5**	**28**	**14.7**	**44.2**	**11.4**	**28**
AM-003	**12.1**	**36.3**	**11.5**	**30**	**12.0**	**36.1**	**11.4**	**30**	**12.2**	**36.5**	**11.5**	**29**	**12.1**	**36.0**	**11.4**	**30**
AM-004	**11.8**	**35.7**	**11.9**	**25**	**11.8**	**35.5**	**11.9**	**25**	**11.7**	**35.0**	**11.8**	**24**	**11.9**	**35.8**	**11.8**	**26**
AM-005	**13.2**	**39.5**	**12.0**	**32**	**13.2**	**39.2**	**12.0**	**33**	**13.0**	**39.0**	**11.9**	**32**	**13.3**	**39.8**	**12.1**	**32**
AM-006	**13.8**	**41.4**	**11.5**	**27**	**13.7**	**41.0**	**11.5**	**26**	**13.9**	**41.6**	**11.4**	**28**	**13.9**	**41.5**	**11.5**	**25**
AM-007	**12.9**	**38.6**	**12.0**	**34**	**12.8**	**38.5**	**12.1**	**34**	**12.8**	**38.3**	**12.0**	**33**	**12.8**	**38.3**	**12.1**	**34**
EN-001	**14.8**	**44.2**	**11.5**	**52**	**14.8**	**44.4**	**11.5**	**54**	**14.7**	**44.2**	**11.4**	**48**	**14.8**	**44.3**	**11.5**	**23**
EN-014	**14.9**	**44.5**	**11.5**	**47**	**14.7**	**44.3**	**11.4**	**50**	**14.9**	**44.7**	**11.3**	**50**	**14.8**	**44.5**	**11.4**	**27**
AR-006	**15.9**	**48.0**	**11.5**	**58**	**15.8**	**46.0**	**11.5**	**62**	**16.2**	**48.3**	**11.6**	**56**	**16.1**	**48.0**	**11.5**	**27**
AR-017	**11.4**	**33.3**	**11.8**	**52**	**11.0**	**32.7**	**11.7**	**56**	**11.2**	**33.0**	**11.7**	**49**	**11.6**	**33.5**	**11.5**	**26**
AR-018	**11.0**	**33.4**	**11.8**	**45**	**10.9**	**33.0**	**11.9**	**42**	**11.2**	**33.7**	**11.7**	**46**	**11.5**	**34.2**	**11.8**	**25**
AR-022	**10.5**	**31.2**	**12.0**	**52**	**10.2**	**31.0**	**11.9**	**48**	**10.9**	**32.7**	**12.0**	**45**	**11.5**	**34.4**	**11.8**	**29**

AR-023	**13.2**	**39.1**	**11.6**	**28**	**13.2**	**39.0**	**11.6**	**27**	**13.4**	**39.5**	**11.8**	**26**	**13.3**	**39.2**	**11.8**	**26**
AR-026	**14.6**	**43.0**	**11.3**	**48**	**14.2**	**42.5**	**11.5**	**52**	**14.5**	**43.2**	**11.5**	**52**	**14.7**	**43.5**	**11.4**	**25**
AR-030	**11.7**	**34.2**	**11.5**	**50**	**11.4**	**33.8**	**11.4**	**54**	**11.9**	**35.5**	**11.5**	**48**	**11.8**	**34.6**	**11.5**	**25**
AR-031	**15.3**	**45.7**	**11.6**	**68**	**15.0**	**45.2**	**11.6**	**72**	**15.0**	**45.4**	**11.4**	**64**	**15.2**	**45.8**	**11.4**	**23**
AR-032	**14.8**	**44.1**	**11.3**	**46**	**14.4**	**43.8**	**11.3**	**52**	**14.7**	**44.0**	**11.2**	**45**	**14.9**	**44.6**	**11.1**	**26**
AR-033	**11.5**	**34.0**	**11.7**	**44**	**11.2**	**33.7**	**11.5**	**46**	**11.4**	**33.9**	**11.8**	**46**	**11.6**	**34.2**	**11.6**	**28**
AR-034	**15.2**	**45.6**	**11.2**	**48**	**15.0**	**45.2**	**11.3**	**45**	**15.3**	**45.5**	**11.2**	**42**	**15.3**	**45.7**	**11.0**	**22**
VQ-01	**11.5**	**34.2**	**11.8**	**63**	**11.4**	**34.2**	**11.7**	**65**	**11.6**	**34.3**	**11.7**	**62**	**11.4**	**34.3**	**11.8**	**28**
VQ-02	**12.0**	**35.8**	**11.8**	**64**	**11.7**	**35.0**	**11.5**	**65**	**11.8**	**35.7**	**11.7**	**67**	**11.9**	**36.1**	**11.8**	**29**
VQ-03	**14.3**	**42.8**	**11.5**	**28**	**14.0**	**42.1**	**11.5**	**32**	**14.1**	**42.5**	**11.4**	**29**	**14.4**	**42.8**	**11.5**	**27**
VQ-04	**13.9**	**40.2**	**11.2**	**64**	**13.7**	**40.0**	**11.3**	**70**	**14.0**	**40.4**	**11.2**	**64**	**14.2**	**40.5**	**11.0**	**25**
VQ-05	**14.1**	**42.2**	**11.8**	**29**	**14.1**	**42.3**	**11.8**	**27**	**14.1**	**42.3**	**11.9**	**28**	**14.0**	**42.0**	**11.8**	**27**
ZC-01	**12.2**	**36.5**	**11.4**	**45**	**11.9**	**36.1**	**11.4**	**48**	**12.1**	**36.3**	**11.3**	**40**	**12.0**	**36.2**	**11.4**	**27**
ZC-02	**14.6**	**43.6**	**11.8**	**51**	**14.2**	**43.0**	**11.7**	**53**	**14.5**	**44.0**	**11.7**	**50**	**14.7**	**44.3**	**11.7**	**24**
ZC-03	**11.0**	**33.2**	**11.9**	**46**	**11.2**	**33.4**	**11.7**	**50**	**11.3**	**33.7**	**11.9**	**45**	**11.2**	**33.5**	**11.9**	**27**
ZC-04	**15.2**	**45.3**	**11.3**	**48**	**14.9**	**45.0**	**11.4**	**45**	**15.2**	**45.5**	**11.2**	**49**	**15.3**	**45.7**	**11.1**	**25**
ZC-05	**14.0**	**42.2**	**11.4**	**68**	**13.7**	**41.3**	**11.5**	**72**	**14.0**	**42.4**	**11.5**	**64**	**14.2**	**42.1**	**11.5**	**26**
FH-001	**15.0**	**44.7**	**11.3**	**23**	**14.9**	**44.8**	**11.3**	**23**	**15.1**	**45.0**	**11.2**	**23**	**15.0**	**45.2**	**11.2**	**22**
FH-002	**15.3**	**45.0**	**11.3**	**23**	**15.1**	**45.0**	**11.2**	**23**	**15.4**	**44.8**	**11.3**	**22**	**15.2**	**45.3**	**11.4**	**22**
FH-003	**14.8**	**43.7**	**11.3**	**22**	**14.5**	**43.0**	**11.4**	**22**	**14.4**	**44.0**	**11.3**	**23**	**14.8**	**44.1**	**11.3**	**23**
FH-004	**15.1**	**45.0**	**11.4**	**24**	**15.0**	**44.8**	**11.4**	**24**	**15.3**	**44.8**	**11.4**	**24**	**15.2**	**45.0**	**11.4**	**23**
FH-005	**14.2**	**42.8**	**11.6**	**24**	**13.9**	**42.3**	**11.5**	**25**	**14.0**	**42.2**	**11.5**	**24**	**14.3**	**42.5**	**11.5**	**24**
FH-006	**15.0**	**44.6**	**11.4**	**23**	**14.7**	**43.1**	**11.4**	**23**	**14.9**	**44.0**	**11.3**	**24**	**15.1**	**44.9**	**11.4**	**23**
CR-001	**14.9**	**44.8**	**11.3**	**34**	**14.8**	**44.4**	**11.3**	**34**	**14.9**	**44.6**	**11.2**	**33**	**14.9**	**44.6**	**11.1**	**34**
CR-002	**9.6**	**28.9**	**11.7**	**27**	**11.6**	**34.6**	**11.6**	**27**	**13.1**	**39.4**	**11.7**	**28**	**14.9**	**44.6**	**11.1**	**34**
CR-003	**11.9**	**35.6**	**11.9**	**28**	**11.5**	**34.6**	**11.8**	**29**	**11.6**	**34.7**	**11.8**	**30**	**12.0**	**35.9**	**11.8**	**29**
CR-004	**12.4**	**37.0**	**11.4**	**25**	**12.2**	**36.4**	**11.4**	**26**	**12.2**	**36.5**	**11.4**	**25**	**12.5**	**37.3**	**11.3**	**26**
CR-005	**11.9**	**35.5**	**11.7**	**29**	**12.1**	**36.4**	**11.7**	**28**	**12.1**	**36.3**	**11.6**	**28**	**12.2**	**36.4**	**11.8**	**29**
CR-006	**13.0**	**38.9**	**12.1**	**36**	**13.0**	**39.1**	**12.2**	**35**	**13.0**	**38.8**	**12.0**	**36**	**12.9**	**37.6**	**12.1**	**37**
CR-007	**12.8**	**38.3**	**11.6**	**27**	**12.8**	**38.4**	**11.6**	**26**	**12.9**	**38.8**	**11.6**	**28**	**12.8**	**38.3**	**11.7**	**26**
CR-008	**14.4**	**43.3**	**11.3**	**25**	**14.2**	**42.7**	**11.4**	**26**	**14.3**	**42.8**	**11.3**	**24**	**14.5**	**43.6**	**11.3**	**25**
CR-009	**12.2**	**36.4**	**11.8**	**27**	**12.1**	**36.4**	**11.7**	**28**	**12.2**	**36.5**	**11.7**	**29**	**12.0**	**35.9**	**11.7**	**28**
CZ-001	**15.0**	**44.9**	**11.8**	**24**	**14.7**	**44.2**	**11.8**	**25**	**14.8**	**44.5**	**11.8**	**25**	**15.1**	**45.1**	**11.7**	**26**
CZ-002	**14.7**	**44.2**	**11.6**	**28**	**14.5**	**43.4**	**11.6**	**29**	**14.6**	**43.8**	**11.5**	**28**	**14.9**	**44.8**	**11.6**	**27**
CZ-003	**16.6**	**50.2**	**11.0**	**22**	**16.0**	**49.5**	**11.2**	**24**	**16.2**	**50.0**	**11.3**	**22**	**16.7**	**49.7**	**11.2**	**22**
CZ-004	**15.5**	**46.4**	**11.4**	**24**	**15.3**	**45.7**	**11.5**	**22**	**15.3**	**45.9**	**11.4**	**25**	**15.4**	**46.3**	**11.5**	**25**
CZ-005	**13.2**	**39.7**	**11.9**	**31**	**12.9**	**38.7**	**11.8**	**32**	**13.0**	**38.8**	**11.9**	**32**	**13.3**	**40.0**	**11.8**	**31**
CZ-006	**12.7**	**38.0**	**11.4**	**24**	**12.6**	**37.7**	**11.4**	**24**	**12.8**	**38.4**	**11.2**	**23**	**12.7**	**38.2**	**11.2**	**24**
CZ-007	**14.7**	**44.2**	**11.8**	**25**	**14.7**	**44.0**	**11.7**	**24**	**14.8**	**44.4**	**11.7**	**25**	**14.6**	**43.5**	**11.6**	**23**

CZ-008	**15.2**	**45.5**	**11.3**	**26**	**15.3**	**45.7**	**11.4**	**26**	**15.2**	**45.7**	**11.4**	**25**	**15.2**	**45.5**	**11.4**	**25**
CZ-009	**13.4**	**40.0**	**11.6**	**29**	**13.3**	**39.8**	**11.6**	**27**	**13.4**	**40.1**	**11.5**	**28**	**13.4**	**40.2**	**11.6**	**28**
CZ-010	**12.7**	**38.0**	**11.7**	**25**	**12.5**	**37.6**	**11.7**	**25**	**12.5**	**37.4**	**11.8**	**25**	**12.8**	**38.2**	**11.7**	**26**
CZ-011	**14.5**	**43.6**	**11.4**	**24**	**14.3**	**43.1**	**11.4**	**25**	**14.5**	**43.5**	**11.4**	**24**	**14.5**	**43.6**	**11.5**	**24**
JR-001	**14.9**	**41.8**	**11.6**	**27**	**14.2**	**42.6**	**11.6**	**26**	**14.2**	**42.7**	**11.5**	**27**	**14.3**	**42.8**	**11.6**	**27**
JR-002	**13.5**	**40.4**	**11.8**	**27**	**13.1**	**39.2**	**11.8**	**27**	**13.2**	**39.5**	**11.8**	**26**	**13.7**	**41.0**	**11.7**	**27**
JR-003	**13.7**	**41.0**	**11.5**	**26**	**13.6**	**40.8**	**11.6**	**25**	**13.6**	**40.9**	**11.6**	**27**	**13.6**	**40.8**	**11.7**	**28**
JR-004	**12.8**	**38.2**	**11.7**	**25**	**12.5**	**37.5**	**11.7**	**25**	**12.6**	**37.7**	**11.7**	**28**	**12.7**	**38.0**	**11.6**	**25**
JR-005	**13.0**	**38.9**	**11.4**	**28**	**12.7**	**37.9**	**11.4**	**27**	**12.8**	**38.7**	**11.3**	**28**	**13.0**	**38.9**	**11.4**	**28**

12.2.7 Efficacy Response Data Listing By Dosage

Efficacy Response Data Listings									
		Treatment Group							
		SeraSeal		Cauterization					
Patient No.	Dose (IU)	CT (min)	BL (ml)	CT (min)	BL (min)	VS	POB	POI	Lab
JM-01	3k	1	300	5	500	NC	N	N	↑PTT→NL 30d PO
JM-02	3k	1	400	7	700	NC	N	N	↑PTT→NL 30d PO
JM-03	3k	1	300	3	600	NC	N	N	↑PTT→NL 30d PO
JM-04	3k	1	400	8	700	NC	N	N	↑PTT→NL 30d PO
PC-001	3k	1	100	10	300	NC	N	N	↓HGB↓HCT→NL 24h PO
PC-002	7.5k	10	150	30	300	NC	N	N	NC
PC-003	7.5k	1	1	30	200	NC	N	N	NC
PC-004	7.5k	1	1	20	200	NC	N	N	NC
GJ-001	3k	1	150	45	300	NC	N	N	NC
GJ-002	3k	0.03	1	25	300	NC	N	N	NC
GJ-003	6k	1	50	60	150	NC	N	N	NC
GJ-004	6k	1	50	60	400	NC	N	N	NC
JS-001	3k	1	10	22	250	NC	N	N	NC
JS-002	3k	1	50	30	250	NC	N	N	NC
JS-003	3k	1	30	40	250	NC	N	N	NC
JS-004	3k	1	20	20	300	NC	N	N	NC
JM-001	6k	2	10	60	150	NC	N	N	NC
JM-002	3k	1	20	60	200	NC	N	N	NC
JM-003	6k	1	50	60	250	NC	N	N	NC
JM-004	6k	1	1	30	200	NC	N	N	NC
JM-005	3k	1	1	30	50	NC	N	N	NC
JM-006	6k	1	10	30	250	NC	N	N	NC
JM-007	3k	1	5	20	100	NC	N	N	NC
JM-008	3k	1	1	15	50	NC	N	N	NC
LB-001	3k	1	50	60	2000	NC	N	N	NC
LB-002	3k	2	10	0	3000	NC	N	N	NC
LB-003	3k	1	150	60	3000	NC	N	N	NC
LB-004	3k	1	30	20	100	NC	N	N	NC
LC-001	0.9k	1	5	30	100	NC	N	N	NC
LC-002	1.5k	10	5	40	100	NC	N	N	NC
LC-003	3k	10	50	30	100	NC	N	N	NC
LC-004	3k	1	50	30	100	NC	N	N	NC
LC-005	3k	1	50	20	100	NC	N	N	NC
LC-006	3k	1	100	40	200	NC	N	N	NC
ML-001	3k	0.67	50	30	500	NC	N	N	NC
ML-002	3k	0.67	30	40	300	NC	N	N	NC
ML-003	3k	0.83	30	30	300	NC	N	N	NC
ML-004	3k	0.33	200	20	1500	NC	N	N	NC
ML-005	6k	1	30	60	300	NC	N	N	NC
ML-006	6k	0.67	30	30	300	NC	N	N	↓HGB↓HCT→NL 48h PO
ML-007	3k	0.67	50	30	500	NC	N	N	NC
ML-008	6k	1	60	40	600	NC	N	N	↓HGB→NL 24h PO
ML-009	3k	0.5	20	30	300	NC	N	N	↓HGB↓HCT→NL 24h PO
ML-010	3k	1	50	30	500	NC	N	N	NC
ML-011	3k	1	20	20	200	NC	N	N	NC
ML-012	3k	0.67	200	20	400	NC	N	N	NC
ML-013	6k	0.83	20	20	300	NC	N	N	NC

ML-014	3k	1	20	20	300	NC	N	N	NC
ML-015	3k	1	20	20	200	NC	N	N	NC
ML-016	3k	1	20	30	300	NC	N	N	NC
ML-017	3k	1	20	30	300	NC	N	N	NC
ML-018	3k	1	20	30	300	NC	N	N	NC
ML-019	6k	1	2000	30	3000	NC	N	N	NC
RG-001	3k	0.33	500	20	1000	NC	N	N	NC
RG-002	3k	1	500	30	1000	NC	N	N	↓HGB↓HCT→NL 48h PO
RG-003	3k	1	400	60	800	NC	N	N	NC
RG-004	3k	1	50	30	600	NC	N	N	↓HGB↓HCT→NL 30d PO
RG-005	3k	1	500	60	800	NC	N	N	↓HGB↓HCT→NL 30d PO
AM-001	3k	1	50	15	250	NC	N	N	NC
AM-002	6k	1	50	30	700	NC	N	N	NC
AM-003	3k	1	50	30	200	NC	N	N	NC
AM-004	3k	1	60	45	1000	NC	N	N	NC
AM-005	3k	1	200	45	2000	NC	N	N	NC
AM-006	6k	1	100	50	700	NC	N	N	NC
AM-007	3k	2	50	60	1500	NC	N	N	NC
EN-001	6k	0.03	250	2	500	NC	N	N	↑PTT→NL 30d PO
EN-014	3k	0.5	250	5	500	NC	N	N	↑PTT→NL 30d PO
AR-006	12k	0.5	500	15	1200	NC	N	N	↑PTT→NL 30d PO
AR-017	6k	0.5	500	5	1000	NC	N	N	↑PTT→NL 30d PO
AR-018	6k	0.5	500	5	1000	NC	N	N	↑PTT→NL 30d PO
AR-022	3k	0.5	250	5	500	NC	N	N	↑PTT→NL 30d PO
AR-023	3k	0.5	150	5	300	NC	N	N	NC
AR-026	3k	0.5	500	5	1000	NC	N	N	↑PTT→NL 30d PO
AR-030	9k	1	500	10	1000	NC	N	N	↑PTT→NL 30d PO
AR-031	6k	0.5	200	5	500	NC	N	N	↑PTT→NL 30d PO
AR-032	6k	1	500	10	1000	NC	N	N	↑PTT→NL 30d PO
AR-033	6k	1	500	10	1000	NC	N	N	↑PTT→NL 30d PO
AR-034	6k	1	150	10	300	NC	N	N	↑PTT→NL 30d PO
VQ-01	3k	0.5	30	15	300	NC	N	N	↑PTT→NL 30d PO
VQ-02	3k	0.5	300	10	800	NC	N	N	↑PTT→NL 30d PO
VQ-03	3k	0.5	200	5	500	NC	N	N	↑PTT→NL 30d PO
VQ-04	3k	0.5	400	5	1000	NC	N	N	↑PTT→NL 30d PO
VQ-05	3k	0.03	5	10	200	NC	N	N	NC
ZC-01	6k	1	500	20	800	NC	N	N	↑PTT→NL 30d PO
ZC-02	6k	1	300	35	600	NC	N	N	↑PTT→NL 30d PO
ZC-03	3k	1	200	15	400	NC	N	N	↑PTT→NL 30d PO
ZC-04	6k	1	500	30	1000	NC	N	N	↑PTT→NL 30d PO
ZC-05	3k	0.5	300	10	800	NC	N	N	↑PTT→NL 30d PO
FH-001	3k	2	10	40	200	NC	N	N	NC
FH-002	6k	1	10	60	250	NC	N	N	NC
FH-003	6k	3	10	60	300	NC	N	N	NC
FH-004	6k	2	10	90	300	NC	N	N	NC
FH-005	9k	5 2	10	60 60	400	NC	N	N	NC
FH-006	9k	2	5	90	250	NC	N	N	NC
CR-001	6k	1	100	30	600	NC	N	N	NC
CR-002	3k	10	500	40	1000	NC	N	N	↓HGB↓HCT→NL 48h PO
CR-003	3k	10	200	30	300	NC	N	N	NC
CR-004	3k	1	200	20	300	NC	N	N	NC
CR-005	3k	1	200	20	400	NC	N	N	NC
CR-006	3k	1	100	10	200	NC	N	N	NC

CR-007	3k	0.03	1	10	200	NC	N	N	NC
CR-008	3k	1	200	15	400	NC	N	N	NC
CR-009	6k	1	50	10	200	NC	N	N	NC
CZ-001	6k	1	400	30	1000	NC	N	N	NC
CZ-002	3k	1	350	30	700	NC	N	N	NC
CZ-003	3k	1	250	60	1000	NC	N	N	NC
CZ-004	3k	1	250	60	700	NC	N	N	NC
CZ-005	6k	1	500	60	1000	NC	N	N	NC
CZ-006	6k	1	30	60	1000	NC	N	N	NC
CZ-007	3k	1	50	40	500	NC	N	N	NC
CZ-008	3k	1	50	45	400	NC	N	N	NC
CZ-009	3k	1	100	60	300	NC	N	N	NC
CZ-010	3k	1	400	30	700	NC	N	N	NC
CZ-011	3k	1	200	30	500	NC	N	N	NC
JR-001	3k	10	200	40	400	NC	N	N	NC
JR-002	6k	10	500	60	800	NC	N	N	NC
JR-003	3k	1	100	15	200	NC	N	N	NC
JR-004	6k	1	200	30	500	NC	N	N	NC
JR-005	6k	1	400	60	800	NC	N	N	NC

CT – clotting time
BL – blood loss
NC – no change
POB – post-operative bleeding
POI – post-operative infection
VS – vital sign
NL – normal limits
PO – post-operative

12.2.8 Adverse Event Listing

In the investigational group there were no adverse events reported.

12.3 CASE REPORT FORMS

12.3.1 CRF's for Deaths, Other Serious Adverse Events, and Withdraw for Adverse Events

Case Report Forms

There were no deaths or serious adverse events in this study.