SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Hemostatic Agent
Device Trade Name:	PerClot® Polysaccharide Hemostatic System
Device Product Code:	LMG
Applicant's Name and Address:	Artivion, Inc. (formerly CryoLife, Inc.) 1655 Roberts Boulevard NW Kennesaw, GA 30144
Date(s) of Panel Recommendation:	None
Premarket Approval Application Number:	P210036
Date of FDA Notice of Approval:	5/19/2023

II. INDICATIONS FOR USE

PerClot® Absorbable Hemostatic Powder

PerClot® Absorbable Hemostatic Powder is indicated in surgical procedures (except neurological and ophthalmic) as an adjunctive hemostatic device to assist when control of suture line bleeding or capillary, venous and arteriolar bleeding by pressure, ligature, and other conventional procedures is ineffective or impractical.

Accessory Tips

The PerClot® 20cm Extender Tip and PerClot 38cm Laparoscopic Tip are intended for the application of PerClot Absorbable Hemostatic Powder onto surgical wound surfaces consistent with the product labeling in open and laparoscopic procedures, respectively.

III. CONTRAINDICATIONS

Do not inject or place PerClot into blood vessels such as artery or vein as potential for embolization and death may exist.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the PerClot® Absorbable Hemostatic Powder labeling and the PerClot® accessory Tips labeling

V. DEVICE DESCRIPTION

PerClot Absorbable Hemostatic Powder (PerClot) is a medical device composed of absorbable polysaccharide granules. The PerClot System is comprised of three (3) components: 1) PerClot (granules/powder); 2) PerClot Delivery System; and the optional 3) PerClot Accessory Tips. The PerClot Delivery System includes a bellows and a standard applicator tip. Refer to the image of the PerClot Delivery System in Figure 1. The PerClot granules are biocompatible, non-pyrogenic and derived from purified plant starch. The granules do not contain any human or animal components. PerClot granules have a molecular structure that rapidly absorbs water, forming a gelled adhesive matrix that provides a mechanical barrier against bleeding and results in the accumulation of platelets, red blood cells, and coagulation proteins (thrombin, fibrinogen, etc.). The gelled adhesive matrix thus promotes the normal, physiological clotting cascade. PerClot granules are enzymatically degraded by alpha-amylase and glucoamylase and by macrophages. Based on preclinical studies, absorption occurs within 96 hours. Absorption is dependent on the amount of material applied on the wound and the site of use.

PerClot is supplied as a bellows pre-loaded with hemostatic powder. The bellows contains at least 1, 3, or 5 grams of material.

- 1g: 1.4-1.6 grams
- 3g: 3.4-3.7 grams
- 5g: 5.4-5.8 grams

An applicator tip is also supplied for application of the hemostatic powder. Contents of the PerClot package are supplied sterile for single-patient use only. Not made with natural rubber latex.

PerClot must be stored between 5°C and 25°C.

Figure 1: PerClot Delivery System (Assembled)

The PerClot Accessory Tips, which include the PerClot 20cm Extender Tip and PerClot 38cm Laparoscopic Tip, are sterile, single-use, malleable tips, designed to deliver PerClot Absorbable Hemostatic Powder onto surgical wound surfaces consistent with the PerClot Absorbable Hemostatic Powder product labeling. Refer to scaled images of the optional applicator tips in Figures 2 and 3.

Figure 2: PerClot 20cm Extender Tip – Optional applicator tip available separately

Figure 3: PerClot 38cm Laparoscopic Tip – Optional applicator tip available separately

VI. ALTERNATIVE PRACTICES AND PROCEDURES

A variety of existing alternative practices for achieving surgical hemostasis exist today. For bleeding along a suture line, the most common conventional method is the application of additional sutures. Direct pressure compression (with and without gauze or sponge) remains a common surgical technique to assist the body in creating its own platelet plug or fibrin clot, depending on the severity of the injury and bleed. Staples and ligating clips can also be used as mechanical methods for achieving hemostasis. Other alternative methods employed when the body's normal coagulation process cannot function properly include heat/energy-based methods such as electrocautery, ultrasonic devices and lasers. When these conventional methods are impractical or ineffective, there are topical agents on the market ranging from cellulose, gelatin and collagen-based products to active thrombin-based agents and chemical sealants.

PerClot Absorbable Hemostatic Powder, like other topical agents, can be used as an adjunctive agent during a variety of procedures where it may not be prudent or possible to

achieve surgical hemostasis with other means. Because it is plant-based, PerClot does not pose the risks associated with the use of hemostats manufactured from human- or animal-derived components.

VII. MARKETING HISTORY

PerClot Absorbable Hemostatic Powder has been on the market outside the United States since 2008 when it was first CE-marked, manufactured, and distributed by Starch Medical (SMI) (San Jose, CA). The device consists of the PerClot Powder (hemostatic granules) and a delivery system, which includes a bellows containing the powder and an applicator tip. PerClot Accessory Tips (20cm Extender Tip and 38cm Laparoscopic Tip) are sold separately.

PerClot Distributed Outside the United States (OUS)

Between September 28, 2010 and May 20, 2021, Artivion has distributed PerClot worldwide to OUS regions. Table 1 provides the countries where the device has been distributed. Adverse events occurring with the commercial PerClot device OUS are collected for evaluation. The device has not been withdrawn from any market for reasons of safety or effectiveness.

Table 1: PerClot OUS Distribution History

Country/Geography		
Australia	Jordan	Philippines
Austria	Kuwait	Poland
Bahrain	Lebanon	Qatar
Belgium	Libya	Russia
Chile	Malaysia	Russian Federation
Colombia	Malta	Saudi Arabia
Costa Rica	Mauritius	Singapore
Cyprus	Mexico	South Africa
Denmark	Morocco	South Korea
Dominican Republic	Myanmar	Spain
Ecuador	Netherlands	Sweden
Finland	New Zealand	Switzerland
France	Nigeria	Thailand
Germany	Norway	Turkey
India	Oman	United Kingdom
Indonesia	Pakistan	Uruguay
Ireland	Palestine	United Arab Emirates
Israel	Panama	Vietnam
Italy	Peru	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Hypophosphatemia
- Pleural Effusion
- Anemia
- Hypotension
- Constipation
- Abdominal Pain
- Nausea
- Hyperglycemia
- Atelectasis
- Hypokalemia
- Acute Kidney Injury
- Dyspnea
- Leukocytosis
- Atrial Fibrillation
- Fever
- Pericardial Effusion
- Compression of Tubular Ducts, Vessels and Nerves with Swelling Causing Obstruction or Neuropathy

For the specific adverse events that occurred in the clinical study, please see section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. LABORATORY STUDIES

Multiple non-clinical studies to support the safety and efficacy of PerClot and the Accessory Tips, including design verification and validation, pre-clinical open and laparoscopic animal studies, biocompatibility, shelf life, packaging testing and sterilization, and endotoxin validation and testing was conducted.

Bench Testing

An overview of the non-clinical testing is provided in Table 2 through Table 4 that demonstrates that the PerClot System components meet the design specifications and are safe and effective for their intended clinical use.

Table 2: Summary of Bench Testing – PerClot Granules

Study	Test Purpose	Acceptance Criteria/Assessment Criteria	Results/Conclusion
The Determination of PerClot Polysaccharide Hemostatic System's Gel Permeability Through a Suture Line	To determine if any of the PerClot gel could penetrate through the sutured incision	PerClot not detected on iodine-stained filter Positive and negative controls behave as expected	**PASS** Powdered and gelled PerClot does not permeate through suture lines on pressurized femoral popliteal arteries or saphenous veins
Evaluation of Potential Permeation of PerClot Polysaccharide Hemostatic System through an Arterial Puncture	To determine if, after the application of the PerClot Polysaccharide Hemostatic System onto an 18-gauge arterial puncture site, the PerClot permeated into the femoral artery	PerClot not detected on iodine-stained filter (PerClot does not seep through 18- gauge puncture into the femoral artery) Negative control behaves as expected	**PASS** Stained filters showed "No PerClot" for all test samples Stained blood vessels showed "No PerClot" for all test samples Some PerClot was visible around the puncture site in the bovine fatty tissue used to wrap the vessel Powdered and gelled PerClot does not permeate beyond the fatty tissue in a pressurized 18-gauge arterial puncture
Testing the Homogeneity of PerClot	To confirm that PerClot Absorbable Hemostatic Powder is a homogeneous product	n=10 samples: ≤ L1% 15%) n=30 samples, if required: ≤ L1% (15%) and no individual content of any dosage unit is less than (1-L2*0.01)M nor more than (1+L2*0.01)M where L2=25.0	**PASS** The results of the n=10 samples yielded a degree of substitution average (label claim) of 0.349 The resulting acceptance value was 4.397% which is less than the acceptance maximum The PerClot powder is homogenous

Study	Test Purpose	Acceptance Criteria/Assessment Criteria	Results/Conclusion
Evaluation of PerClot Performance When Left Open to the Operating Room Environment	To determine if the functional performance of the PerClot granules degrades over time when the PerClot bellows with the attached delivery applicator tips are exposed to the operating room (OR) environment	Rate of Water Absorption: Mass absorbed at 10 sec must be ≥1.100g Mass absorbed at 60 sec must be ≥2.900g Total Water Absorbance: All samples must have a swelling capacity ≥19	**PASS** At 10 seconds, all samples passed rate of water absorption testing with a range of 1.991g – 2.362g At 60 seconds, all samples passed rate of water absorption testing with a range of 3.370g – 4.350g All samples absorbed ≥19 times their weight All samples were able to dispense at least 5g of PerClot granules with a range of 5.14g – 5.41g

Table 3: Summary of Bench Testing – PerClot Delivery System

Study	Test Purpose	Acceptance Criteria/ Assessment Criteria	Results/Conclusion
Design Validation for Containing PerClot in the Primary Container and Dispensing the Marketed Volume	To validate that PerClot Absorbable Hemostatic Powder can be contained inside the primary container during agitation, and the amount of dispensed PerClot granules is greater than or equal to the marketed volume	After agitation, each primary container must be able to deliver > 5.0g of PerClot granules	**PASS** Minimum amounts dispensed: IDE: 5.07g PMA: 5.04g Both IDE and PMA primary containers and delivery tips delivered ≥5.0 g of PerClot granules after conditioning via agitation indicating the primary containers can contain and dispense the marketed weight of granules

Study	Test Purpose	Acceptance Criteria/ Assessment Criteria	Results/Conclusion
Design Validation for PerClot Ease of Removal from Packaging, Assembly, and Use	To validate that PerClot Absorbable Hemostatic Powder meets the user needs: 1) the delivery system must be easy to assemble, 2) must dispense PerClot granules, and 3) PerClot granules are ready to use off the shelf	All scaled testing requirements must be scored with an overall average rating of 3 (Satisfactory) or higher If the bellow and delivery tip cannot be presented aseptically or any sample receives and overall average rating less than 3, the sample will be considered an "Incomplete Task" and evaluated by the team	**PASS** No "Incomplete Tasks" and user needs met. All samples had an overall average rating of 3.0 or greater, ranging from 4.0 to 5.0 in the IDE group and 3.0 to 5.0 in the PMA group All primary operating functions were easily recognizable by the users The average time to complete opening the pouches and fitting the delivery tip to the bellow was 33 seconds
Evaluation of PerClot Coverage When Dispensed Using the New Primary Container and Delivery Tip	To evaluate the coverage of the PerClot granules when they are dispensed using the new primary container and delivery tip	PerClot primary containers must be able to deliver 3.36-4.48g of PerClot granules and cover a 4cm x 4cm application site between 3-4 mm in depth	**PASS** The dispensed weights ranged from 3.43g to 4.36g The dispensed heights (thickness) ranged from 3mm to 4mm All samples covered the $16cm^2$ application site

Table 4: Summary of Bench Testing – PerClot Accessory Tips

Study	Test Purpose	Acceptance Criteria/ Assessment Criteria	Results/Conclusion
Design Validation for PerClot Ease of Removal from Packaging, Assembly, and Use	To validate that the PerClot Accessory Tips meet the system requirements and user interface specifications related to the preparation, use and disposal	All scaled testing requirements must be scored with an overall average rating of 3 (Satisfactory) or higher If the laparoscopic tip cannot be presented aseptically or any sample receives and overall average rating less than 3, the sample will be considered an "Incomplete Task" and will be evaluated by the team	**PASS** No "Incomplete Tasks" and all user needs met All samples had an overall average rating of 3.0 or greater, ranging from 3.8 to 5.0 All primary operating functions were easily recognizable by the users
Evaluation of PerClot Coverage When Dispensed Using the 20cm Extender Tip	To evaluate the coverage of the PerClot granules when dispensed using the 20cm Extender Tip	PerClot Extender Tips must be able to deliver 3.36-4.48g of PerClot granules and cover a 4cm x 4cm application site between 3-4 mm in depth	**PASS** The dispensed weights ranged from 3.37g to 4.32g The dispensed heights (thickness) ranged from 3mm to 4mm All samples covered the $16cm^2$ application site
Evaluation of PerClot Coverage When Dispensed Using the 38cm Laparoscopic Tip	To evaluate the coverage of the PerClot granules when dispensed using the 38cm Laparoscopic Tip	PerClot Extender Tips must be able to deliver 3.36-4.48g of PerClot granules and cover a 4cm x 4cm application site between 3-4 mm in depth	**PASS** The dispensed weights ranged from 3.46g to 4.12g The dispensed heights (thickness) ranged from 3mm to 4mm All samples covered the $16cm^2$ application site

Study	Test Purpose	Acceptance Criteria/ Assessment Criteria	Results/Conclusion
Evaluation of the Flexibility and Rigidity of the PerClot 38cm Laparoscopic Tip	To verify that the PerClot 38cm Laparoscopic Tip has been designed such that the extruded tube portion of the assembly is rigid enough to prevent kinking during positioning of the tip to the site of the bleeding while allowing enough flexibility to allow tip advancement through a 5mm trocar	The 38cm laparoscopic tip must be able to be successfully inserted into and through the 5mm trocar At each location: • the extruded tube and the distal tip of the 38cm laparoscopic tip must not kink during positioning to occlude the delivery of the PerClot granules • PerClot granules must be able to be dispensed through the 38cm laparoscopic tip The 38cm laparoscopic tip must be able to be successfully removed through the 5mm trocar in a single piece (i.e., distal tip is still attached to the extruded tubing) After removal from the trocar, the distal tip must not be visually deformed such that the distal tip would occlude delivery of the PerClot granules The amount of PerClot dispensed must be ≥ the marketed volume of the bellow used	**PASS** The 38cm laparoscopic tip was able to be successfully inserted into and through the 5mm trocar At each location, the extruded tube and the distal tip of the 38cm laparoscopic tip did not kink during positioning At each location, PerClot granules were able to be dispensed through the 38cm laparoscopic tip The 38cm laparoscopic tip was able to be successfully removed through the 5mm trocar in a single piece After removal from the trocar, the distal tip was not visually deformed The amount of PerClot dispensed was ≥ the marketed volume of the bellow used (5g) with a range of 5.15g to 5.75g

Biocompatibility Testing

Biological evaluation was conducted in compliance with ISO 10993-1:2018, Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process. To evaluate the biological safety of the PerClot Absorbable Hemostatic Powder, consideration was given to the following: type of patient contact and intended clinical use; potential hazards associated with the materials of construction, the history of clinical use of the materials of construction, manufacturing process, the results of biocompatibility and chemical characterization testing performed, and the clinical history of the PerClot Absorbable Hemostatic Powder. The testing demonstrated that the PerClot Absorbable Hemostatic Powder is biocompatible as summarized in Table 5 below.

The PerClot Granules are categorized according to ISO 10993-1:2018 as implant medical device with prolonged ≥24 hours but not >30 days) contact with tissue/bone and blood based on its intended clinical use. The assessment of the PerClot granules is separate from that of the delivery system. The PerClot Delivery System is categorized according to ISO 10993-1:2018 as an externally communicating device with limited ≤24 hours) contact with tissue. The PerClot Standard Applicator Tip and Accessory Tips are categorized according to ISO 10993-1:2018 as an externally communicating device with limited ≤24 hours) contact with both tissue and blood path, indirect. Table 5 identifies the biological endpoints the results for test articles that underwent biocompatibility testing.

Table 5: Summary of Biocompatibility Testing

Endpoint	Applicable ISO 10993 Standard	Result
PerClot Granules		
Physical and Chemical Information	ISO 10993-1: Evaluating and Testing within a Risk Management Process	**PASS** Negligible toxicological risk
Cytotoxicity	ISO 10993-5: Tests for in vitro cytotoxicity	**PASS** Non-cytotoxic
Sensitization	ISO 10993-10: Tests for irritation and skin sensitization	**PASS** Non-sensitizer
Intracutaneous Irritation	ISO 10993-10: Tests for irritation and skin sensitization	**PASS** Non-irritant
Material Mediated Pyrogenicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-pyrogenic
Acute System Toxicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-toxic
Sub-Acute Systemic Toxicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-toxic Non-irritant
Implantation	ISO 10993-6: Tests for local effects after implantation	**PASS** At 28 days +/-2 days: Ranked Reactivity Score was 0.0 for the liver/serosa and parenchyma The Test Article was characterized as a non-irritant and was nonreactive as compared to the Control Article

Hemocompatibility	ISO 10993-4: Selection of tests for interactions with blood	**PASS** Non-hemolytic
Genotoxicity	ISO 10993-3: Tests for genotoxicity, carcinogenicity, and reproductive toxicity	**PASS** Non-genotoxic
PerClot Delivery System		
Cytotoxicity	ISO 10993-5: Tests for in vitro cytotoxicity	**PASS** Non-cytotoxic
Sensitization	ISO 10993-10: Tests for irritation and skin sensitization	**PASS** Non-sensitizer
Intracutaneous Irritation	ISO 10993-10: Tests for irritation and skin sensitization	**PASS** Non-irritant
Material Mediated Pyrogenicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-pyrogenic
Acute System Toxicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-toxic
Hemocompatibility	ISO 10993-4: Selection of tests for interactions with blood	**PASS** Non-hemolytic
PerClot Standard Tip and Accessory Tips		
Cytotoxicity	ISO 10993-5: Tests for in vitro cytotoxicity	**PASS** Non-sensitizer
Sensitization	ISO 10993-10: Tests for irritation and skin sensitization	**PASS** Non-sensitizer
Intracutaneous Irritation	ISO 10993-10: Tests for irritation and skin sensitization	**PASS** Non-irritant Non-pyrogenic
Material Mediated Pyrogenicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-pyrogenic

Acute System Toxicity	ISO 10993-11: Tests for systemic toxicity	**PASS** Non-toxic
Hemocompatibility	ISO 10993-4: Selection of tests for interactions with blood	**PASS** Hemolytic index of 0.2%; Non-hemolytic

B. ANIMAL STUDIES

Pre-clinical animal studies were conducted to support the safety and efficacy of PerClot and the Accessory Tips for their intended use in open and laparoscopic procedures. These studies demonstrate the safety and efficacy of the PerClot System and establish that benefit of its use outweighs the risk in open and laparoscopic procedures.

An overview of the non-clinical animal studies is provided in Table 6.

Table 6: Summary of Non-Clinical Animal Studies

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
A GLP Preclinical Evaluation of the Effectiveness and Safety of a Polysaccharide Hemostat to Achieve Hemostasis of an Abdominal Aorta Lesion in Pig	Swine (pigs) Total Used: n=14 (13 + 1 backup) Test: PerClot Polysaccharide Hemostatic System (PerClot Granules and Delivery System) Control: Gelfoam Plus n=1 Acute* treated with test n=7 survival treated with test (including 1 backup) n=6 survival treated with control	The primary efficacy endpoint was hemostasis of the treatment site within 5 minutes after hemostat application Any scoring or acceptance criteria related to histopathology are described separately in the individual study reports	Hemostasis: All animals in both the PerClot and control groups achieved the primary efficacy endpoint of hemostasis by 5 minutes PerClot was as safe as the control article when implanted chronically for a minimum of 14 days PerClot was absorbed by all animals according to histology, while the control article had some residual material at the time of necropsy The implant of neither PerClot or control article initiated an immune

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
	*Acute animal not included in the safety assessments of the test or control article		response
A GLP Preclinical Evaluation of the Effectiveness and Safety of a Polysaccharide Hemostat to Achieve Hemostasis of a Kidney Lesion in a Pig	Swine (pigs) Total Used: n=15 (12+ 3 backup) Test: PerClot Polysaccharide Hemostatic System (PerClot Granules and Delivery System) Control: Gelfoam Plus n=9 survival treated with test (including 3 backups) n=6 survival treated with control	The primary efficacy endpoint was hemostasis of the treatment site within 5 minutes after hemostat application Any scoring or acceptance criteria related to histopathology are described separately in the individual study reports	Hemostasis: PerClot: 5 minutes: 78% PerClot was still effective within 10 minutes of application Control: 5 minutes: 83% PerClot was as safe as the control article when implanted chronically for a minimum of 14 days PerClot was absorbed by all animals according to histology, while the control article still had some animals that had residual material at the time of necropsy The implant of neither PerClot nor control article initiated an immune response Clinical pathology (blood testing and animal morbidity and mortality) did not indicate a negative response to the implant of either PerClot or the control article
A GLP Preclinical Evaluation of the Effectiveness and Safety of a Polysaccharide	Swine (pigs) Total Used: n= 19 (17 + 2 backup) Test:	The primary efficacy endpoint was defined as the achievement of hemostasis by 5 minutes Any scoring or	Hemostasis: PerClot: 1 minute: 44% 3 minutes: 56%

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
Hemostat to Achieve Hemostasis of a Liver Lesion in a Pig	PerClot Polysaccharide Hemostatic System (PerClot Granules and Delivery System) Control: Gelfoam Plus n=13 survival treated with test (including 2 backups) (Total 13 animals with test and 16 wounds) n=6 survival treated with control	acceptance criteria related to histopathology are described separately in the individual study reports	5 minutes: 69% 10 minutes: 81% Control: 1 minute: 83% 3 minutes: 100% 5 minutes: 100% PerClot was as safe as the control article when implanted chronically for a minimum of 14 days PerClot was absorbed by all animals according to histology, while some animals implanted with the control article had residual material present at the time of necropsy There was a mild to moderate foreign body response noted by histology in the control animals The implant of neither PerClot nor control had an immune response in regard to the clinical pathology evaluation
A GLP Evaluation of the Effectiveness of Two Plant Based Hemostats in a Pig Bleeding Model	Swine (pigs) Total Used: n= 15 n= 3 bleeding group n=6 treated with test n=6 treated with control Pre-determined sized liver injuries of the following dimensions were	The primary endpoint was the achievement of hemostasis by 5 minutes after Hemostat application; and secondary endpoints were hemostasis at the site of application evaluated at 1,3,7, and 10 minutes	Hemostasis: PerClot: 1 minute: 52.78% 3 minutes: 72.22% 5 minutes: 88.89% 7 minutes: 94.45% 10 minutes: 97.23%

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
	used throughout the study. Each test system had 6 different sizes of injuries each created on their liver. Each test system had one of each of these injuries created on their liver: • 0.3 cm depth by 1.0 cm diameter • 0.5 cm depth by 1.0 cm diameter • 0.3 cm depth by 1.5 cm diameter • 0.5 cm depth by 1.5 cm diameter • 0.5 cm depth by 2.0 cm diameter • 1.0 cm depth by 2.0 cm diameter Test: PerClot Polysaccharide Hemostatic System (PerClot Granules and Delivery System Control: Surgicel Original Absorbable Hemostat		Control: 1 minute: 27.78%, 3 minutes: 44.45%, 5 minutes: 91.67% 7 minutes: 91.67%, 10 minutes: 97.23% For the 10-minute bleeding evaluation group, total blood loss throughout the entire evaluation period ranged from 1.22g to 163.18g When the collected 30 second fluid mass was 10.0g or less, both PerClot and control were at least 90% effective for the achievement of the primary endpoint of hemostasis by 5 minutes All three bleeding severity methods (hemoglobin concentration, mass and bleed scoring) were used to assess the blood loss from the pre-determined sized liver injuries The bleeding severity assessment methods did not predict time to hemostasis. There were no strong relationships between bleeding severity and the amount of PerClot or control applied
Assessment of Blood Glucose Levels During Degradation of Starch Based	New Zealand White Rabbits Total used n=15 n=6 received the test article	Evaluation of blood glucose levels	Mean baseline blood glucose levels were similar for all three groups (138.56 mg/dL, 147.33 mg/dL, and 139.33 mg/dL for PerClot,

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
Hemostatic Agents in a Rabbit Model	n=6 received the control article n=3 were operated on as sham controls <u>Test:</u> PerClot Hemostatic system (PerClot Granules and Delivery System) <u>Control:</u> Arista AH (Arista) – P050038 (also referenced as HemoStase) Absorbable Hemostatic Particles		Control, and sham groups, respectively) Blood glucose levels 1 hour postoperatively were significantly higher than baseline blood glucose for all three groups ($p<0.05$), with glucose levels remaining significantly higher at 2 hours postoperatively for animals treated with PerClot or Control The 1 hour and 2 hour glucose levels in animals treated with either PerClot or Control were significantly higher than glucose levels in sham operated control animals with control treated animals having higher glucose levels than PerClot treated animals 2 hours post-operatively By 48 hours, glucose levels for all three groups were similar and remained so for the remainder of the study At time of necropsy, no remaining article was grossly observed in any of the animals treated with either PerClot or control Overall, no adverse events were noted in response to implanted PerClot for any animals for the duration of the study
Determination of Systemic Blood	New Zealand White Rabbits Total used n=15	Evaluation of blood glucose levels	Baseline blood glucose levels were similar for all

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
glucose Levels During Degradation of Starch Based Hemostatic Agents in a Rabbit Model	n=6 received the test article n=6 received the control article n=3 were operated on as sham controls <u>Test:</u> PerClot Hemostatic system (PerClot Granules and Delivery System) <u>Control:</u> Arista (also referenced as HemoStase) Absorbable Hemostatic Particles		three groups (153.61 mg/dL, 148.17 mg/dL, and 141.89 mg/dL for PerClot, Control, and Sham groups, respectively) and all three treatment groups had mean baseline blood glucose levels within normal range Blood glucose levels 1 hour post-operatively were significantly higher than baseline blood glucose for all three groups ($p<0.05$), with glucose levels remaining relatively high at 2 hours post-operatively for animals treated with PerClot or Control Glucose levels of PerClot and Control animals at 2 hours were almost equivalent while slightly higher than glucose levels in Sham operated control animals By 4 hours, glucose levels for all three groups were similar and remained normal for the remainder of the study. It was concluded that known structural differences in the polysaccharide molecules and the rates of breakdown of the two products did not result in elevated systemic blood glucose levels during the degradation of PerClot and control in a rabbit model As all groups experienced brief elevation of blood

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
			glucose levels at 1 and 2 hours post-surgery, postoperative stress and excitement most likely attributed to those slight elevations This study demonstrated that implantation of starch based hemostatic agents into the body do not significantly alter systemic blood glucose levels during degradation for extended periods of time and that degradation of the particles occurs within 96 hours after application
Laparoscopic Application of the PerClot Absorbable Hemostatic Powder (5g) in a Swine Hemorrhagic (Liver) Model	Swine (Pigs) Total Used = 8 (7 + 1 backup) n=4 implanted with the test article n=3 implanted with the control article n=1 termination prior to procedure start <u>Test:</u> PerClot Hemostatic Powder (PerClot Granules and Delivery System) PerClot 38cm Laparoscopic tip (Accessory Tip) <u>Control:</u> Arista Absorbable Hemostatic Powder Arista FlexiTip Applicator,	Acceptance criteria included but was not limited to the following: <u>Safety & Efficacy</u> -Rating of Yes or No on End Use Rating Scale with success defined as a % -Evidence of clinically significant events -Complete cessation of bleeding (hemostasis) -Average score of 2 or below for adhesions <u>Usability</u> -Average Rating of 3 or above in the end-user rating scale	The PerClot Absorbable Hemostatic Powder (5g) and PerClot 38cm Laparoscopic Tip met the safety and efficacy criteria set forth in the protocol for comparison with the Arista Absorbable Hemostatic Powder (5g) and FlexiTip Applicator, 38cm in a healthy swine model over 28 days from treatment. All PerClot and control animals had easily removable (score 1) adhesions associated with the liver wounds created for the surgical model. The adhesions were mainly from the liver wound sites to the omentum and there were no adhesions observed remote from the surgical site. There were no findings of concern in the non-target tissues (non-treated regions of the

Study	Study Design	Acceptance Criteria/ Endpoint(s)	Results/Conclusion
	38cm		liver, hepatic lymph nodes, kidneys, spleen, pancreas, or lungs). The observed easily removable adhesions are expected consequence due to prior experimental manipulations and therefore do not represent a clinically significant safety concern. There was no evidence of significant (Grade 3 or above) adhesion formation found in any of the study animals regardless of assignment to receive PerClot or Control Articles and therefore the acceptance criteria was met. Unintended dispersion (spilling remote from the target surgical site) and tip leakage was evaluated; 96.8% of the PerClot treated animals met the success criteria for this endpoint, vs 91.6% of the control treated animals. In conclusion, this study demonstrated that the PerClot Absorbable Hemostatic Powder (5g) and PerClot 38cm Laparoscopic Tip did not introduce any new safety risks when compared to the predicate Arista Absorbable Hemostatic Powder (5g) and FlexiTip Applicator, 38cm.

C. ADDITIONAL STUDIES

Shelf-life Testing

Real-time testing conducted in support of devices' shelf-life has demonstrated that the product and packaging meet the required specifications for the stated life of the product.

Real-Time stability testing (PerClot Granules) and Real-Time and Accelerated stability testing (optional applicator tips) is ongoing on test articles following sterilization. Interim Real-Time stability data available at time of PMA approval establishes a shelf-life of 1 year for PerClot Granules when stored between 5°C and 25°C. Accelerated aging studies have established a shelf-life of 3 years for the optional applicator tips, when stored between 5°C and 25°C.

Sterile barrier system integrity testing was completed in compliance with ISO 11607- 1: 2019, *Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems*.

All package integrity testing conducted for the PerClot System and PerClot Accessory Tips demonstrate that these devices are safe and effective for their intended use in open and laparoscopic procedures.

Sterilization

The PerClot filled bellows, snap-fit adaptor and cap and the standard Applicator Tip are terminally sterilized using an Electron Beam (E-Beam) irradiation in accordance with ISO 11137, *Sterilization of Health Care Products: Requirements for Validation and Routine Control of - Radiation Sterilization*.

The Accessory Tips (20cm Extender Tip and 38cm Laparoscopic Tip) are sterilized via Ethylene Oxide in accordance with ISO 11135: *Sterilization of health-care products — Ethylene oxide —Requirements for the development, validation and routine control of a sterilization process for medical devices*.

All sterilization testing conducted for the PerClot System and PerClot Accessory Tips demonstrate that these devices meet a sterility assurance level (SAL) of 10^{-6} and are safe and effective for their intended use in open and laparoscopic procedures.

Other Essential Non-Clinical Testing and Assessments

Based on the results of these tests the following is concluded: the PerClot System is MR Safe; the PerClot System does not contain materials of animal origin, the PerClot Absorbable Hemostatic Powder does not contain phthalates; specifically, the components of the PerClot System do not pose a risk to the patient from exposure to phthalates; and the PerClot System is not made with natural rubber latex. The PerClot system does not pose a risk of significant adhesions, if per the IFU, once hemostasis is achieved, excess PerClot is removed from the site of application by irrigation and aspiration and inaccurate delivery, leakage or dispersion of PerClot Absorbable Hemostatic Powder is not likely.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

PerClot has an extensive clinical history which includes the clinical trial conducted under IDE G110072 in the US, additional clinical studies conducted Outside-the-US (OUS), clinical literature from the SMI-marketed product, and over 10 years of commercial use OUS with a safe history. The clinical history of reported scientific literature and unpublished clinical trials, including the IDE trial, totals more than 650 patient treatments over a 12-year period with positive clinical outcomes. The studies supporting the safety and efficacy of PerClot include:

- A prospective, multicenter, multidisciplinary, randomized, controlled (Arista) clinical IDE investigation (CLOT Trial; G110072) for subjects undergoing open elective cardiac, general, or urological surgical procedures, with a total of 324 subjects randomized to PerClot (n=161) or Arista (n=163) subjects at 19 US centers.

- Four unpublished clinical studies conducted in Europe totaling 119 PerClot subjects and three unpublished clinical studies conducted in China totaling 148 PerClot subjects. Surgical areas covered in these studies are discussed in Section XI.

- Nine published literature articles (8 clinical trials and 1 systematic review) totaling 255 PerClot subjects. Surgical areas covered in these studies are discussed in Section XI.

- Over 10 years of marketing history in more than 50 countries with a safe history.

Summary of Primary Clinical Study (CLOT Trial)

A clinical trial was conducted to establish a reasonable assurance of safety and efficacy of PerClot as an adjunctive hemostatic device to assist when control of suture line bleeding or capillary, venous and arteriolar bleeding by pressure, ligature, and other conventional procedures is ineffective or impractical, excluding neurological and ophthalmic surgeries, in the US under IDE G110072. Data from this study forms the primary clinical basis for the PMA submission.

A. Study Design

Patients were treated and enrolled between March 2015 and January 2019. The database for this PMA reflected data collected through February 2021 and included 324 patients. There were 24 investigational sites with 19 sites enrolling patients into the study.

The CLOT Investigation, a pivotal study of the hemostatic agent PerClot, was designed as a prospective, multicenter, multidisciplinary, randomized, active-controlled (Arista) clinical investigation for subjects undergoing open elective cardiac, general, or urological surgical procedures. The primary objective of this investigation was to demonstrate non-inferiority in the achievement of hemostasis of the treated bleeding site at 7 minutes in subjects receiving PerClot compared to subjects receiving Arista in multiple surgical disciplines when used as an adjunct to conventional means of achieving hemostasis such as pressure or ligature. For

this trial, hemostasis was defined as complete cessation of bleeding and was assessed at the time of surgery by the treating physician.

Subjects were randomized in a 1:1 ratio to PerClot or Arista with randomization stratified by bleeding severity (severity score 1 vs. 2) and therapeutic area (cardiac, general, or urology).

The study was sponsored by Artivion, Inc. and was conducted in compliance with United States Food and Drug Administration (FDA) regulations 21 CFR Parts 50, 54, 56, and 812, and also International Council for Harmonization (ICH) E6 Good Clinical Practices (GCP). Artivion collaborated with Contract Research Organizations (CRO) for study management, data management, site activation, DSMB facilitation, site monitoring, and data verification.

A DSMB with independent medical experts and an expert statistician operated throughout the course of the study to review unblinded data regarding trial conduct, patient selection, and safety and efficacy endpoints. These data were 100% source data monitored throughout the course of the study.

The clinical trial used Arista Absorbable Hemostatic Particles as the active control device. Arista is an ideal comparative device for the following reasons:

- The two products are based on the same raw materials (potato starch) and do not contain any pharmaceutical components, such as thrombin or fibrinogen.
- The two products are used under the same conditions and have the similar principles of operation.
- The products are similar in terms of clinical, biological and technical characteristics.
- Arista is a legally marketed alternative with similar indications for use.

The study enrolled subjects undergoing an elective surgical procedure in one of three different therapeutic areas (general, cardiac, or urology) with bleeding categorized by a bleeding severity score of 1 or 2. The bleeding site area and bleeding severity were rigorously defined and measured in each case prior to determination of subject eligibility preceding enrollment. The bleeding anatomic site could be no more than 25 cm^2 and the area for hemostatic application could be no more than 47 cm^2.

The bleeding severity score was defined by ranges of bleeding flux which was measured and calculated by weighing dedicated gauze with known absorption properties before and after applying the gauze for a measured period of time (see Table 7). Subjects with ooze (>0.000040-0.0056 g/(cm^2 s)) or slight bleeding (>0.0056-0.013 g/(cm^2 s)) were eligible, but subjects with moderate, severe, or life-threatening bleeding were not. These rigorous measurement procedures provide assurance that the bleeds treated in the trial met eligibility criteria and are accurately classified.

Table 7: Bleeding Severity Score Definition

Bleeding Severity Score	Bleeding Flux (g/cm^2 per second)
0=No Bleeding	0-0.000040
1=Ooze	>0.000040-0.0056
2=Slight Bleeding	>0.0056-0.013
3=Moderate Bleeding	>0.013-0.041
4=Severe Bleeding	>0.041-0.063
5=Life-Threatening Bleeding	>0.063

1. Subject Inclusion and Exclusion Criteria

Patient selection criteria were based on the inclusion and exclusion criteria listed below.

Preoperative Inclusion Criteria

- Subject is undergoing one of the following open elective cardiac, general, or urological surgical procedures:
    - Cardiac procedure (Epicardium);
    - Cardiac procedure (Aortic Anastomosis or Aortotomy Suture Line);
    - Liver resection;
    - Total splenectomy;
    - On-clamp partial nephrectomy; or
    - Radical nephrectomy.
- Subject is willing and able to give prior written informed consent for investigation participation; and
- Subject is > 22 years of age.

Preoperative Exclusion Criteria

- Subject with known sensitivity to starch or starch-derived materials;
- Subject who has a clinically significant coagulation disorder or disease, defined as a platelet count <100,000 per microliter, International Normalized Ratio >1.5, or a PTT more than 1.5 times outside the laboratory's normal reference range;

- Subject who used corticosteroids (excluding inhalers, eye-drops, and dermatologic corticosteroids) within 6 weeks prior to surgery;
- Subject who has been treated with an investigational product and has not completed the entire follow-up period for that investigational product;
- Subject who is pregnant (as confirmed by a pregnancy test), planning on becoming pregnant during the follow-up period, or actively breast-feeding; and
- Subject with poor blood glucose control as per glycosylated hemoglobin > 9%.

Intraoperative Inclusion Criteria

- Subject is undergoing one of the following elective procedures:
    - Cardiac procedure (Epicardium);
    - Cardiac procedure (Aortic Anastomosis or Aortotomy Suture Line);
    - Liver resection;
    - Total splenectomy;
    - On-clamp partial nephrectomy; or
    - Radical nephrectomy
- Subject in whom all visible vessels or suture holes, greater than or equal to 2mm in diameter have been ligated, or suture line gaps greater than or equal to 2mm have been ligated;
- Subject in whom there is bleeding at the specified area for each surgical procedure after any applicable conventional means for hemostasis are attempted as specified by the intraoperative protocol;
- Subject in whom the anatomic site is equal to or less than 25cm^2;
- Subject in whom the anatomic application site is equal to or less than 47cm^2; and
- Subject in whom the bleeding flux from the identified bleeding site is > 0.000040[$g/(cm^2 \cdot s)$] and ≤0.013[$g/(cm^2 \cdot s)$].

Intraoperative Exclusion Criteria

- Subject undergoing a cardiac procedure in which there is no aortic anastomosis or aortotomy suture line to evaluate using the bleeding severity scale (i.e., not for treatment at the distal coronary artery bypass graft anastomosis);

- Subject in whom any major intraoperative bleeding incidences during the surgical procedure occurred (i.e., subject with assignment of an American College of Surgeons Advanced Trauma Life Support Hemorrhage Class of II, III, or IV Hemorrhage);

- Subject who has an active or potential infection at the surgical site, or whose surgical wound is defined as a wound classification of CO (Contaminated) or D (Dirty or Infected) based upon the Center for Disease Control and Prevention's wound classification system;

- Subject who has undergone platelet receptor GP IIb/IIIa antagonist therapy less than 48 hours prior to surgery.

2. Patient Follow-up Schedule

Follow-up occurred intra-operatively, post-operatively and at discharge (up to 14 days post-randomization) and 6-weeks post-randomization. Oncology subjects had a survival assessment at 24 months post-randomization. Five patients enrolled under the original protocol version had follow-up at 1 and 3 months rather than 6 weeks post-randomization.

3. Clinical Endpoints

The primary efficacy endpoint was the proportion of patients with complete hemostasis at 7 minutes post-application. The primary analysis was a non-inferiority comparison with a margin of 10% in order to demonstrate that the PerClot was clinically comparable or better than Arista with respect to the primary efficacy endpoint. The primary hypothesis is that the proportion of subjects achieving hemostasis of the first treated lesion by 7 minutes in the PerClot subjects is no more than 10% lower than the proportion of subjects achieving hemostasis within 7 minutes in Arista subjects:

H_0: $P_{PerClot} < P_{Arista} - 10\%$

Ha: $P_{PerClot} \geq P_{Arista} - 10\%$

Non-inferiority comparison of the hemostasis rate between PerClot and Arista was performed using the Farrington-Manning method in the As Treated population**.** The primary non-inferiority endpoint was met if the one-sided p-value < 0.025. A total sample size of 324 was planned to provide >80% power for this test assuming a 90% hemostasis rate for both PerClot and Arista and a 5% attrition.

A secondary endpoint was the complete hemostasis at 5 minutes post-application, also using a non-inferiority comparison with 10% non-inferiority margin. An additional hemostasis assessment was performed at 12 minutes to check whether hemostasis was maintained at 5 minutes after the primary endpoint assessment time of 7 minutes. If the primary endpoint was met, the secondary endpoint was evaluated and was met if the one-sided p-value < 0.025.

The primary efficacy analysis was performed in several analysis populations. The intention-to-treat (ITT) analysis population included all randomized subjects and subjects were analyzed according to the study arm to which they were randomized. The ITT population consisted of all 324 patients that were randomized with 161 PerClot and 163 Arista subjects. The As Treated (AT) analysis population included all subjects who were randomized and treated with either PerClot or Arista, with subjects analyzed according to the treatment group for the treatment received (even if this differed from randomization assignment). The Per Protocol (PP) analysis population included all subjects who were randomized and treated with either PerClot or Arista and had no major protocol deviations. Due to the primary endpoint being a non-inferiority comparison, study success is based on the non-inferiority hypothesis being met in the AT analysis population.

The study was designed to assess safety through reporting on adverse events, including their relationship to the therapeutic device, seriousness, and severity. Safety and efficacy were further characterized by prospective data collection of key supplemental safety parameters including: operative time, maintenance of hemostasis 5 minutes after primary endpoint assessment at 7 minutes, alternate means used to achieve hemostasis, estimated blood loss, units of blood transfused, re-operation, and hospitalization time. The safety assessment was performed over a period of 6 weeks after the surgery to provide sufficient time for bleeding complications to manifest. Additionally, all-cause mortality assessments through 24 months were completed for oncology patients.

B. Accountability of PMA Cohort

In total, the study consented 582 subjects and enrolled 324 subjects across 19 Sites. Study attrition and withdrawal were low in the study with 13 subjects 4%) exiting the study early. Seven subjects discontinued participation prematurely for a reason other than death (2 lost to follow-up, 2 withdrawn after randomization before any hemostatic agent was applied, 1 voluntarily withdrew, 1 unable to return for an in-person visit due to remaining in a long term care facility, and 1 cancelled 6-week appointment with the transplant team and followed up with their primary care physician. Six subjects died during study follow-up through 6 weeks (1 PerClot and 5 Arista). Compliance with mortality reporting through up to 24 months was 99.4% (177/178).

Randomization for the trial was stratified by bleeding severity score and therapeutic area to help ensure balance within these sub-categories. The therapeutic areas included General Surgery (N=155), Urology (N=83) and Cardiac Surgery (N=86). Subjects enrolled had a bleeding severity score of 1 in approximately 57% of cases and a bleeding severity score of 2 in approximately 43% of cases. As shown in Table 8, approximately 50% of the subjects were undergoing a general surgery procedure, with approximately 25% in each of the other therapeutic areas (cardiac and urology). Use in cardiac cases included the application of the hemostatic agents to a surgical graft. The study was designed to pool data across the therapeutic areas and two bleeding severity scores. It was not powered to compare the relative safety and efficacy of PerClot and Arista within the individual arms of the study.

Table 8: Randomization Strata*

Variable	Summary Statistics	All Subjects (N=324)	PerClot (N=161)	Arista (N=163)
Bleeding Severity Score				
1	% (n/N	57.1% (185/324)	57.8% (93/161)	56.4% (92/163)
2	% (n/N	42.9% (139/324)	42.2% (68/161)	43.6% (71/163)
Therapeutic Area				
Cardiac	% (n/N	26.5% (86/324)	26.7% (43/161)	26.4% (43/163)
General	% (n/N	47.8% (155/324)	46.6% (75/161)	49.1% (80/163)
Urology	% (n/N	25.6% (83/324)	26.7% (43/161)	24.5% (40/163)

*Comparability of the PerClot and control groups were assessed using Fisher's exact tests of proportions for categorical variables

C. Study Population Demographics and Baseline Parameters

Patients were 59 years old on average, 62.7% male, and 88.9% white. No statistically significant differences were observed between study arms. No statistically significant differences were observed between arms on the height, weight, temperature or systolic blood pressure of enrolled patients (see Table 9).

Malignant tumor was the most common indication for surgery (33.0%). Cardiovascular disease (26.2%) and metastatic tumor (22.5%) were also common. Together, these three indications accounted for 81.8% of all surgeries with each of the remaining indications accounting for <10%. Surgery at a site that had been previously operated on was fairly common at 18.5%. No statistically significant differences were observed between the PerClot and Arista arms.

Table 9: Physical Exam*

Variable	Summary Statistics	All Subjects (N=324)	PerClot (N=161)	Arista (N=163)
Height (cm)	Mean ± SD (n) Median (Range)	173.0 ± 9.88 (324) 172.7 (140, 208)	173.3 ± 10.09 (161) 172.7 (140, 196)	172.7 ± 9.69 (163) 172.7 (147, 208)

Variable	Summary Statistics	All Subjects (N=324)	PerClot (N=161)	Arista (N=163)
Weight (kg)	Mean ± SD (n) Median (Range)	86.5 ± 20.15 (324) 84.5 (39, 150)	86.0 ± 19.90 (161) 83.5 (46, 135)	87.0 ± 20.44 (163) 84.8 (39, 150)
Temperature (°C)	Mean ± SD (n) Median (Range)	36.6 ± 0.40 (319) 36.6 (35, 38)	36.6 ± 0.42 (160) 36.6 (35, 38)	36.6 ± 0.38 (159) 36.6 (35, 37)
Systolic (mmHg)	Mean ± SD (n) Median (Range)	133.3 ± 19.78 (323) 131.0 (86, 196)	135.3 ± 18.48 (160) 133.0 (94, 186)	131.4 ± 20.86 (163) 130.0 (86, 196)
Diastolic (mmHg)	Mean ± SD (n) Median (Range)	76.3 ± 11.92 (323) 76.0 (42, 120)	77.7 ± 11.98 (160) 78.0 (42, 120)	74.9 ± 11.75 (163) 75.0 (47, 113)

*Comparability of the PerClot and control groups were assessed using t-tests of means or Wilcoxon tests for continuous factors and Fisher's exact tests of proportions for categorical variables

Use of blood modifiers, insulin, blood sugar lowering medications, or reversal drugs was fairly common in the enrolled population (66.4%). Current smoking was uncommon (10.2%), while former smoking was more common (41.4%). Approximately 1 in 5 patients (20.7%) had Type II diabetes and a similar percentage (17.9%) had undergone chemotherapy within the past 6 months.

D. Safety and Efficacy Results

1. Effectiveness Results

Primary Endpoint

In the AT population, the observed PerClot hemostasis rate at 7 minutes post-application is 90.6% versus 92.0% in Arista, a difference of -1.4% for the three therapeutic areas pooled. However, poolability of data across therapeutic areas and across sites was assessed and the pooling of data across the three therapeutic areas was not supported by the data due to variability in treatment difference between PerClot and Arista across therapeutic areas. Therefore, primary efficacy data was not pooled across the three therapeutic areas for hypothesis testing. Hemostasis rate at 7 minutes post-application by therapeutic area and treatment group is presented in Table 10.

The difference between PerClot and Arista varies across therapeutic area with a range from -9.3% (urology) to 16.7% (cardiac . Comparisons between PerClot and Arista

within each individual therapeutic area were not statistically powered for formal noninferiority assessments.

Table 10: Hemostasis at 7 minutes: By therapeutic area – AT population

Therapeutic Area	PerClot % (n/N)	Arista % (n/N)
General	93.3% (70/75)	100.0% (80/80)
Cardiac	85.7% (36/42)	69.0% (29/42)
Urology	90.7% (39/43)	100.0% (40/40)

Secondary Endpoint

Hemostasis at 5 minutes post-Application

In the AT population, PerClot demonstrated a comparable hemostasis rate at 5 minutes post-application versus Arista. Hemostasis rate at 5 minutes post-application by therapeutic area and treatment group is presented in Table 11.

Table 11: Hemostasis at 5 minutes: By therapeutic area – AT population

Therapeutic Area	PerClot %(n/N)	Arista %(n/N)
General	92.0% (69/75)	90.0% (72/80)
Cardiac	83.3% (35/42)	64.3% (27/42)
Urology	93.0% (40/43)	97.5% (39/40)

The difference between PerClot and Arista by therapeutic area varies with a range from -4.5% (urology) to 19% (cardiac). Comparisons between PerClot and Arista within each individual therapeutic area were not statistically powered.

Additional Assessment of Hemostasis

Maintained Hemostasis at 12 minutes post-Application

An additional hemostasis assessment was performed at 12 minutes to check whether hemostasis was maintained at 5 minutes after the primary endpoint assessment time of 7

minutes. This hemostasis assessment was defined as a supplemental safety measure to assess re-bleeding with results between PerClot and Arista more consistent across therapeutic areas. Hemostasis maintenance results by therapeutic area are provided at 12 minutes (Table 12). The 7 minute time point stands out as having the most variable results across therapeutic areas. Achieving hemostasis at 7 minutes that is not maintained through 12 minutes is of limited clinical value. Accounting for the 6 cases (2 general surgery and 4 urology) in which Arista did not maintain hemostasis from 7 to 12 minutes and the 1 case (1 general surgery) in which PerClot did not maintain hemostasis, the hemostasis results at 12 minutes demonstrate that the results of the PerClot across the three therapeutic areas are reasonably consistent, with poor performance of Arista in cardiac epicardial cases being the primary reason for variation in performance across therapeutic areas.

Table 12: Hemostasis Maintenance at 12 minutes: By therapeutic area – AT population

Therapeutic Area	PerClot %(n/N)	Arista %(n/N)
General	92.0% (69/75)	97.5% (78/80)
Cardiac	85.7% (36/42)	69.0% (29/42)
Urology	90.7% (39/43)	90.0% (36/40)

These findings suggest that the consistently good performance of PerClot across therapeutic areas at 5, 7, and 12 minutes provides evidence that PerClot affords therapeutic benefit that is anticipated to be comparable to Arista in repeated future use of the product.

2. Safety Results

The safety profile of both adjunctive hemostatic devices was comparable with no type of adverse event or severity of adverse event having a statistically significant higher rate in the PerClot arm compared to Arista. Furthermore, all supplemental safety measures further supported the conclusion of comparable safety and effectiveness with no differences in total operative time, use of alternate means to achieve hemostasis, total estimated blood loss, total units of blood transferred, need for re-operation, or total days hospitalized. In the study, there were 30 re-operations that occurred in 27 subjects. Re-operations for bleeding were assessed to determine if the bleeding occurred at the hemostatic agent application site.

There was a total of 6 deaths reported during study follow-up through 6 weeks. Of these deaths, 5 occurred in the Arista arm and 1 in the PerClot arm. At 24 months for the oncology patients, the Kaplan-Meier estimate of survival was 76% in the PerClot arm versus 74% in the Arista arm. Device deficiencies were rare in the clinical study occurring in <1% of distributed PerClot devices.

There were no unanticipated adverse device effects (UADEs) reported in the study. Non-serious AEs were common with 66.7% of subjects having 1 or more non-serious adverse event. Serious AEs were less common with 27.2% of subjects having 1 or more serious adverse event. Given that all patients in the study were undergoing a surgical procedure, a substantial number of events and a wide variety of types of events were expected to occur (see Table 13 and Table 13.1).

There was also a total of 34 device-related adverse events consisting of 17 SAEs and 17 non-SAEs. These events occurred in 21 separate subjects (21/324=6.5%). All 34 events were categorized as "Possibly related" with choices of "Possibly related", "Probably related" and "Definitely related" for the certainty with which an AE was related to the product.

For the PerClot cohort, a total of 21 adverse events (AEs) in 12 different subjects "Possibly related" to PerClot were reported in the study (see Table 14). Anemia, thromboembolic event, and pleural effusion were the only three types of AEs that had more than one occurrence. The number of device-related AEs were also comparable between the study arms. The observed rates of device-related adverse events by arm were 3.7% PerClot and 3.1% Arista for non-serious adverse events related to the device and 3.7% PerClot and 2.5% Arista for serious adverse events related to the device (Table 13). Therefore, a total of 7.5% (12/161) PerClot and 5.5% (9/163) Arista subjects experienced an adverse event, either serious or non-serious, that was "Possibly related" to the hemostatic device during the study.

Table 13: Overall Adverse Event Classification Summary*

	# Events (# Subjects, % Subjects)		
Adverse Event Category	**All Subjects (N=324)**	**PerClot (N=161)**	**Arista (N=163)**
Non-Serious AE	909 216, 66.7%)	457 114, 70.8%)	452 102, 62.6%)
Non-Serious Device Related AE	17 11, 3.4%)	10 6, 3.7%)	7 5, 3.1%)
Serious AE	152 88, 27.2%)	69 44, 27.3%)	83 44, 27.0%)
Serious Device Related AE	17 10, 3.1%)	11 6, 3.7%)	6 4, 2.5%)

*Comparison of safety between treatment arms was based on Fisher's exact tests for the proportion of subjects with serious device-related adverse events, unanticipated adverse device effects, and frequent adverse events (≥ 5% overall incidence

Table 13.1. Reported Adverse Event Summary (rates>5%).

	# Events (#Subjects, % Subjects)		
	All Events		
Adverse Event Category	**All Subjects (N=324)**	**PerClot (N=161)**	**Arista (N=163)**
Hypophosphatemia	46 (45, 13.9%)	22 (22, 13.7%)	24 (23, 14.1%)
Pleural Effusion	38 (38, 11.7%)	20 (20, 12.4%)	18 (18, 11.0%)
Anemia	32 (32, 9.9%)	19 (19, 11.8%)	13 (13, 8.0%)
Hypotension	32 (31, 9.6%)	12 (12, 7.5%)	20 (19, 11.7%)
Constipation	29 (28, 8.6%)	16 (16, 9.9%)	13 (12, 7.4%)
Abdominal Pain	28 (28, 8.6%)	14 (14, 8.7%)	14 (14, 8.6%)
Nausea	27 (27, 8.3%)	13 (13, 8.1%)	14 (14, 8.6%)
Hyperglycemia	26 (26, 8.0%)	14 (14, 8.7%)	12 (12, 7.4%)
Atelectasis	25 (24, 7.4%)	15 (14, 8.7%)	10 (10, 6.1%)
Hypokalemia	24 (23, 7.1%)	12 (11, 6.8%)	12 (12, 7.4%)
Acute Kidney Injury	21 (21, 6.5%)	11 (11, 6.8%)	10 (10, 6.1%)
Dyspnea	21 (21, 6.5%)	12 (12, 7.5%)	9 (9, 5.5%)
Leukocytosis	21 (21, 6.5%)	9 (9, 5.6%)	12 (12, 7.4%)
Atrial Fibrillation	19 (19, 5.9%)	10 (10, 6.2%)	9 (9, 5.5%)
Fever	17 (17, 5.2%)	12 (12, 7.5%)	5 (5, 3.1%)
Total	**909 (216, 66.7%)**	**457 (114, 70.8%)**	**452 (102, 62.6%)**

Table 14: Adverse Event Categories with Device-related Adverse Events – PerClot (Treatment)

	All AEs in Treatment Arm Subjects (N=161) # Events (# Subjects, % Subjects)			
Adverse Event Category	**Not related**	**Possibly related**	**Probably related**	**Definitely related**
Anemia	16 (16, 9.9%)	3 (3, 1.9%)	0	0
Thromboembolic Event	0	3 (3, 1.9%)	0	0
Pleural Effusion	21 (20, 12.4%)	2 (2, 1.2%)	0	0
Hyperglycemia	13 (13, 8.1%)	1 (1, 0.6%)	0	0
Hypoxia	6 (6, 3.7%)	1 (1, 0.6%)	0	0
INR Increased	6 (6, 3.7%)	1 (1, 0.6%)	0	0
Respiratory Failure	2 (2, 1.2%)	1 (1, 0.6%)	0	0
Sepsis	2 (2, 1.2%)	1 (1, 0.6%)	0	0
Activated Partial Thromboplastin Time Increased	0	1 (1, 0.6%)	0	0
Distributive Shock	0	1 (1, 0.6%)	0	0
Gastric Perforation	0	1 (1, 0.6%)	0	0
Hematoma Infection	0	1 (1, 0.6%)	0	0
Implant Site Fluid Collection	0	1 (1, 0.6%)	0	0
Pericardial Tamponade	0	1 (1, 0.6%)	0	0
Perihepatic Fluid Collection	0	1 (1, 0.6%)	0	0
Pneumonia	0	1 (1, 0.6%)	0	0

In addition to the deaths reported as part of safety reporting during study follow-up, there were additional deaths reported at the 24-month survival assessment for oncology subjects. As stated previously, there were 184 of 324 randomized subjects that were oncology subjects. The Kaplan-Meier estimate of survival at 24 months was 76% (20 deaths) in the PerClot arm versus 74% (25 deaths) in the Arista arm (see Figure 4). The difference in the survival rate by arm was small, with Arista patients having similar survival compared to PerClot patients. The study was not specifically designed or powered to compare survival.

Supplementary safety information is provided in Table 15. A total of 322 of the 324 enrolled subjects were assessed for supplementary safety. Overall, all supplemental safety endpoints were comparable across PerClot and Arista study arms, providing evidence of comparable safety performance. None of the re-operations were due to bleeding at the hemostatic agent application site for either product. PerClot performance with vascular grafts was studied in the CLOT Trial (n=6), but this subset was not statistically powered. All patients met the primary and secondary endpoints, and no device related AEs were observed in this subset of subjects.

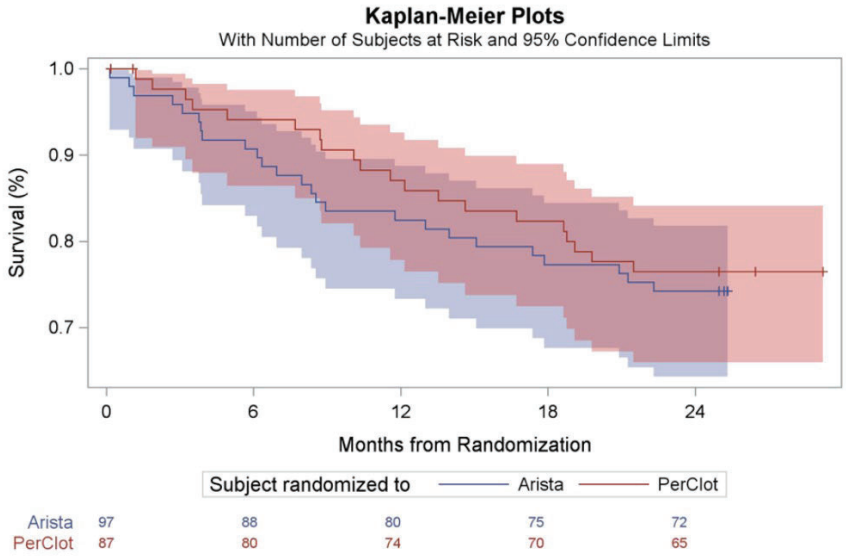

Figure 4: Kaplan-Meier Plot of Survival in Oncology Subjects Through 24 months

Table 15: Supplemental Safety Summary*

Variable	Summary Statistics	All Subjects (N=324)	PerClot (N=161)	Arista (N=163)
Total Operative Time (minutes)	Mean ± SD (n) Median (Range)	257.2 ± 124.61 (322) 233.5 (59, 733)	254.2 ± 126.40 (160) 234.5 (61, 692)	260.2 ± 123.13 (162) 233.5 (59, 733)
Hemostasis at 5 minutes (per investigator)	% (n/N	87.6% (282/322)	90.0% (144/160)	85.2% (138/162)
Hemostasis at 7 minutes (per investigator)	% (n/N	91.3% (294/322)	90.6% (145/160)	92.0% (149/162)
Hemostasis Maintained at additional 5 minutes	% (n/N	89.1% (287/322)	90.0% (144/160)	88.3% (143/162)

Variable	Summary Statistics	All Subjects (N=324)	PerClot (N=161)	Arista (N=163)
Used Alternate Means to Achieve Hemostasis	% (n/N	10.2% (33/322)	10.0% (16/160)	10.5% (17/162)
Stitches	% (n/N	1.9% (6/322)	1.9% (3/160)	1.9% (3/162)
Manual pressure applied	% (n/N	1.6% (5/322)	1.9% (3/160)	1.2% (2/162)
Other hemostatic device	% (n/N	4.7% (15/322)	3.8% (6/160)	5.6% (9/162)
Other	% (n/N	4.7% (15/322)	6.3% (10/160)	3.1% (5/162)
Total Estimated Blood Loss (mL)	Mean ± SD (n) Median (Range)	477.6 ± 546.76 (322) 300 (0, 4500)	471.4 ± 476.91 (160) 350 (0, 2200)	483.6 ± 609.38 (162) 300 (0, 4500)
Total Units Blood Transfused	Mean ± SD (n) Median (Range)	0.4 ± 0.94 (322) 0 (0, 4)	0.4 ± 0.93 (160) 0 (0, 4)	0.4 ± 0.95 (162) 0 (0, 4)
Reoperation	% (n/N	8.4% (27/322)	10.6% (17/160)	6.2% (10/162)
Total Hospitalization Time (days)	Mean ± SD (n) Median (Range)	6.8 ± 5.96 (318) 5 (1, 66)	7.0 ± 6.58 (158) 5.5 (2, 66)	6.6 ± 5.29 (160) 5 (1, 37)

*Comparability of the PerClot and control group subjects were assessed using t-tests of means or Wilcoxon tests for continuous factors and Fisher's exact tests of proportions for categorical variables

Study Summary

PerClot Absorbable Hemostatic Powder demonstrated effectiveness as an adjunctive hemostatic device. For the primary endpoint, PerClot demonstrated comparable performance versus Arista. Comparability was also demonstrated for the secondary endpoint with a complete hemostasis rate at 5 minutes. Hemostasis for both groups was maintained at a high rate through the 12-minute assessment for both arms. PerClot and Arista showed comparable safety and efficacy for both mild (Severity Score 1) and moderate (Severity Score 2) bleeds, for men and women, and all races.

The safety profile of both adjunctive hemostatic devices was comparable with no type of adverse event or severity of adverse event having a statistically significant higher rate in the PerClot arm compared to Arista. Furthermore, all supplemental safety measures further supported the conclusion of comparable safety and effectiveness with no differences in total operative time, use of alternate means to achieve hemostasis, total

estimated blood loss, total units of blood transferred, need for re-operation, or total days hospitalized.

The results of the CLOT Trial of PerClot Absorbable Hemostatic Powder demonstrated safety and efficacy as an adjunctive hemostatic device by demonstrating comparable performance versus Arista.

3. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 110 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Additional European and Chinese Studies

Additional clinical information for PerClot is sourced from outside the United States (OUS) clinical studies (Table 16).

Table 16: Total Available Clinical Data for PerClot

Source	Number of Studies / Reference Articles	Total PerClot
European Studies	4	119
China Studies	3	148
Published Literature	9	255
Total		**522**

Four European (n=119 PerClot) and Three Chinese (n=148 PerClot) clinical trials are available totaling 267 patients. These studies cover a wide range of therapeutic areas as shown in Table 17.

Table 17: Additional Clinical Studies Using PerClot

Study	Surgical Area	# of PerClot
Studies in Europe		
Roberts D., "A post-market surveillance study evaluating the safety and effectiveness of PerClot to control mild bleeding in subjects undergoing endoscopic sinus surgery."[1]	ENT	N=12
Ponce J. and Scambia G., "A prospective, multi-center, randomized, safety and effectiveness study of PerClot compared to usual care when used during gynecological procedures."[2]	Gynecological surgery	N=44 (20 laparoscopic)
Mair H., et al., "Use of PerClot, a plant-based polysaccharide hemostat, for bleeding control of the sternum in high risk patients."[3]	Coronary surgery requiring median sternotomy	N=21
Busch F. "Safety and effectiveness of PerClot an absorbable adhesive forming hemostatic microporous polysaccharide in spinal surgery."[4]	Head and Neck surgery (Spinal)	N=42 patients N=127 bleeding events
Studies in China		
Southwest Hospital Tangdu Hospital "Clinical Trial of Absorbable Polysaccharides Haemostatic."[5]	Surgical trauma	N=44
Third Military Medical University Tangdu Hospital "Absorbable Polysaccharide Hemostatic Material"[6]	General surgery	N=89
Fourth Army Medical University Lu J. and Wang Q. "Clinical evaluation of hemostatic performance in hepatic surgery."[7]	Splenectomy for portal hypertension	N=15
Total		**N=267**

Additional Published Scientific Literature

A literature search was conducted to identify any published clinical data related to PerClot. In total, 9 articles were identified (8 clinical trials and 1 systematic review). This real-world clinical evidence (RWE) included multiple therapeutic areas such as ENT surgery, cardiovascular / vascular surgery, head and neck surgery, plastic surgery, and orthopedic surgery. In total, 255 PerClot subjects are included in published literature (Table 18).

Table 18: Therapeutic Areas and Subjects in Published Literature

Therapeutic Area	Articles (n)	Subjects (n)
ENT surgery (Pagella[8], Van Ahnen[9])	2	12+30 (42)

Cardiovascular / vascular surgery (Janczak[10], Tscholl[11])	2	26+51 (77)
Head and neck surgery (Rao[12])	1	57
Laparoscopic abdominal surgery (Duran[13], Puchkov[14])	2	31+16 (47)
Plastic surgery (Malik[15])	1	Not reported
Orthopedic surgery (Aktas[16])	1	32
Total	**9**	**255**

Supplemental Clinical Information - Laparoscopic

Several supplemental clinical studies have been conducted OUS to support the assessment of PerClot when administered laparoscopically. As shown in Table 19, PerClot was used successfully in 67 procedures from these three OUS studies, further supporting the laparoscopic clinical outcomes.

Table 19: PerClot Laparoscopic OUS Post-market Usage

Reference	Surgical Area	# of Laparoscopic PerClot Uses
Ponce J. and Scambia G., "A prospective, multi-center, randomized, safety and effectiveness study of PerClot compared to usual care when used during gynecological procedures."[2]	Gynecological surgery	N=20
Duran, et al., "Comparative study of different means of hemostasia from the liver bed in the course of cholecystectomies complicated laparoscopic."[13]	Laparoscopic abdominal surgery (Cholecystectomy)	N=31
Puchkov, et al. "Methods of treatment of the stump of the adrenal gland."[14]	Laparoscopic abdominal surgery (Adrenalectomy)	N=16
TOTAL		**N=67**

Published literature shows that PerClot is used in a wide range of real-world applications. No unexpected adverse events were reported in the clinical studies. PerClot was effective in achieving hemostasis with a positive safety profile compared to traditional closure methods. This evidence supports the continued use of PerClot at a physician's discretion in any procedure where demands for hemostasis fits the device parameters of PerClot and no known contra-indications are known.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Efficacy Conclusions

The PerClot Polysaccharide Hemostatic System (PerClot System) consisting of the PerClot Absorbable Hemostatic Powder (PerClot), a containment and delivery system inclusive of all applicator tips, packaging and labeling has demonstrated a comparable hemostasis rate at 5 and 7 minutes when compared to the Arista control arm. Further, the hemostasis maintenance rate in both the treatment (PerClot) and control (Arista) arms at 12 minutes was similar to the hemostasis rate observed at 7 minutes.

B. Safety Conclusions

The risks identified and assessed for the PerClot System are based on nonclinical laboratory and animal studies, as well as data collected in clinical studies conducted to demonstrate the safety and efficacy of the device in support of PMA approval. The safety profile of the PerClot Absorbable Hemostatic Powder was found to be similar to that of the control Arista with regard to the rate and types of Adverse Events and Serious Adverse Events. In addition, there were no unanticipated adverse device effects or safety concerns identified with the device's containment/delivery system or applicator tips.

C. Benefit-Risk Determination

When PerClot was used as an adjunct to hemostasis during open cardiac, general, or urological surgical procedures to control oozing or slight bleeding in the pivotal study, the benefits of PerClot included achieving hemostasis within 5 and 7 minutes of application compared to the control group in the overall population of the three arms combined. It was comparable to the Arista group for the primary endpoint of hemostasis at 7 minutes. The secondary endpoint of hemostasis at 5 minutes was also found to be comparable to the Arista group. The additional endpoint of maintenance of hemostasis at 12 minutes was similar to the hemostasis rate observed at 7 minutes for both groups, although numerically more patients did not maintain hemostasis through 12 minutes in the Arista arm. When the individual surgical arms were compared at each time point, the hypothesis test between PerClot and Arista could not be evaluated. However, hemostasis exceeded 90% for each arm at all time points providing an acceptable result for mild to moderate bleeding even though the statistical analysis of the combined arms were not poolable. The safety profile of both adjunctive hemostatic devices was comparable with no type of adverse event or severity of adverse event having a statistically significant higher rate in the PerClot arm compared to Arista.

Potential risks of hemostatic devices include: Hypophosphatemia, Pleural Effusion, Anemia, Hypotension, Constipation, Abdominal Pain, Nausea, Hyperglycemia, Atelectasis, Hypokalemia, Acute Kidney Injury, Dyspnea, Leukocytosis, Atrial Fibrillation, Fever, and Pericardial Effusion. All supplemental safety measures of PerClot further supported the conclusion of comparable safety and effectiveness with no differences in total operative time, use of alternate means to achieve hemostasis, total estimated blood loss, total units of blood transferred, need for re-operation, or total days hospitalized.

The PerClot arm compared to the Arista arm showed no increased mortality, no thromboembolic events or wound healing complications. The benefits of the reduction of intraoperative bleeding outweigh the potential risks.

Based on results reported in IDE G110072, the safety profile of both adjunctive hemostatic devices was comparable with no type of adverse event or severity of adverse event having a statistically significant higher rate in the PerClot arm compared to Arista. Furthermore, all supplemental safety measures further supported the conclusion of comparable safety and effectiveness with no differences in total operative time, use of alternate means to achieve hemostasis, total estimated blood loss, total units of blood transferred, need for re-operation, or total days hospitalized.

Supplement clinical evidence supporting safety and effectiveness includes clinical studies conducted Outside-the-US (OUS) and supporting clinical literature. In total, PerClot was evaluated in more than 650 patients including an IDE pivotal clinical trial, nine (9) published clinical studies and seven (7) unpublished clinical studies. The supplemental clinical evidence includes approximately 67 patient treatments reported on applications in laparoscopic surgery. The entirety of the US and OUS clinical experience and the long history of safe treatment in commercial use (OUS) demonstrates that PerClot is overall acceptable for use in mild and moderate bleeding with no major bleeding episodes and no patients returning post-operatively for major bleeding. Furthermore, PerClot was effective in achieving hemostasis with a positive safety profile compared to traditional hemostatic measures.

Given the comparable results of PerClot and Arista in the randomized IDE study, the body of evidence in published and unpublished OUS studies and the long history of safe treatment in commercial use OUS, PerClot has been demonstrated to be safe and effective for its intended use in open and laparoscopic surgery.

Patient Perspectives

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for surgical procedures (except neurological and ophthalmic) as an adjunctive hemostatic device to

assist when control of suture line bleeding or capillary, venous and arteriolar bleeding by pressure, ligature, and other conventional procedures is ineffective or impractical the probable benefits outweigh the probable risks.

D. Overall Conclusions

E. The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Given the available information from non-clinical and clinal data from Artivion studies, SMI studies and the published literature, the data support that for the PerClot Polysaccharide Hemostatic System, specifically the PerClot Absorbable Hemostatic Powder and the PerClot Applicator Tips, the benefits outweigh the risk for use in open and laparoscopic surgical procedures (except neurological and ophthalmic) as an adjunctive hemostatic device to assist when control of suture line bleeding or capillary, venous and arteriolar bleeding by pressure, ligature, and other conventional procedures is ineffective or impractical.

XIV. CDRH DECISION

CDRH issued an approval order on 5/19/2023.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order

XVI. REFERENCES

[1] Roberts D., "A post-market surveillance study evaluating the safety and effectiveness of PerClot to control mild bleeding in subjects undergoing endoscopic sinus surgery" – PCT1401.000-M (06/14) – Report on file.

[2] Ponce J. and Scambia G., "A prospective, multi-center, randomized, safety and effectiveness study of PerClot compared to usual care when used during gynecological procedures" – PCT1501.000-C (01/15) – Report on file.

[3] Mair H., et al., "Use of PerClot, a plant-based polysaccharide hemostat, for bleeding control of the sternum in high risk patients" – Unpublished manuscript on file.

[4] Busch F., "Safety and effectiveness of PerClot an absorbable adhesive forming hemostatic microporous polysaccharide in spinal surgery" – Unpublished manuscript on file.

[5] "Clinical Trial of Absorbable Polysaccharides Haemostatic." – Clinical trial (n=142 patients) conducted in China – Report on file.

[6] "Absorbable Polysaccharide Hemostatic Material" Clinical trial (n=288 patients) conducted in China – Report on file.

[7] Lu J. and Wang Q., "Clinical evaluation of hemostatic performance in hepatic surgery." Clinical trial (n=45 patients) conducted in China – Report on file.

[8] Pagella F., et al., "Endoscopic surgical treatment of epistaxis in hereditary haemorrhagic telangiectasia: our experience." Acta Otorhinolaryngologica Italica.2021;41:59-68.

[9] von Ahnen T., et al., "Comparison of an intraoperative application of a haemostatic agent (PerClot) with conventional haemostatic procedure after thyroid resection." Surgical Science.2015;6:239-246.

[10] Janczak D., et al., "Modern topical hemostatic agents–a breakthrough in vascular surgery" 26 Polim. Med. 2013, 43, 4, 221–225.

[11] Tscholl V., et al., "Prospective randomized study evaluating the effects of PerClot (Polysaccharide Hemostatic System) application in patients with high bleeding risk undergoing cardiac rhythm device implantation." International Journal of Cardiology.2017;248:84-91.

[12] Rao K., et al. "Use of PerClot in head and neck surgery: a Scottish centre experience." European Archives of Oto-Rhino-Laryngology.2021;278:1965-1969.

[13] Duran J., et al., "Comparative study of different means of hemostasia from the liver bed in the course of cholecystectomies complicated laparoscopic." Seclaendosurgery.com (2016), #50

http://www.seclaendosurgery.com/secla/index.php?option=com_content & view = article & id = 645 & Itemid = 543 ISSN: 1698-4412.

[14] Puchkov K.V. and Estratov R.M., "Methods of treatment of the stump of the adrenal gland." Surgical Practice.2016;2:5-10.

[15] Malik M., et al., "Routine postoperative management of blepharoplasty: a review of current evidence-based practice." Facial Plastic Surgery.2021:epub.

[16] Aktas E., et al., "Polysaccharide hemostatic system reduces blood loss in high-body-mass-index patients undergoing simultaneous bilateral total knee arthroplasty." J Orthop Sci (2012) 17:432-436.