SeraSeal
Clinical Evaluation Report

General Information

Trade name:	SeraSeal
Generic name:	Surgical plant polysaccharide haemostatic agent (GMDN 38771)
Type:	Topical hemostatic sealant, single component
Model:	4003
Execution version:	14/4/2020
Manufacture:	Wortham Laboratories, Inc. 6340 Bonny Oaks Dr Chattanooga, TN 37416

Description of the assessed medical device and its intended use

Description (Ref: SeraSeal Technical File: Section A1, Page 11-15)

Composition: agar, bovine Factor IIa, VIIa, IXa, Xa, and Betadine – bound to the bovine proteins as a stabilizer with no free iodine in solution.

SeraSeal is a sterile, single use topical hemostatic agent, intended for invasive and noninvasive bleeding wounds, and can be applied to all tissues of the body. SeraSeal is removed by irrigation/suction 1-2 minutes after hemostasis has occurred.

Agar, the complex sugar in SeraSeal, when added to a bleeding wound, will cross-link with the ions of platelet phosholipds, and cations from amine groups in fibrinogen/fibrin monomers and tissue proteins, forming an α-1,6-linked galactophospho and α-1,6-galactoamine forming a gelatin barrier over the wound. This barrier reduces blood from escaping through the opening of the wound, allowing the patient's cascade system to form a fibrin clot sooner. The Factors IIa, VIIa, IXa, and Xa, function in an ancillary way, by facilitating the agar to cross-link with the platelets and fibrinogen, lending strength to the gelatin barrier, and by biologically facilitating only the blood outside of the wound, which has already been activated by tissue thromboplastin from platelets and damaged cells due to trauma, to assist in forming a clot. The clotting cascade is a biological activity system, and the clotting factors in the product are participating in this biological activity as a catalyst to form a fibrin clot. Further, platelets do an internal surface translocation, where more phospholipids are available to cross-link with agar, and covalent lysine to glutamine linkages between gama chains of adjacent fibrin molecules and between adjacent alpha chains create clot stabilization.

Intended therapeutic indications and claims

SeraSeal was used in a gynecological clinical case to treat a patient with a 29 cm x 45 cm tumor, in a myomectomy procedure, at the public health facility ISSSTE in Mexico. A 3 ml vial of SeraSeal was used in place of cauterization, to control all bleeding throughout the procedure. As a result, the patient's blood loss was reduced by 75%.

Context of clinical evaluation and choice of clinical data types

SeraSeal was developed as a primary hemostatic agent to control severe to life-threatening hemorrhages in a broad range of tissues. Tumors are highly vascularized and known for large blood loss. When the Department of Gynecology reviewed their standard myomectomy clinical cases on the volume of blood loss, SeraSeal demonstrated to be superior to cauterization to control bleeding. By avoiding cauterization, SeraSeal does not damage the uterine tissue, preventing adhesions, known as Ashermon's syndrome. Adhesions adhere to the uterus and cause menstrual difficulties or fertility problems in the future.

Essential Requirements Medical Device Directive 93/42/EED – Annex 1:

- No. 7.4: Medical devices that contain medicinal substance.
- No. 8.2: Tissues of animal origin must originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissue.
- No. 9.1: If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system must be safe and must not impair the specified performances of the devices. Any restrictions on the use must be indicated on the label or in the instructions for use.
- No. 13.6 (c): If the device must be installed with or connected to other medical devices or equipment in order to operate as required for its intended purpose, sufficient details of the characteristics to identify the correct devices or equipment to use in order to obtain a safe combination.
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Summary of the clinical data and appraisal

Blood loss in an abdominal myomectomy, SeraSeal was evaluated against cauterization, tourniquet, and Vassopressin, as a hemostatic agent. There was a 76%, 68%, and 58% reduction of blood loss, respectively.

SeraSeal was used in place of cauterization throughout the surgical procedure, successfully controlling all hemorrhages, and demonstrating SeraSeal as a primary hemostatic agent.

Due to the size of the fibroid tumor and its high vascularization, blood transfusion was not required.

By avoiding cauterization, the patient may potentially avoid future menstrual difficulties or fertility problems.

Publications:

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Technical File – Cross Reference

Section Part B8: Clinical Investigations, pages 569-808.

Data analysis

Performance

The statistical analyses were performed using Student's unpaired t-test. Continuous variables were reported as mean ± standard deviation (SD). Categorical variables were reported as number and percentage of patients.

Parameters	**SeraSeal n = 1**	**Cauterization n = 24**	**Tourniquet n =24**	**Vasopressin n = 24**
Blood loss (ml)				

Range	140 – 160	200 – 800	370 -560	300 - 520
Mean	50 ± 10	630 ± 392.42	467.9 ± 74.5	356.5 ± 58.36
Blood transfusion requirement				
No transfusion	1 (100%)	16 (66.67%)	19 (79.17%)	22 (91.67%)
One unit whole blood	0 (0.00%)	8 (33.33%)	5 (20.83%)	2 (8.33%)

Safety

There were no adverse events during the application of SeraSeal, including throughout the 30-day evaluation period.

Product Literature and Instructions for Use

The product literature and Instructions for Use are consistent with the clinical data and cover all the hazards and other clinically relevant information that may impact on the use of SeraSeal.

Appraisal Plan

The appraisal plan consisted of an assessment of the methodological quality of the clinical study, and a clinical evaluation method of appraisal.

Assessing the methodological quality used six questions:

- Was the study original?
- Whom is the study about?
- Was the design of the study sensible?
- Was systematic bias avoided or minimized?
- Was assessment "blind"?
- Were preliminary statistical questions dealt with?

Method used to appraise and weight clinical data:

Table 1: Appraisal Criteria for Suitability

Suitability Criteria	Description	Grading System
Appropriate device	**Was the data generated from the device in question?**	**D1 Actual device** **D2 Comparable device** **D3 Other device**
Appropriate device application	**Was the device used for the**	**A1 Same use**

	same intended use (e.g., methods of deployment, application, etc.)?	**A2 Minor deviation** **A3 Major deviation**
Appropriate patient group	**Was the data generated from a patient group that is representative of the intended treatment population (e.g., age, sex, etc.) and clinical condition (i.e., disease, including state and severity)?**	**P1 Application** **P2 Limited** **P3 Different population**
Acceptable report/data	**Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?**	**R1 High quality** **R2 minor deficiencies** **R3 Insufficient information**

Table 2: Appraisal Criteria for Data Contribution

Data Contribution Criteria	Description	Grading System
Data source type	**Was the design of the study appropriate?**	**T1 Yes** **T2 No**
Outcome measures	**Do the outcome measures reported reflect the intended performance of the device?**	**O1 Yes** **O2 No**
Follow up	**Is the duration of follow-up long enough to assess whether duration of treatment effects and identifies complications?**	**F1 Yes** **F2 No**
Statistical significance	**Has a statistical analysis of the data been provided and is it appropriate?**	**S1 Yes** **S2 No**
Clinical significance	**Was the magnitude of the treatment effect observed clinically significant?**	**C1 Yes** **C2 No**

Assessing the methodological quality

Was the study original?
SeraSeal was compared to cauterization and other hemostatic methods: tourniquet and Vassopressin.
The numerical result adds to the meta-analysis of previous studies.
The population of the study was similar in ages, sex, and ethnic groups.

Whom is the study about?
Only subjects undergoing a myomectomy procedure to remove a fibroid tumor(s).
Subjects with underlying morbidity issues were included.
All subjects were admitted to the hospital for active vaginal bleeding.

Was the design of the study sensible?
The surgeon in this study routinely uses cauterization as a primary method to control bleeding, as well as alternative secondary methods: tourniquet and Vassopressin.

What was measured?
Blood loss and blood transfusion requirements were measured.

Was systematic bias avoided or minimized?

Bias was avoided by reviewing historical myomectomy surgical cases that used cauterization, tourniquet, and Vassopressin to control bleeding.

Was assessment "blind"?
The assessment of the study was blinded by withholding review of historical cases until SeraSeal was evaluated.

Were preliminary statistical questions dealt with?
Sample size: SeraSeal – Sufficient for the size and number of blood vessels of the tumor
Cauterization - The number of patients was significant
Tourniquet – The number of patients was significant
Vassopressin – The number of patients was significant

Duration of follow-up: Adequate = 30 days
Completeness of follow-up: • Incorrect entry: no
- **Suspected adverse reaction: no**
- **Loss of patient motivation: no**
- **Withdrawal by clinician for clinical reasons: no**
- **Loss to follow up (patient moves): no**
- **Death: no**

Appraise and weight of the clinical data

The appraisal of both the suitability and contribution datasets demonstrated a level 1evaluation in an overall performance and safety of SeraSeal.

Conclusions

The data from this clinical case study clearly demonstrated SeraSeal's composition to be an effective and safe primary hemostatic agent, an alternative to cauterization.

The risks identified in the risk management documentation have been addressed by the clinical data.

It is proposed that SeraSeal be used to treat gynecological active bleeding. The clinical evidence demonstrates conformity with relevant Essential Requirements, the performance and safety of SeraSeal, as claimed, and the risks associated with the use of SeraSeal are acceptable when weighed against the benefits to the patient.

Leon Wortham

4/14/2020
Date