

SEP 8 1998

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K982865

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510(k) Summary of Safety and Effectiveness

1. General Information

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Device Generic Name: Bioabsorbable GTR Barrier Kit (used to form a Bioabsorbable GTR Barrier)

Device Trade Name: ATRISORB® Bioabsorbable Guided Tissue Regeneration (GTR) Barrier Kit (used to form an ATRISORB® Bioabsorbable GTR Barrier)

510(k) Clearance Number for Unmodified Device: K955838

510(k) Clearance Number for Modified Device: K _____

Date Prepared: July 1, 1998

Predicate Device: GORE-TEX® Periodontal Material

1. Description

1.1. Formulation

The ATRISORB® polymer formulation is a sterile, synthetic flowable polymeric formulation which is bioabsorbable and has been developed for GTR procedures by Atrix Laboratories, Inc. It consists of a polymer of lactic acid, poly(DL-lactide) (PLA), dissolved in *N*-methyl-2-pyrrolidone (NMP).

2.2. Device

The finished device is provided in two different packaging configurations. The first configuration is the ATRISORB® GTR Barrier Kit (case kit) used to form either with the barrier-forming case (extraoral) or by direct application over bone grafting material. The second configuration is the ATRISORB® GTR Barrier multipack (multipack) used only for the direct application technique.

The ATRISORB® GTR Barrier Kit configuration contains a foil-pouched, single-patient use dose pack containing 0.5 g of ATRISORB® polymer formulation, a pouched tray that contains a barrier forming case and three units of 0.9% sodium chloride solution (pH range 3.5 - 6.0), and an instructions for use booklet.

The barrier forming case has two sections of porous pads held in the cavities of the case and two spacers that are loose in the case. A label with a 1 mm grid pattern is affixed to the underside of the case. This grid is visible through the case and allows an area on the inside of the case to be used for trimming the formed barrier

The ATRISORB® GTR Barrier multipack configuration consists of three foil-pouched, single patient use dose packs containing 0.5 g of the ATRISORB® polymer formulation, three 18 gauge cannulae, and an instructions for use booklet.

3. Mechanics

The ATRISORB® GTR barrier functions as a guided tissue regeneration barrier by isolating the regenerative surgical site from the adjacent gingival connective tissue and epithelium. This facilitates population of the surgical site with cells from the periodontal ligament and adjacent alveolar bone that lead to regeneration.

The ATRISORB® polymer formulation is a flowable solution. A preformed GTR barrier, with consistent thickness, is prepared by using a barrier forming kit. The flowable formulation partially precipitates when it is "sandwiched" between two porous pads which are wetted with sodium chloride solution contained in a barrier forming case. The barrier thickness is determined by the thickness of the spacers which hold the two porous pads apart. The barrier, which is prepared in approximately three to six minutes, can be trimmed to the required size and morphology of the defect. The formed ATRISORB® GTR barrier is applied to the defect.

Another method of forming the barrier can be accomplished in situ where the tissue fluid aids in the precipitation of the barrier at the defect site. For defects where bone replacement graft material has been applied, the flowable formulation can be applied directly over the grafting material. Extraoral formation (formed in the case) is required when grafting materials are not used, as the unprecipitated formulation would flow into the defect.

With either method of application, the formed barrier is a film which covers the defect. Once in place, it continues to solidify and the resulting barrier precludes the migration of epithelial or connective tissue cells through it, and simultaneously isolates the periodontal compartment, thereby facilitating regeneration. The chemistry of the ATRISORB® polymer formulation is such that, after setting, the polymer component subsequently bioabsorbs through the process of hydrolysis. Bioabsorption occurs over the course of several months. The barrier is present and intact during the critical period when periodontal regenerative cells are proliferating during the wound healing cascade from adjacent periodontal sources.

4. Intended Use

The clinical indications for the ATRISORB® GTR Barrier are for GTR procedures in the surgical treatment of Class II furcations, or 2 and/or 3 walled intra-osseous defects and dehiscence defects to aid in the regeneration and integration of periodontal tissue components.

The indications for the ATRISORB® GTR barrier are equivalent to the indications for the predicate device, expanded polytetrafluoroethylene (e-PTFE) GORE-TEX® Periodontal Material (W.L. Gore & Assoc., Flagstaff, AZ).

The indications that differ are for bioabsorbability and elimination of a second surgical procedure to remove a non-bioabsorbable material. Results of preclinical and clinical trials support the claim of bioabsorbability and good tissue compatibility.

The predicate device, GORE-TEX® Periodontal Material, is indicated as an implantable material to aid in the healing of periodontal defects. The GORE-TEX® Periodontal Material is non-bioabsorbable and requires a second surgical procedure to remove it.

5. Summary of In Vitro Studies

5.1. Cytotoxicity

The study evaluated the toxic effects of the ATRISORB® GTR barrier upon mature monolayer tissue cultures of L929 cells. The ATRISORB® GTR barrier is mildly cytotoxic; however, these results are not consistent with results from more meaningful, in vivo implantation and clinical studies on the barrier.

5.2. Sensitization

A guinea pig maximization test, based on the method of Magnusson and Kligman (1970), was used to evaluate the potential of the ATRISORB® polymer formulation to elicit delayed dermal contact sensitization. The ATRISORB® polymer formulation is not a skin sensitizer.

5.3. Genotoxicity

The study evaluated the mutagenicity of an extract of the ATRISORB® polymer formulation. The ATRISORB® polymer formulation is not mutagenic.

5.4. Pyrogenicity - *Limulus* Amebocyte Lysate Test (LAL)

The LAL test estimated the concentration of bacterial endotoxins in an extract of the ATRISORB® GTR barrier. The ATRISORB® GTR barrier is non-pyrogenic according to this test method.

5.5. Hemolysis

The ATRISORB® GTR barrier causes hemolysis in an in vitro test system, but it is highly unlikely to cause hemolysis in patients treated with the barrier. The study evaluated the ATRISORB® GTR barrier's hemolytic potential using human blood in an in vitro system with limited buffering capacity. The barrier does not have significant contact with the blood path and the NMP concentrations in this assay may have been far greater than that which could be attained in the human body.

Based upon this analysis, the ATRISORB® GTR barrier's in vitro hemolytic activity does not represent a risk to patients treated with the barrier in accordance with the barrier's intended use.

5.6. Sterilization

The ATRISORB® GTR Barrier Kit and ATRISORB® GTR Barrier are terminally sterilized by Cobalt-60 gamma irradiation. The cannulae in the ATRISORB® GTR Barrier configuration are provided sterile by the manufacturer and are not further processed.

5.7. Bioburden

Bioburden determination is performed prior to sterilization following USP procedures.

6. Summary of In Vivo Implantation Studies

6.1. Subchronic Implantation

The study evaluated the biocompatibility of the ATRISORB® GTR barrier when surgically implanted subcutaneously in the rat. During the course of the study, no toxicity was observed around any of the test implantation sites which could be directly related to the barrier. No overt toxicity was observed in the rats during the course of the study.

The subcutaneous implantation of the ATRISORB® GTR barrier in rats for a period of ten days did not result in toxicity.

6.2. Chronic Implantation and Biodegradation

The study evaluated (1) the degradation kinetics of the ATRISORB® GTR barrier, and (2) response of tissue in contact with the barrier. The controls for the study were USP plastic strips. Histological examination of the test and control excised implant sites showed no signs of biologically significant changes or abnormal tissue. There was no significant difference between the ATRISORB® GTR barrier sites and control sites with respect to tissue effects.

The study demonstrated that the ATRISORB® GTR barrier does not elicit toxicity (dermal or systemic) when subcutaneously implanted in rabbits for up to twelve months and biodegradation of the ATRISORB® GTR barrier should be complete by 13-14 months.

7. Summary of Animal Efficacy Studies

7.1. Histology Study

This study compared the safety, clinical results, and histologic effects of ATRISORB® GTR barriers to sham operated controls in six adult beagle dogs with naturally occurring Class II periodontal furcation defects.

A periodontal surgeon selected and prepared 16 study sites as follows: a full thickness flap created after gingival incision was reflected, plaque and calculus were removed with ultrasonic devices, and roots planed by hand. Preformed ATRISORB® GTR barriers were applied to eight test sites, all study sites were closed and sutured. Post-surgery periodontal maintenance consisted of topical applications of Peridex® oral rinse to all study sites for two months, then the teeth were brushed using a modified Bass technique with brushes soaked in Peridex® oral rinse. Site integrity, clinical conditions, and toxicity were evaluated throughout the remainder of the study. All of the animals were sacrificed after six months of observation.

The ATRISORB® GTR barrier demonstrated clinically and statistically superior results in pocket depth, horizontal furcation depth, and improved attachment levels. The ATRISORB® GTR barrier significantly increased the

amount of periodontal regeneration (i.e., new bone, cementum, and periodontal ligament formation) in the furcation defect. No signs of toxicity were observed.

7.2. Biodegradation and Safety Study

The object of this study was to evaluate the potential for clinical application, clinical management, safety and biocompatibility of a biodegradable polymer barrier preformed in a barrier forming device to facilitate guided tissue regeneration at periodontal defects in the mandible and/or maxilla in the dog. Seven beagle dogs were used in the study and 17 naturally occurring defects were treated. Twelve periodontal furcation defects were treated surgically with ATRISORB® GTR barriers to determine if the barriers formed with three prototype kits compared favorably to 5 sham operated controls in terms of safety and biocompatibility.

The ATRISORB® GTR barrier was well tolerated in all periodontal test sites and produced no increases in localized inflammation compared to control sites.

Use of the ATRISORB® GTR barrier in treating periodontal defects in the dog resulted in no clinical or histological evidence of adverse healing and generally confirmed complete bioabsorption of the barrier by the end of one year.

Histological examination confirmed that barriers were completely absorbed at 12 months with the exception of one small spicule found in one out of twelve test sites.

7.3. Pilot Study

This study was a pilot study designed to examine four compositions of ATRISORB® polymer formulation used to prepare the ATRISORB® GTR barrier for potential to promote connective and/or bone tissue regeneration in the periodontal region.

Thirty-nine defects were treated in six beagle dogs. All dogs were terminated between 9 and 12 months following initial barrier placement. The study showed that new periodontal supporting tissues became reconstituted on root and furcation surfaces in surgically-induced and naturally-occurring periodontal defects after using the ATRISORB® GTR barrier.

7.4. Feasibility Study

The objective of this study was to evaluate the safety and potential of a synthetically formulated flowable polymer barrier to facilitate periodontal regeneration in naturally occurring and induced wound sites in the canine and

molar regions of dogs over a period of 3 months. Two dogs were used with a total of 16 sites (8 barrier sites and 8 control sites) being treated.

The results of this study demonstrated the potential safety and the ability of the synthetically formulated flowable polymers to facilitate periodontal tissue regeneration.

8. Summary of Pivotal Trial

A pivotal clinical trial under an FDA Investigational Device Exemption was conducted to evaluate the safety and efficacy of the ATRISORB® GTR Barrier Kit in a multicenter clinical trial.

The primary object of the study was to demonstrate that the ATRISORB® GTR barrier is substantially equivalent to GORE-TEX® periodontal material for guided tissue regeneration (GTR) treatment of Class II furcation defects in humans. The primary clinical end points were vertical and horizontal attachment level, with secondary clinical end points being pocket depth, bleeding on probing, gingival margin location, and gingival index.

The investigation was a multicenter study with a parallel design. Individuals with a Class II furcation defect were treated with either ATRISORB® GTR barrier or GORE-TEX® periodontal material according to a randomized treatment assignment. Outcomes of healing were evaluated at regular intervals up to one year after the regenerative procedure. Comparisons of clinical results between the two products were made in order to demonstrate substantial equivalency between the ATRISORB® GTR barrier and GORE-TEX® periodontal material in guided tissue regeneration treating Class II furcation defects.

One hundred sixty-two subjects were randomized and entered into this 52-week study; 82 subjects received the ATRISORB® GTR barrier and 80 subjects received GORE-TEX® periodontal material. Subjects were selected if they met the following entry criteria:

- A Class II furcation with vertical pocket depth \geq 5 mm and attachment loss at the site and the horizontal depth of the furcation was \geq 3 mm
- Between the ages of 25 and 75
- In good general health

Radiographs were taken within the two months prior to Screening or at the Screening or Baseline visit, and provided evidence of crestal alveolar bone loss associated with periodontitis.

The study demonstrated that ATRISORB® GTR barrier is substantially equivalent to the predicate device, GORE-TEX® periodontal material for the treatment of periodontal defects using guided tissue regeneration procedures.

The safety results over the 52-week duration of the study support the benign safety profile associated with the use of the ATRISORB® GTR barrier.

8.1. Summary of the Statistical Analysis of the Data from the Pivotal Clinical Trial

The following tabulation presents the data for ATRISORB® GTR barrier vs. GORE-TEX® periodontal material at Baseline and Week 52. Vertical attachment level gain significantly satisfied the condition of clinical equivalence between the two treatment groups at Week 52. The mean increase at Week 52 for subjects treated with ATRISORB® GTR barrier was 0.38 mm greater than the mean for subjects treated with GORE-TEX® periodontal material. The null hypothesis that GORE-TEX® periodontal material was clinically superior by at least 0.5 mm was rejected with a p-value of less than 0.001. The one-sided confidence interval for the difference between the ATRISORB® GTR barrier and the GORE-TEX® periodontal material indicates that any difference greater than 0.08 mm in favor of GORE-TEX® periodontal material can be ruled out with 95% confidence.

Horizontal attachment level gain significantly satisfied the condition of clinical equivalence between the two treatment groups at Week 52. The mean increase at Week 52 for subjects treated with ATRISORB® GTR barrier was slightly greater (0.04 mm) than the mean for subjects treated with GORE-TEX® periodontal material. The null hypothesis that GORE-TEX® periodontal material was clinically superior by at least 0.5 mm was rejected with a p-value of 0.017. The one-sided confidence interval for the difference in treatment effects indicates that any difference greater than 0.38 mm can be ruled out with 95% confidence.

Pocket depth improvement significantly satisfied the condition of clinical equivalence for the two treatment groups at Week 52. The mean decrease at Week 52 was 0.18 mm greater for ATRISORB® GTR barrier subjects than the mean decrease for subjects treated with GORE-TEX® periodontal material.

Mean Values for Periodontal Measurements										
Measurement	Time Point	ATRISORB® GTR Barrier			GORE-TEX® Periodontal Material			GORE-TEX® Periodontal Material Minus ATRISORB® GTR Barrier Difference	P-value*	One-sided* Confidence Interval
		N	Mean	S.E.	N	Mean	S.E.			
Vertical Attachment Level	Baseline**	76	5.82	0.21	73	5.74	0.20	-0.08	0.009	0.30
	Week 52	66	2.00	0.19	64	1.63	0.20	-0.38	<0.001	0.08
Horizontal Attachment Level	Baseline**	76	4.57	0.14	73	4.77	0.15	0.20	0.010	0.34
	Week 52	66	2.11	0.20	64	2.06	0.16	-0.04	0.017	0.38
Pocket Depth	Baseline**	76	5.55	0.11	73	5.55	0.10	-0.00	0.024	0.43
	Week 52	66	2.26	0.16	64	2.08	0.15	-0.18	0.001	0.19
Gingival Margin	Baseline**	76	-0.26	0.19	73	-0.19	0.19	0.07	<0.001	0.15
	Week 52	66	-0.26	0.15	64	-0.45	0.18	-0.20	0.002	0.20
Bleeding on Probing	Baseline**	76	1.34	0.09	72	1.17	0.09	-0.18	<0.001	0.12
	Week 52	66	0.85	0.14	64	0.81	0.11	-0.04	0.001	0.25
Plaque Index	Baseline**	76	0.68	0.08	73	0.84	0.09	0.15	0.015	0.42
	Week 52	66	0.15	0.12	64	0.30	0.12	0.15	0.018	0.42
Gingival Index	Baseline**	76	1.32	0.08	72	1.19	0.08	-0.12	<0.001	0.10
	Week 52	66	0.48	0.13	63	0.38	0.11	-0.10	<0.001	0.17

Note: Null hypothesis for p-value calculation: Difference between treatment means \leq 0.5 mm
 *p-values and confidence intervals calculated from one-sided t-distribution
 †All means and standard errors are raw means and standard errors

Gingival margin recession significantly satisfied the condition of clinical equivalence for the two treatment groups at all time points. The mean increase at Week 52 for subjects treated with ATRISORB® GTR barrier was 0.2 mm less than the mean increase for subjects treated with GORE-TEX® periodontal material.

Bleeding on probing score significantly satisfied the condition of clinical equivalence for the two treatment groups at all time points. The mean change at Week 52 for subjects treated with ATRISORB® GTR barrier was slightly greater (0.04 mm - 0.06 mm) than the mean change for subjects treated with GORE-TEX® periodontal material.

Gingival index score significantly satisfied the condition of clinical equivalence for the two treatment groups at all time points. The mean change at Week 52 for subjects treated with ATRISORB® GTR barrier was slightly greater (0.07 - 0.10) than the mean change for subjects treated with GORE-TEX® periodontal material.

Plaque index score significantly satisfied the condition of clinical equivalence for the two treatment groups at all time points. The mean change at Week 52 for subjects treated with ATRISORB® GTR barrier was 0.15 less than the mean change for subjects treated with GORE-TEX® periodontal material.

8.2. Postoperative Complications

Postoperative symptoms or complications that were reported were those commonly associated with oral or periodontal surgical procedures, such as intra oral swelling and pain which usually resolved spontaneously without treatment or in some cases the clinician prescribed antibiotics. These events occurred in both test and control treatments.

There were no sensitivity reactions or immune responses associated with the use of the ATRISORB® GTR barrier.

9. Direct Application

Case studies were conducted with the direct application of the barrier over bone grafting material. Eighteen subjects with a total of twenty-two periodontal defects of varying complexity were treated and it was determined that the material was suitable for the intended periodontal purpose as determined by clinical measurements and re-entry surgeries. These cases were followed and no adverse sequela were observed. These data demonstrate that the direct application of the ATRISORB® GTR Barrier has clinical utility and is a suitable alternative to forming the barrier in the precipitation case.

10. Conclusions

The claims for the ATRISORB® GTR Barrier Kit and the ATRISORB® GTR Barrier are equivalent to the claims for the predicate device, GORE-TEX® Periodontal Material. Additional claims for the ATRISORB® GTR Barrier are for bioabsorbability and elimination of a second surgical procedure to remove the non-bioabsorbable GORE-TEX® Periodontal Material. The features of the ATRISORB® GTR Barrier compared to the GORE-TEX® Periodontal Material are described below.

Human clinical trials have demonstrated that the ATRISORB® GTR Barrier is equivalent to the non-bioabsorbable GORE-TEX® Periodontal Material as an implantable material intended to aid in the healing of periodontal defects.

The ATRISORB® GTR Barrier is bioabsorbed, eliminating the need for a second surgical procedure such as that required to remove the non-bioabsorbable membrane, GORE-TEX® Periodontal Material.

Preclinical and clinical trial studies have demonstrated the ATRISORB® GTR Barrier to be safe and effective in the treatment of periodontal defects when formed either using the barrier forming case or the direct application technique.

The ATRISORB® GTR Barrier is non-pyrogenic and is biocompatible.

In vitro, animal, and clinical studies have demonstrated that the ATRISORB® GTR Barrier is safe and effective for its stated indications and is substantially equivalent to the predicate device, GORE-TEX® Periodontal Material.



OCT 10 2007

Food and Drug Administration
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Elyse Wolff, MT (ASCP)
Regulatory Project Leader
Atrix Laboratories, Incorporated
2579 Midpoint Drive
Fort Collins, Colorado 80525-4417

Re: K982865
Trade Name: ATRISORB® Bioabsorbable Guided Tissue
Regeneration (GTR) Barrier
Regulation Number: 872.3930
Regulation Name: Bone Grafting Material
Regulatory Class: 2
Product Code: NPK
Dated: July 1, 1998
Received: August 13, 1998

Dear Ms. Wolff:

This letter corrects our substantially equivalent letter of September 8, 1998.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

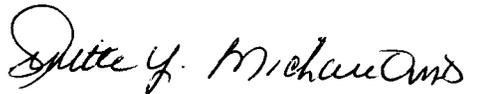
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to continue marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0115. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>

Sincerely yours,



Chiu Lin, Ph.D.

Director

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Infection Control and Dental Devices

Office of Device Evaluation

Center for Devices and

Radiological Health



Protecting and Promoting Public Health

K982865

510(k) Number (if known): ~~K955838~~ (Unmodified Device)

Device Name: ATRISORB® GTR Barrier

Indications For Use:

ATRISORB® GTR Barrier is indicated for the surgical treatment of periodontal defects to aid in the regeneration and integration of tissue components in guided tissue regeneration procedures. ATRISORB® GTR Barrier is not intended for use in defects outside the indications statement.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Susan Runge

(Division Sign-Off)
Division of Dental, Infection Control,
and General Hospital Devices

510(k) Number K982865

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use

