Labeling for PepGen P-15

CAUTION - Federal law (USA) restricts this device to sale by or on the order of a licensed physician or dentist.

DESCRIPTION

PepGen P-15™ is bovine derived hydroxylapatite, which contains P-15, a synthetic peptide. Hydroxylapatite is the major mineral component of tooth enamel and bone. P-15 is a synthetic short chain peptide, a biomimetic of a cell binding region of Type I collagen. PepGen P-15 is manufactured as radiopaque, rounded particles sized between 250 and 420 microns.

INDICATIONS - PepGen P-15 particles are intended to be used for the treatment of intrabony periodontal osseous defects due to moderate or severe periodontitis.

CONTRAINDICATIONS – None known.

WARNINGS
To prevent cross contamination or transmission of infectious agents, DO NOT INSERT SYRINGE THAT HAS CONTACTED BODY FLUIDS OR OTHER CONTAMINANTS INTO VIAL/SYRINGE CONNECTOR. DO NOT EXPRESS PEPGEN P-15 PARTICLES FROM SYRINGE BACK INTO VIAL.

Use of PepGen P-15 has not been evaluated in early onset periodontitis (such as juvenile periodontitis), uncontrolled diabetes, or other uncontrolled systemic diseases, disorders or treatments or other immunosuppressive therapy, and infection or vascular impairment at the surgical site.

PepGen P-15 particles should be implanted only by dental and medical practitioners familiar with bone graft techniques. The particle size of PepGen P-15 particles should not be altered.

PRECAUTIONS

1. DO NOT USE if sterile package is opened or damaged. To prevent possible cross contamination, discard or return damaged package and the enclosed device.

2. Syringes and filler caps are single use items. Do not resterilize or reuse syringe or filler caps.

3. The safety and effectiveness of PepGen P-15 around endosseous dental implants has not been studied.

ADVERSE REACTIONS - In the multicenter PepGen P-15 clinical trial (31 patients), no instances of any tissue reaction, inflammation, particle migration or loss with the grafts, or other local reactions were observed in the one-year post-operative period.

The following complications have been reported in the literature with regard to periodontal surgical grafting procedures: implant migration, particle extrusion, wound dehiscence, loss of vestibular depth, sterile abscess, infection, and varying levels of mental nerve anesthesia including permanent paresthesia or anesthesia.

CLINICAL STUDY RESULTS

Two clinical studies were conducted to evaluate PepGen P-15. Both studies used the same inclusion and exclusion criteria, as well as the same surgical procedures.

A multicenter (3 sites) randomly controlled clinical trial in humans having moderate or severe periodontitis, and treatment planned for reconstructive periodontal surgery, were used to compare 3 treatments in a same mouth design. Thirty one patients, with a mean age of 51.5 (range 37 – 76), were studied. There were 16 males and 15 females. Each patient served as his or her own control. PepGen P-15 was compared to a positive control, decalcified freeze dried bone allograft (DFDBA), and open surgical debridement, a negative control. At a 6-7 month re-entry and follow-up soft tissue measurements was made. Thirty of these patients were reevaluated at 12 months. Analysis compared measurements of defect repair, percentage of defect repair; and measurement of crestal change, gingival recession, attachment level change, and probing depth.

A second clinical study was undertaken to evaluate clinical utility or usefulness of adding P-15 peptide to OsteoGraf N-300 to create PepGen P-15. Thirty three, including twelve male and twenty one female patients, with a mean age of 48.7 years (range of 38 – 81 years), were studied. Clinical comparisons were made of PepGen P-15 and OsteoGraf N-300. This study demonstrated statistically significant improvement in percent defect fill, when using PepGen P-15 as compared to OsteoGraf N-300.

TABLE 1
Clinical Study #1
Defect Results

	PepGen P-15 (a)	DFDBA (b)	DEBR (c)	P*
Original Defect	3.6 mm	4.0 mm	3.8 mm	
Residual Defect	0.7 mm	1.5 mm	1.3 mm	a/b, a/c
Amount Defect Fill	2.8 mm	2.0 mm	1.5 mm	a/b, a/c
% Defect Fill	72.3%	51.5%	40.3%	a/b, a/c
Crestal resorption	0.1 mm	0.5 mm	1.0 mm	a/c, b/c
%Defect Resolved	79.9%	64.6%	66.0%	a/b, a/c

(a) PepGen P-15 was formerly known as OsteoGraf CS-300.
(b) DFDBA = decalcified freeze dried bone allograft
(c) DEBR = defect debridement (no graft material)
P* indicates that when comparing data in column a compared to data in column b, data in column b compared to column c, or data in column a compared to column c, a Parametric one way ANOVA with Student Neuman-Keuls and nonparametric Kruskall-Wallis ANOVA by Ranks with Dunn's post-test used for analysis, indicated statistical significance.

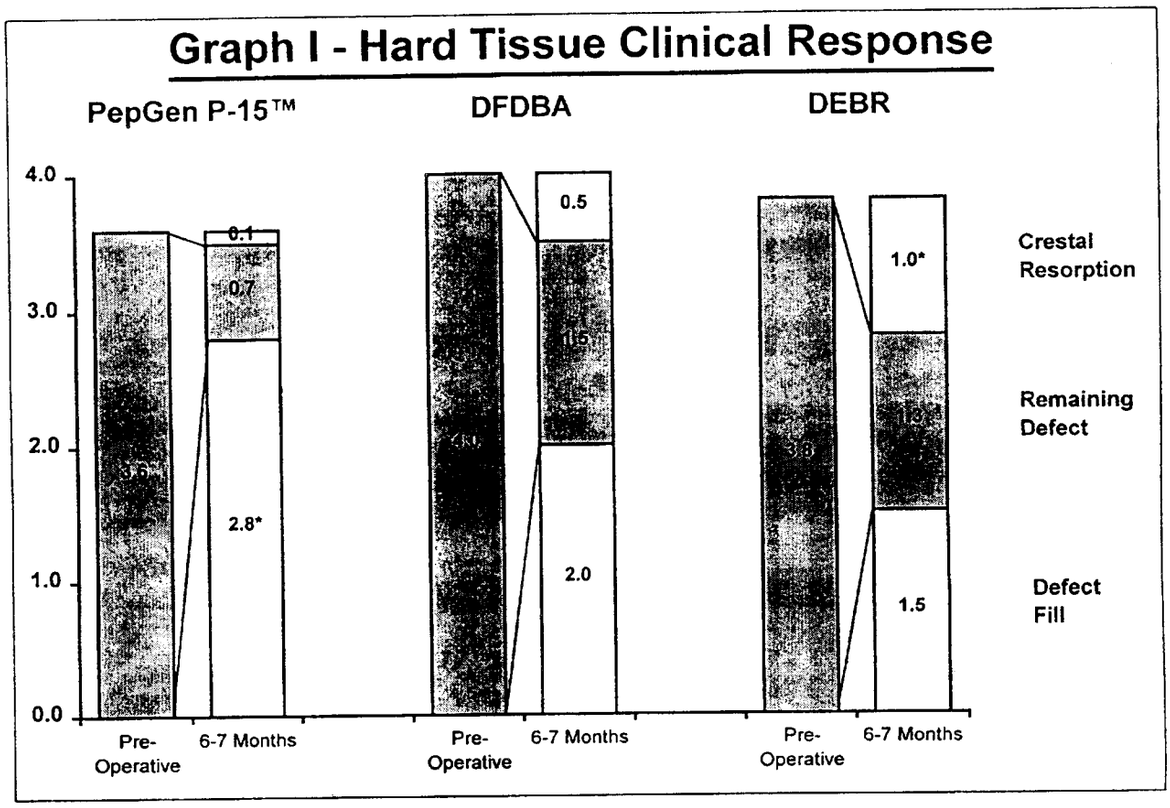
TABLE 2
Clinical Study #1
Cases Demonstrating "Positive Results" with Respect to Defect Fill

Treatment		≥90%	≥50%	<50%	<20%	% Successful*
PepGen P-15	Number	9	18	4	0	87%
	Percent	29	58	13	0	
DFDBA	Number	5	13	4	9	58%
	Percent	16	42	13	29	
DEBR	Number	2	11	10	8	41%
	Percent	6	35	32	26	

DFDBA = decalcified freeze dried bone allograft
DEBR = defect debridement (no graft material)
Positive results are defined as the percentage of cases with greater than 50% defect fill. Successful* outcomes were defined as the percentage of patients having "positive results".

Table 2 demonstrates the percentage of patients in the study having a positive, or greater than 50% defect fill, with respect to the three treatment modalities studied. While the benchmark bone filling material, DFDBA, was successful 58 percent of the time, PepGen P-15 was successful 87% of the time. PepGen P-15 appears to be providing an incremental improvement in grafting success over the benchmark grafting material.

Graphs 1 and 2 are representations of results obtained form Study #1. Osseous response to PepGen P-15 is demonstrated in Graph 1, and soft tissue response is demonstrated in table 2.

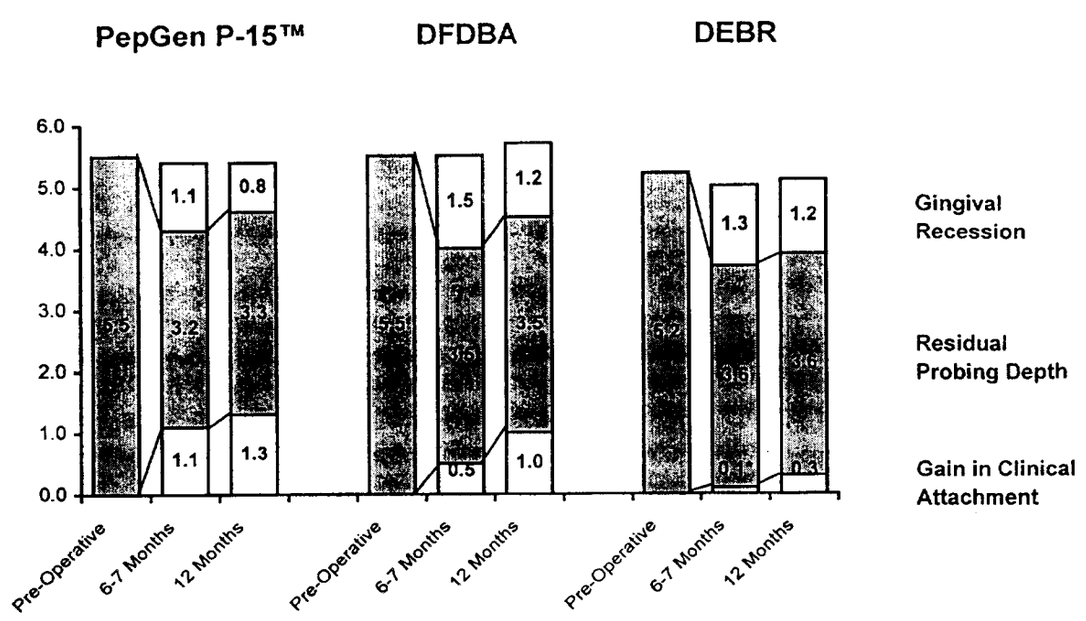


2.8* at 6 – 7 months represents a statistically significantly greater percent defect fill.
1.0* at 6 – 7 months represents a statistically significantly increased amount of crestal resorption.

Graph 1 shows the amounts of crestal resorption, defect fill, and the amount of defect remaining after each treatment. Crestal resorption and the amount of defect remaining reflect the success of each treatment modality. They are not reflected in pocket probing depth measurements or in probing attachment level, which have a soft tissue component.

Graph 2, below take into consideration the soft tissue component of the response to periodontal bone grafting modalities. Gingival recession was not significantly different among the treatments studied, but DFDBA and PepGen P-15 demonstrated statistically significantly more original defect fill as compared to open debridement alone.

Graph II - Soft Tissue Clinical Response



0.1*at 6 – 7 months represents a statistically significantly less gain in clinical attachment than either DFDBA or PepGen P-15.

DIRECTIONS FOR USE

PREPARING PepGen P-15 PARTICLES FOR USE

PepGen P-15 particles are supplied in sterile vials. Unfilled OsteoGraf syringes are supplied separately. In all operations involving PepGen P-15 particles, appropriate aseptic technique must be observed.

Precaution: DO NOT USE IF STERILE PACKAGE IS OPENED OR DAMAGED.
Discard or return damaged package and the enclosed device.

Vial Package without Syringe

Remove vial from sterile package using sterile technique. Dispense desired quantity of PepGen P-15 particles into sterile dish. PepGen P-15 particles should be wetted with sterile saline or sterile water to facilitate delivery to the surgical site, using conventional instruments such as curettes or plastic amalgam carriers.

Vial Package With Syringe

Remove vial (with its vial/syringe connector) and syringe from sterile package using sterile technique. Retract syringe plunger. Remove cap from vial/syringe connector and insert syringe barrel into connector. Transfer desired amount of PepGen P-15 particles to syringe and disconnect syringe from vial. Place filter cap onto syringe barrel. To facilitate delivery, PepGen P-15

particles should be wetted. Draw sterile saline or sterile water up through filter cap until liquid level is slightly above level of PepGen P-15 particles. Expel excess liquid by depressing plunger lightly. Do not compact PepGen P-15 particles or jamming may result when delivery is attempted. When wetted, the PepGen P-15 particles are easily expelled from the syringe. Prepare a sufficient number of syringes in advance to minimize delay of the surgical procedure. Do not reload syringes.

PRECAUTION: Syringes and filter caps are designed for single use only.
DO NOT RESRERILIZE OR REUSE SYRINGES OR FILTER CAPS.

Vial Autoclaving

PepGen P-15 particles remaining in vial may be autoclaved up to three times and used for subsequent procedures if the following procedures are followed:

1. Keep vial and cap clean at all times — **do not insert** syringe that has contacted body fluids or other contaminants into vial/syringe connector.
2. Keep contents of vial clean at all times — **do not express** PepGen P-15 particles from syringe back into vial.

Syringes and filter caps are designed for single use only. **DO NOT AUTOCLAVE OR REUSE SYRINGES OR FILTER CAPS.** To autoclave PepGen P-15:

- Remove cap from vial.
- Assure vial, cap, and contents are clean.
- Place vial and cap in paper autoclave bag.
- Steam autoclave at 121°C (250°F), saturated steam, for 30 minutes.
- Replace cap on vial while both are still in autoclave bag.

NOTE: To determine the efficacy of autoclaving, **the use of biological indicators is recommended.**

SURGICAL GUIDELINES

Preoperative Procedure

Dental and medical practitioners are responsible for treatment planning, proper patient preparation, surgical techniques, and postoperative care when using PepGen P-15 particles. The patient must be an acceptable surgical risk. Oral disease must be eliminated or under control before surgery. Examination and evaluation of the oral cavity are necessary to identify hard and soft tissue pathology and to plan the surgical procedure.

Operative Procedures

The surgical placement of PepGen P-15 is similar to osseous grafting procedures using other particulate materials. Recommended site preparation is to use conventional flap curettage techniques assuring that the site is completely debrided and the root surfaces are thoroughly planed and smoothed removing all calculus and necrotic cementum. The bone defect site should be irrigated with sterile saline or sterile water. Bleeding should be controlled to minimize loss of particles from the site.
Intramarrow penetration should be performed through the bony walls of the defect where needed to allow the egress of pluripotential marrow reticular cells.

Particle placement should be carried out by condensing the previously wetted PepGen P-15 into the defect with a plastic amalgam carrier, spatula, or other conventional instrument. Suctioning should be limited to the periphery of the site. Filling should not proceed beyond the top of the surrounding walls of bone to reduce the chances of particle migration and excessive tension on tissue flaps. Tissue flaps should be positioned back in place and secured with sutures with an objective of obtaining primary coverage of the defect. Placing a periodontal dressing is recommended to help reduce the chances of particle loss.

Postoperative Care

An appropriate analgesic, antibiotic, and home care regimen should be followed. Using appropriate surgical dressings while the soft tissues are healing can help prevent particle loss.