MATRIX

i=FACTOR®+

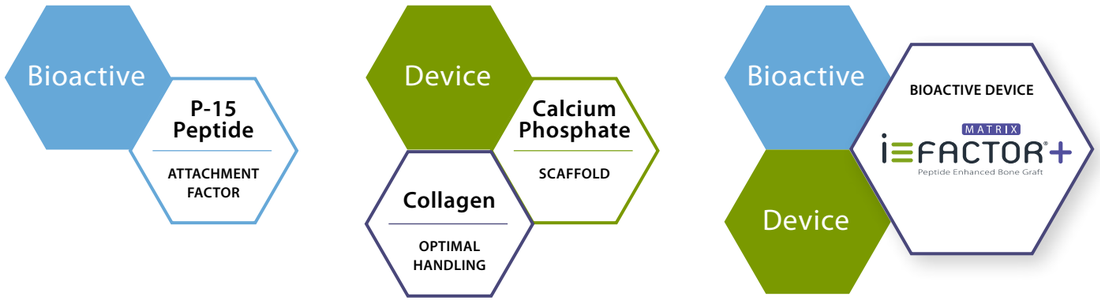
POWERED BY P15™ osteogenic cell binding peptide

THE BONE HEALING POWER OF P-15 OSTEOGENIC CELL BINDING PEPTIDE

CERAPEDICS

Enhancing the Science of Bone Repair

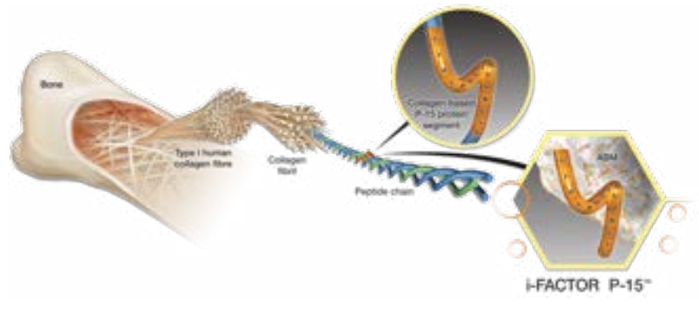
i-FACTOR+ MATRIX:
An Active Biologic which Utilizes P-15 Osteogenic Cell Binding Peptide



i-FACTOR+ MATRIX's Powerful Cell Attachment Capability: P-15 Peptide

i-FACTOR+ MATRIX technology is based on the biological activity of a 15 amino acid peptide naturally found in Type I human collagen.

This protein segment (P-15) is responsible for the attachment and proliferation of osteogenic cells. These cells bind to the synthetic P-15 found in i-FACTOR+ MATRIX.



i-FACTOR+ MATRIX has a Unique Mechanism of Action

i-FACTOR+ MATRIX increases the opportunity for cell binding in the fusion site by making an abundance of P-15 available to osteogenic cells. The ability of P-15 to enhance cell binding hastens the process of new bone formation and closely resembles the natural process of bone regeneration.[1,2,3,4]

ATTRACT

P-15 facilitates and expedites ingrowth of bone by promoting the immigration of reparative cells from the surrounding tissues.[2]

ATTACH

Cells have a high affinity for P-15. Once attached cells continue to organize the matrix via tractional forces. Cell attachment and migration is facilitated by a natural hepatotactic mechanism. [2,3,4]

ACTIVATE

P-15 enhances bone formation by facilitating cellular attachment with subsequent increase in cell binding, proliferation, and differentiation of cells increasing TGFβ-1, BMP-2, and BMP-7 levels that positively influence all processes of new bone formation.[5]

✓ i-FACTOR Putty, with P-15 Osteogenic Cell-Binding Peptide, has Level 1 Human Clinical Evidence

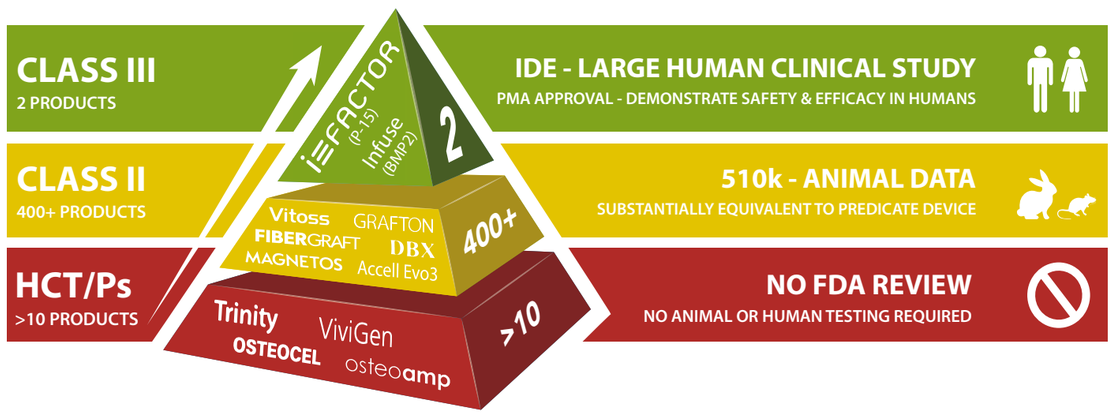
Physicians are encouraged to find the highest level of evidence to support the safe and effective use of a product in a clinical setting. i-FACTOR Putty, which contains P-15 osteogenic cell-binding peptide, has published Level 1 human clinical evidence. Our new i-FACTOR MATRIX product utilizes the same P-15 technology but combines this with a collagen matrix that provides optimal handling in the form of a flexible and moldable carrier. The majority of bone grafts on the market have much lower levels of evidence.

Level 1	Randomized controlled human clinical trial	Fewer High Level Studies (Increased Cost and Quality)
Level 2	Prospective cohort study	Number of Studies
Level 3	Retrospective cohort study	
Level 4	Case studies	
Level 5	Mechanism-based reasoning	
Level 6	Animal studies, in vitro studies	Many Low Level Studies (Lower Cost and Quality)

✓ Only 2 FDA Class III PMA Approved Spinal Bone Grafts

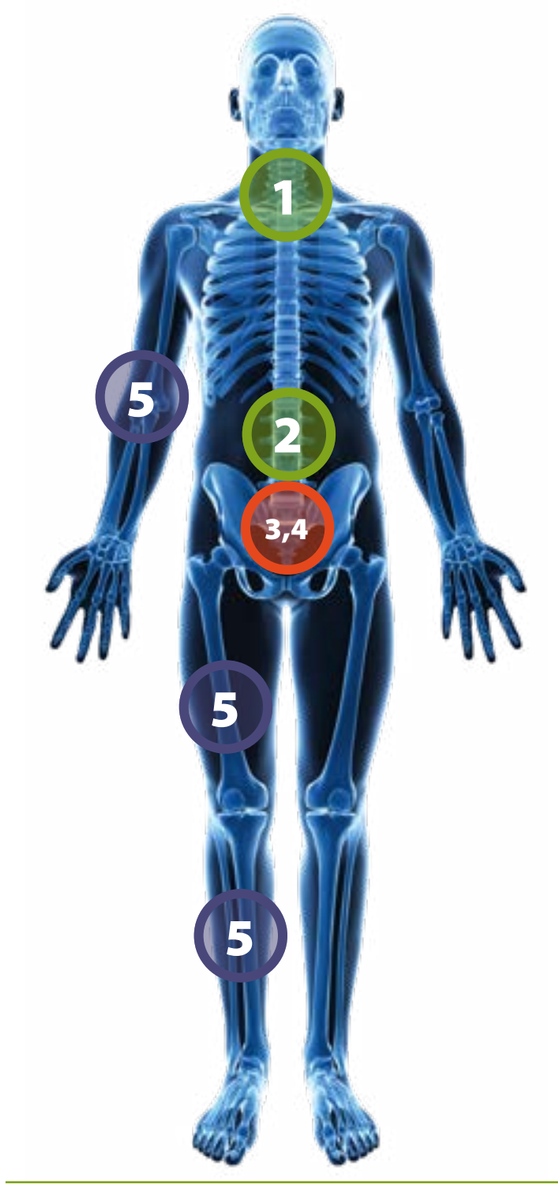
The FDA regulatory process is globally recognized by physicians due to its clear classification systems and stringent demand for quality data to support product claims. There are three FDA regulatory pathways for orthobiologics: Class III (PMA), Class II (510k), and HCT/P (tissue-based products). Class III devices have the most rigorous regulatory pathway to market requiring a PMA backed by Level 1 data from an Investigational Device Exemption (IDE) human clinical trial.

i-FACTOR+ MATRIX leverages the same P-15 based technology as found in our original i-FACTOR Putty product, which has met the most robust FDA study requirements and is one of only two Class III Drug-Device Combination bone grafts approved for the US spine market. The only other spinal bone graft in this category is Medtronic's InFuseTM (BMP-2). The majority of bone grafts on the market are cleared via the 510k pathway like VITOSS or meet no review under HCT/Ps like ViviGen and OsteoAmp.



The Clinically Proven Power of P-15: Osteogenic Cell Binding with i-FACTOR

The osteogenic cell binding power of P-15 has been proven in i-FACTOR Putty. The same P-15 technology is utilized in i-FACTOR+ MATRIX.



Spine

1 ACDF (n = 319)[6,7]
ACDF
- 319 patients
- *"i-FACTOR subjects demonstrated higher overall success rate than control (autograft) subjects (68.75% and 56.95% respectively, p = 0.0382)"*

2 PLF (n = 98)[8]
PLF
- *"This RCT indicates i-FACTOR being significantly superior to allografted bone in enhancing intertransverse fusion (p = 0.000)"*

3 ALIF (n = 110)[9]
ALIF
- 110 patients
- *"…high fusion rate and clinical improvements comparable to the published results for ALIF using autograft or BMP"*

4 PLIF (n = 40)[10]
PLIF
- 40 patients
- *"i-FACTOR is associated with faster formation of bridging bone when compared to autologous bone in patients undergoing PLIF"*

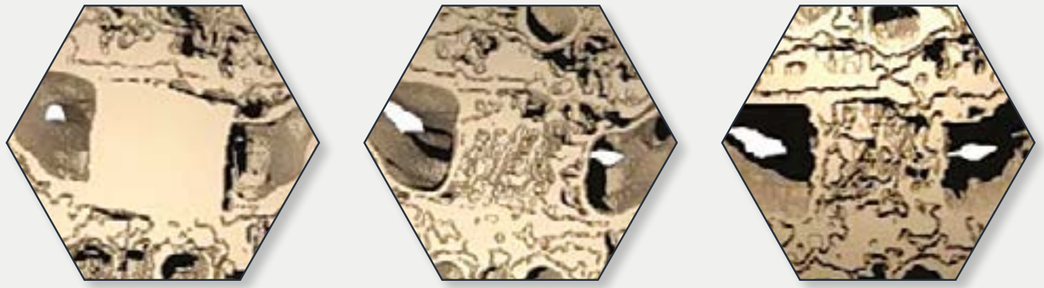
Orthopedics

NON-UNION[11]
5 Treatment of non-union and delayed union (n = 22)
- *"P-15 appears to offer a safe, economical, and clinically useful alternative to autograft in the repair of ununited fractures"*

Level 1 Prospective Study Published Case Series

Fusion Characteristics Similar to Mature and Healthy Bone

To evaluate the quality of bone within the interbody space, 3D CT imaging technology was taken from a patient following a single level ACDF. Detailed analysis determined that the porosity, trabecular orientation, and structure of new bone that P-15 developed was characteristic of mature and healthy normal bone within six months.[12]



Why Should I Choose i-FACTOR+ MATRIX?

i-FACTOR MATRIX uses the same P-15 based technology as i-FACTOR Putty but with the added advantage of:

- ✓ Optimized ABM particles through increased porosity and surface area
- ✓ Enhanced handling characteristics and graft site retention
- ✓ Adaptability to all spine and general orthopedic techniques

Indication

i-FACTOR+ MATRIX Bone Graft is intended to fill bony voids or gaps in extremities and spine that are not intrinsic to the stability of the bony structure. Sufficient internal or external fixation is required.

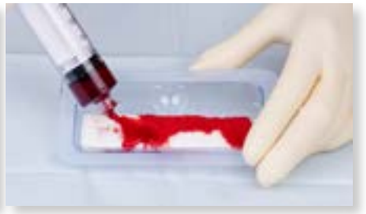
i-FACTOR+ MATRIX may be mixed with autogenous bone and/or autogenous bone marrow aspirate (BMA).

Available Sizes

MATRIX i-FACTOR+ Peptide Enhanced Bone Graft

PRODUCT CODE	PRODUCT DESCRIPTION	VOLUME
930-010	i-FACTOR MATRIX+	1.0cc
930-025	i-FACTOR MATRIX+	2.5cc
930-050	i-FACTOR MATRIX+	5.0cc
930-100	i-FACTOR MATRIX+	10.0cc

Cerapedics is an advanced orthobiologics company focused on developing and commercializing its proprietary small peptide (P-15) technology platform. i-FACTOR® Peptide Enhanced Bone Graft is the only biologic bone graft in orthopedics that incorporates P-15 osteogenic cell binding peptide to stimulate the natural bone healing process. This novel mechanism of action is designed to support safer and more predictable bone formation compared to commercially available bone growth factors.



References

1. Bhatnagar RS, Qian JJ, Wedrychowska A, Sadeghi M, Wu YM, Smith N. Design of biomimetic habitats for tissue engineering with P-15, a synthetic peptide analogue of collagen. Tissue Eng. 1999 Feb; 5(1)53-65
2. Qian JJ, Bhatnagar RS. Enhanced cell attachment to anorganic bone mineral in the presence of a synthetic peptide related to collagen. J Biomed Mater Res. 1996 Aug; 31(4):545-54
3. Guido S, Tranquillo RT. A Methodology for the Systematic and Quantitative Study of Cell Contact Guidance in Oriented Collagen Gels. Correlation of Fibroblast Orientation and Gel Birefringence. J Cell Sci. 1993; 105:317-331
4. Tranquillo RT, Durrani MA, Moon AG. Tissue Engineering Science: Consequences of Cell Traction Force. Cytotechnology. 1992; 10(3): 225-250
5. Guerra FA, Krauser JT, Cabrita AM. Small Peptide (P-15) Bone Substitute Efficacy in a Rabbit Cancellous Bone Model. ORS 2005 Annual Meeting, Poster #0212
6. Arnold PM, Sasso RC, Janssen ME, Fehlings MG, Smucker JD, Vaccaro AR, Heary RF, Patel AL, Goulet B, Kalfas IH, Kopjar B. Efficacy of i-FACTOR™ Bone Graft versus Autograft in Anterior Cervical Disectomy and Fusion. Results of the Prospective Randomized Single-blinded Food and Drug Administration Investigational Device Exemption Study. Spine. 2016; 41(13): 1075-1083
7. Arnold PM, Sasso RC, Janssen ME, Fehlings MG, Heary RF, Vaccaro AR, Kopjar B. i-FACTOR™ Bone Graft vs Autograft in Anterior Cervical Discectomy and Fusion: 2-Year Follow-up of the Randomized Single-Blinded Food and Drug Administration Investigational Device Exemption Study. Neurosurgery. 2018 Sep 1; 83(3):377-384. doi: 10.1093/neuros/nyx432. PubMed PMID: 28945914
8. Jacobsen MK, Andresen AK, Jespersen AB, Støttrup C, Carreon LY, Overgaard S, Andersen MØ. Spine J. 2020 Jan 28. pii: S1529-9430(20)30021-8. doi: 10.1016/j.spinee.2020.01.009
9. Mobbs RJ, Maharaj M, Rao PJ. Clinical outcomes and fusion rates following anterior lumbar interbody fusion with bone graft substitute i-FACTOR, an anorganic bone matrix/P-15 composite. J Neurosurg Spine. 2014 Dec; 21(6):867-76
10. Lauweryns P, Raskin Y. Prospective analysis of a new bone graft in lumbar interbody fusion: results of a 2-year prospective clinical and radiological study. Int J Spine Surg. 2015 Feb 3; 9
11. Gomar F, Orozco R, Villar JL, Arrizabalaga F. P-15 small peptide bone graft substitute in the treatment of non-unions and delayed union. A pilot clinical trial. Int Orthop. 2007 Feb; 31(1):939. Epub 2006 Jun 8
12. Kesteloot G, Parish AJB, Johnson S, McNally DS. Three-dimensional remodelling of i-FACTOR Peptide Enhanced Bone Graft substitute in cervical fusions. Accepted as poster, Annual Scientific Meeting of the Belgian Society of Neurosurgery, March 2016

Corporate Headquarters
11025 Dover Street, Suite 1600
Westminster, CO 80021 USA
P: (303) 974-6275
E: customerservice@cerapedics.com

www.cerapedics.com

CE 2797 Internationally available

Europe, Middle East, Africa, Asia Pacific and Canada
London, England
E: emea@cerapedics.com

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