



PART OF THE *Johnson & Johnson* FAMILY OF COMPANIES

ViviGen[®] and ViviGen Formable[®]

Cellular Bone Matrix

The right cells.
The right time. The right forms.

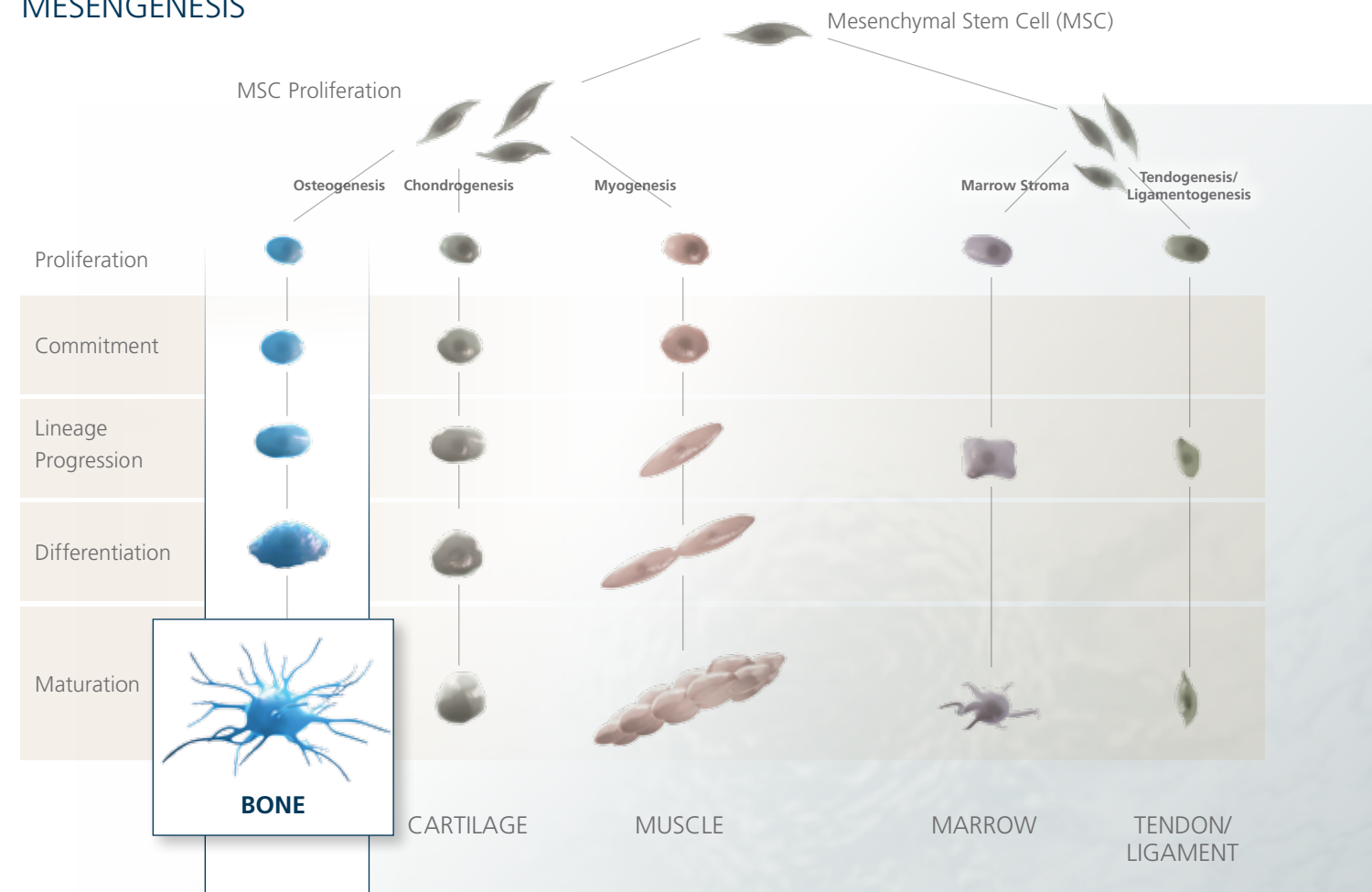


LifeNet Health[®]
Saving Lives. Restoring Health. Giving Hope.

The Bone Cell Advantage

A body of evidence has emerged supporting the fact that bone cells are the preferred cells for bone formation compared to undifferentiated Mesenchymal Stem Cells (MSCs), because they are fully differentiated and are committed solely to laying down bone matrix.

MESENGENESIS



Pre-Clinical Studies Suggest Bone Cells

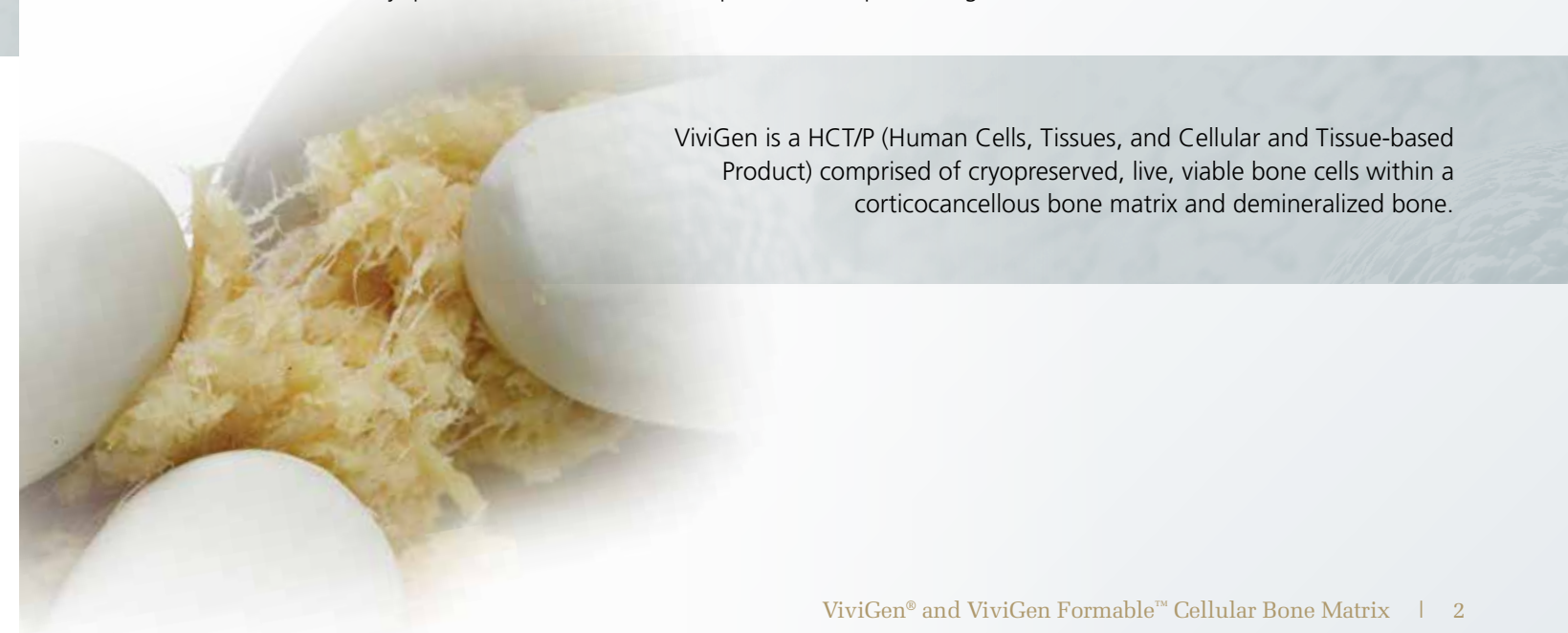
- Remain at the defect site longer⁴, directly participate in the bone formation process and deposit a higher quality of bone than MSCs⁵
- Secrete chemotactic factors such as IGF-1, which may play a major role in recruitment of osteoblasts during bone formation^{6,7}
- Secrete cytokines to stimulate angiogenesis⁶ and work in concert to facilitate further MSC differentiation⁸
- Maintain viability, proliferation potential and osteoblastic function later in life compared to an MSC^{9,10,11,12}

The ViviGen Advantage

ViviGen is the first and only cryopreserved cellular allograft which contains viable lineage committed bone cells. It directly participates in the bone formation process as early as day 7. It is ready for use intraoperatively in 5 minutes or less.^{1,15}

Key Selling Points

- ViviGen contains lineage committed bone cells; it is NOT a MSC-based product.
- ViviGen provides all 3 elements for bone formation:
 - 1. Viable Cells (Osteogenic)**
The processing of ViviGen removes bone marrow components including Mesenchymal Stem Cells while retaining the desirable bone cells (osteoblasts, osteocytes and bone lining cells).¹
 - 2. Corticocancellous Chips (Osteoconductive)**
Provide a natural scaffold for cell attachment, migration and proliferation.
 - 3. Demineralized Bone (Osteoinductive)**
A patented demineralization process exposes natural growth factors within the bone matrix that recruit host cells and stimulate bone forming activity.
- Optimized packaging allows all ViviGen sizes to thaw in 5 minutes or less.¹
 - Why is rapid thaw time important?
 - The rapid thaw prevents ice crystals from forming within the cell which maintains viability.¹⁵
 - Competitive products can take up to 30 minutes to thaw depending on size.^{14,16}
- ViviGen has 96% cell viability post cryopreservation and thaw.¹
 - LifeNet Health's optimized process and packaging protect bone cell viability from donor recovery to clinical use in the OR.
 - ViviGen reaches cryopreservation before the competitors start processing.¹⁴



ViviGen is a HCT/P (Human Cells, Tissues, and Cellular and Tissue-based Product) comprised of cryopreserved, live, viable bone cells within a corticocancellous bone matrix and demineralized bone.

The Right Cells

In Vitro Assays

ViviGen Bone Cells are Viable

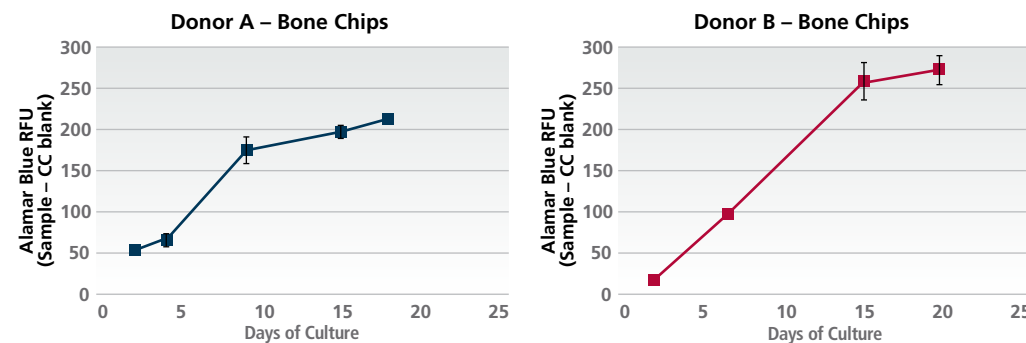
The ViviGen derived cells were able to migrate from the bone chips and attach to the culture plate, demonstrating that they survived the freezing and thawing process.¹

ViviGen Bone Cells are able to Proliferate

Assays that can demonstrate the proliferation potential of cells are the ultimate test of viability, since they test cell function and not just membrane integrity. Results show that ViviGen cells not only survived cryopreservation and processing, but can also proliferate over time.¹



Representative picture of cell migration, attachment, and growth of ViviGen derived cells.



Representative ViviGen bone matrix from 2 different donors were thawed and tested for growth potential by the Alamar blue assay. ViviGen derived bone cells proliferate over time.

ViviGen is Osteogenic¹

ViviGen derived cells were analyzed to assess their capacity to generate bone. A substantial deposition of calcium was seen in the ViviGen cells as early as day 7. When allowed to differentiate to 14 - 21 days, extensive matrix deposits were evident by their positive red staining for calcium in the entire well¹. In contrast, the comparative control of human bone marrow mesenchymal stem cells (hMSCs) were found to begin the deposition of extracellular calcium however, they detached from the culture wells after 21 days. No additional calcium deposition was found compared to those on day 14.¹



Osteogenic capacity of ViviGen derived cells from two donors post processing, cryopreservation and thawing. Cells were allowed to grow until 75-85% confluent and then exposed to osteogenic media. Cells were then fixed at 7, 14, or 21 days and stained for calcium deposits with alizarin red. Human bone marrow mesenchymal stem cells (hMSCs, Lonza) were used as a comparative control.

The Right Time

Processing Time is Important

RECOVERY
≤ 24 HRS

PROCESSING
≤ 48 HRS

CRYOPRESERVATION
≤ 72 HRS

- Donor recovery and processing time directly affects cell viability.¹³
- ViviGen is recovered, processed, and placed into cryopreservation within 72 hours.¹
- ViviGen is cryopreserved 24 hours faster than competitive cellular allografts.¹⁴

Rapid Thawing is Crucial for Cell Viability¹³

The thin walls of the ViviGen pouch allow for an efficient energy transfer resulting in a thaw time of less than 5 minutes for all sizes. This rapid thaw prevents ice crystals from forming intracellularly, ultimately maintaining cell viability.



The Right Forms

A comprehensive solution to meet surgeons' clinical needs

ViviGen contains osteoinductive, demineralized bone particulate.

This particulate allows the graft to be placed into a contained void.



ViviGen Formable® Cellular Bone Matrix contains osteoinductive, precision-machined, demineralized fibers.

These demineralized fibers provide a putty like consistency allowing the graft to be shaped and molded.



ViviGen and ViviGen Formable provide the same advantages with alternative formulations to meet surgeons' clinical needs.

Safety

LifeNet Health prides themselves on their safety record over the last 30+ years. They hold the longest continuous accreditation from the American Association of Tissue Banks, and have a comprehensive range of measures in place to validate the safety of their allograft bio-implants; this includes stringent donor screening methods and release criteria. To obtain suitable donors, LifeNet Health maintains an extensive network of recovery partners. Additionally, LifeNet Health is a leading, federally designated Organ Procurement Organization. LifeNet Health only accepts donors from federally designated Organ Procurement Organizations and qualified tissue recovery partners. These partners are regularly audited to document that their recovery process meets current FDA regulations, AATB standards and LifeNet Health's own stringent guidelines.

Donor Criteria

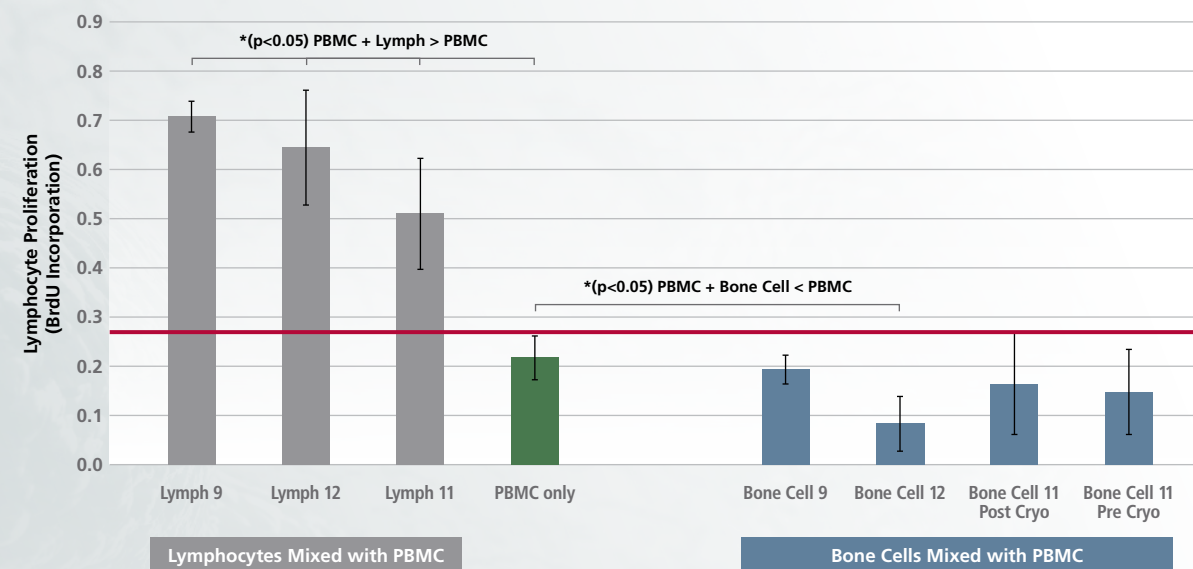
Every donor for ViviGen must meet LifeNet Health's strict medical and behavioral risks assessment in addition to microbial and serological testing.

Aseptic Processing

LifeNet Health utilizes aseptic techniques in ISO certified clean rooms. Each lot of final product is tested for sterility.

ViviGen Cells are Non-Immunogenic¹

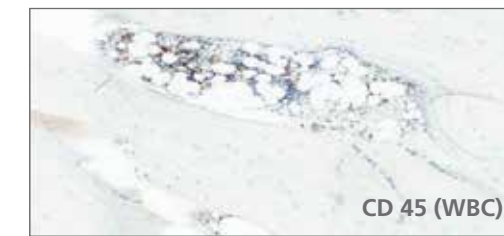
Mixed Lymphocyte Reaction Study^{1,13}



Mixed lymphocyte reaction. Lymphocytes from ViviGen donors were combined with PBMC to elicit an immune reaction (grey bars). ViviGen derived bone cells from the same donors were mixed with PBMC (blue bars). PBMC alone was used as a negative control (green bar).

Lymphocytes from ViviGen donors were combined with peripheral blood mononuclear cells (PBMC) to illicit an immune reaction. As expected, lymphocytes stimulated a statistically significant proliferative response from the non-matched PBMCs. ViviGen derived bone cells from the same donors were also mixed with PBMC resulting in no proliferation. This illustrates the absence of an immune response from the ViviGen derived bone cells.¹

ViviGen Processing Removes Marrow Components¹



Marrow components present pre-processing



Marrow components removed post-processing, cryopreservation and thawing

Staining for CD45, a type I transmembrane protein present on all hematopoietic cells, confirmed the presence of hematopoietic cells in the bone matrix prior to processing. Post processing, cryopreservation and thawing, marrow components including CD45 positive cells were absent, which confirmed the marrow components were negligible. This demonstrates the processing reduces the number of potentially immunogenic cells from the bone marrow, also reducing the risk of eliciting an immune response.¹

Features and Benefits

FEATURES	BENEFITS
Osteogenic	Contains viable, lineage committed bone cells that are able to proliferate in vitro post cryopreservation and thaw
Osteoconductive	Contains corticocancellous chips that provide a natural scaffold for cell attachment, cell migration and cell proliferation
Osteoinductive	Demineralization of the cortical bone exposes the natural growth factors within the matrix
Safety	Every lot is aseptically processed and all final product is tested for sterility using USP <71> standards
Packaging	The rapid heat transfer not only allows for all sizes to thaw in less than 5 minutes, but is also vital for cell viability
Processing Time	ViviGen reaches cryopreservation within 72 hours maximizing cell viability 24 hours sooner than competitive products
Maximized Cell Viability	The processing of ViviGen is focused on protecting viable, lineage committed bone cells from recovery to implantation ¹
Multiple forms	ViviGen and ViviGen Formable provide a comprehensive solution to meet surgeons' clinical needs

Ordering

	ITEM NUMBER	DESCRIPTION
ViviGen	BL-1500-001	1cc
	BL-1500-002	5cc
	BL-1500-003	10cc
	BL-1500-004	15cc
ViviGen Formable	BL-1600-001	Small
	BL-1600-002	Medium
	BL-1600-003	Large
	BL-1600-004	X-Large



All Vivigen orders are placed with LifeNet Health directly by phone:
1-888-847-7831, fax: 1-888-847-7832 or email: orders@lifenethealth.org.
Business hours are Monday through Friday, from 7am to 7pm EST.

Shipping

Free Next-Day Delivery

Vivigen is shipped for next day delivery by 10:30am free of charge.
Next day early AM is also available upon request.

1. Data on file LifeNet Health DHF 12-008, DHF 15-001
 2. Dirckx N, Van Hul M, Maes C. Osteoblast recruitment to sites of bone formation in skeletal development, homeostasis, and regeneration. *Birth Defects Res C Embryo Today*. 2013 Sep;99(3):170-91.
 3. Rupani A, Balint R, Cartmell SH. Osteoblasts and their applications in bone tissue engineering. *Cell Health and Cytoskeleton* 2012;4:49-61.
 4. *Biomaterials* 31 (2010) 242-249
 5. *J Tissue Engineering & Regenerative Medicine* 5 (2011) 831-844
 6. *Biomaterials* 32 (2011) 8150-8160
 7. *Bone* 43 (2008) 869-895
 8. *European Cell and Materials* 23 (2012) 13-27
 9. *J. Orthopaedic. Research*. 8 (1990), 234-237
 10. *Bone* 25 (1999), 667-673
 11. *J. Orthopaedic. Research*. 22 (2004), 30-38.
 12. *Biochem. J.* 333 (1998), 787-794.
 13. *Human Reproduction* vol.3 no.6 pp. 795-802, 1988
 14. Trinity Evolution® Product Brochure
 15. Chen SS. Advantage of Vivigen™ Packaging. Results from In Vitro Studies. LifeNet Health® Institute of Regenerative Medicine White Paper.
 16. Vivigen IFU, LifeNet Health
- Findings from an in vitro assay are not always predictive of human clinical results.



www.depuyshnthes.com

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