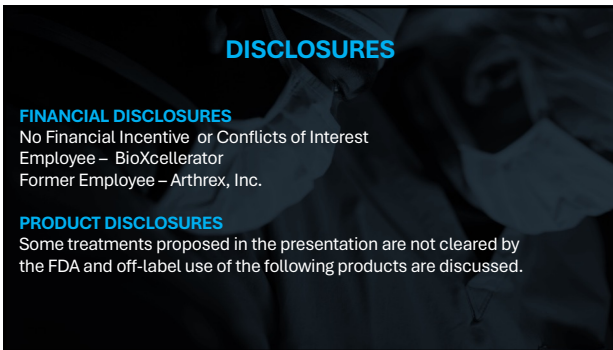


1



2



3

JUST SAY NO!

Kenalog-40
Triamcinolone Acetonide
Kenalog-40
10 mg per 0.5 mL

Kenalog-40
Triamcinolone Acetonide
Kenalog-40
10 mg per 0.5 mL

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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“Regenerative medicine is focused on developing and applying new treatments to heal tissues and organs and restore function lost due to aging, disease, damage or defects.”
– Mayo Clinic

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

5

CELLULAR PRODUCTS
PRP, BMA/BMC

AMNION


ADIPOSE MSCs

UMBILICAL CORD MSCs


**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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CARTILAGE & BONE GRAFTS
Autograft, Allograft



SCAFFOLDS
Dermis, Amnion, Xenograft



**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

7

FDA Regulation

Minimally-Manipulated
Not Combined With Another Substance
Homologous Use
Administration During Same Procedure As Harvest

***No storage, expansion or culture**

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

8

FDA Regulation of PRP

510K Clearance of PRP Machines

“...for producing platelet-rich preparations intended to be used to mix with bone graft materials to enhance bone graft handling properties in orthopedic practices. **The use of PRP outside this setting, for example, an office injection, would be considered "off label."**

J. Knee Surg. 2015 Feb;28(1):29-34. doi: 10.1055/s-0034-1390030. Epub 2014 Sep 30.

US definitions, current use, and FDA stance on use of platelet-rich plasma in sports medicine

Knut Beltzel ¹, Donald Allen ², John Apostolakis ², Ryan P Russell ², Mary Beth McCarthy ², Gregory J Galle ², Mark P Cote ², Augustus D Mezzocane ²

9

PLATELET "RICH" PLASMA
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?
Leukocyte-Rich vs. Leukocyte-Poor

J.Clin.Orthop.Trauma, 2019 Oct; 10(Suppl 1): S7-S12. PMID: PMC6823808
 Published online 2019 May 13. doi: 10.1016/j.jcot.2019.05.008 PMID: 31700202

Leukocyte-rich PRP versus leukocyte-poor PRP - The role of monocyte/macrophage function in the healing cascade

José Fábio Lana,¹ Stephany Cares Huber,² Joseph Purita,³ Claudia H. Tambelli,⁴ Gabriel Silva Santos,^{5,*} Christian Paulus,⁶ and Joyce M. Annichino-Bizzacchi⁴

**REGENERATIVE MEDICINE
 IN ORTHOPEDICS**

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PLATELET "RICH" PLASMA
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?
Leukocyte-Rich vs. Leukocyte-Poor

Curr Rev Musculoskelet Med, 2018 Dec; 11(4): 624-634.
 Published online 2018 Oct 23. doi: 10.1007/s12178-018-9527-7

Current Clinical Recommendations for Use of Platelet-Rich Plasma

Adrian D. K. Le,^{1,2} Lawrence Erweza,¹ Malcolm R. DeBaun,¹ and Jason L. Drago^{2†}

**REGENERATIVE MEDICINE
 IN ORTHOPEDICS**

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AMNION

**UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
 Food and Drug Administration**

Amniotic fluid is considered to be a secreted or extracted human product, and therefore it does not meet the definition of an HCTIP. So instead, amniotic fluid is regulated as a drug, device, and/or biological product, depending on factors such as its intended use.

FDA CBER Webinar: Information for Practitioners — FDA's Regulatory Oversight of Regenerative Medicine Products
 November 17, 2022

Food and Drug Administration (gov)
 Feb 17, 2023

???????

**REGENERATIVE MEDICINE
 IN ORTHOPEDICS**

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AMNION

WARNING LETTER

**Stratus Biosystems, LLC dba
CellGenuity Regenerative Science**

MARCS-CMS 831303 – JUNE 06, 2023

During an inspection of your firm, Stratus Biosystems, LLC (dba CellGenuity Regenerative Science or CellGenuity), located at 613 S Main St, Ste 215, Grapevine, TX 76051-7275, conducted between October 26, 2022 and November 30, 2022, the United States Food and Drug Administration (FDA) documented your manufacture of products for allogeneic use, including an umbilical cord and amniotic membrane derived product, AmnioAMP-WJ™, and an amniotic fluid derived product, AmnioAllograft (collectively, "your products"). You distribute your products to healthcare providers and facilities throughout the United States. These products are intended for injection and are purported to be sterile.

PRODUCT INSERT

DESCRIPTION
CLARIX FLO is a sterile, particulate human amniotic membrane and umbilical cord tissue product that is aseptically processed in compliance with current Good Tissue Practices (cGTP) from the same donated human tissue (placenta) after determination of eligibility and placenta/cord suitability. There is no pooling of tissues from different donors during recovery or throughout the manufacturing process. CLARIX FLO does not contain living cells. CLARIX FLO is terminally sterilized via gamma sterilization with a Sterility Assurance Level (SAL) of 10⁻⁶.

*Though injected, cleared by the FDA under a scaffold

REGENERATIVE MEDICINE
IN ORTHOPEDICS

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AMNION

Journal of Pain Research

Dovepress

CASE SERIES

Clinical Outcomes of Amniotic Membrane/Umbilical Cord Particulate in Spinal Disorders: A Retrospective Study

Amanta Ross, Vikki Gambrell, Chris Main

Anti-Inflammatory Cytokines
Growth Factors
Peptide Complexes

*NO LIVE CELLS

REGENERATIVE MEDICINE
IN ORTHOPEDICS

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“STEM CELLS”

MSCs?

MESENCHYMAL STEM CELLS?
MESENCHYMAL STROMAL CELLS?
MEDICINAL SIGNALING CELLS?

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“ STEM CELLS ”

EFFECTS

- Reduce Inflammation
- Stabilize Native Cells
- Regenerate New Cells

The diagram illustrates the mechanisms of action of Mesenchymal Stem Cells (MSCs). A central MSC cell is shown interacting with various target cells and tissues. Key mechanisms include:

- Paracrine activity:** MSCs release soluble factors like TGF- β 1, IL-10, and Angiogenic factors to influence target cells.
- Cell-cell contact:** MSCs interact with immune cells and endothelial cells.
- Mitochondrial transfer:** MSCs transfer mitochondria to target cells.
- MSC Integration:** MSCs integrate into target tissue and differentiate into target cells.
- Extracellular vesicles/Exosomes:** MSCs release vesicles that interact with target cells.

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“ STEM CELLS ”

Mechanism of Action

- Paracrine Activity
- Cell-Cell Contact
- Mitochondrial Transfer
- MSC Integration
- Extracellular Vesicles/Exosomes

The diagram illustrates the mechanisms of action of Mesenchymal Stem Cells (MSCs). A central MSC cell is shown interacting with various target cells and tissues. Key mechanisms include:

- Paracrine activity:** MSCs release soluble factors like TGF- β 1, IL-10, and Angiogenic factors to influence target cells.
- Cell-cell contact:** MSCs interact with immune cells and endothelial cells.
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- MSC Integration:** MSCs integrate into target tissue and differentiate into target cells.
- Extracellular vesicles/Exosomes:** MSCs release vesicles that interact with target cells.

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BONE MARROW ASPIRATE / CONCENTRATE
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?

Definition: Marrow concentrate containing anti-inflammatory proteins & growth factors, MSCs

Harvest Site?
How Much Aspirate?
Cell Count, Purity & Potency?
Clinical Indication?

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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BONE MARROW ASPIRATE / CONCENTRATE
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?

ILIAC CREST
FEMUR
TIBIA
SHOULDER

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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BONE MARROW ASPIRATE / CONCENTRATE
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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BONE MARROW ASPIRATE / CONCENTRATE

Orthop. Clin North Am. 2017 Jul;48(3):311-321. doi: 10.1016/j.orth.2017.03.005.
PMID: 2880216

Role of Bone Marrow Aspirate in Orthopedic Trauma

Review
Patrick C Schottel¹, Stephen J Warner²

Cell Count Multifactorial
Harvest Most Invasive
"Live" Cells
Exosomes, Growth Factors, AI Cytokines

► **PROLIFERATION
REPAIR
REGENERATION**

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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ADIPOSE – DERIVED MSCs
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?
Definition: ...Resized Fat.




...is used to provide cushion and support to help the natural healing process by supporting the repair, replacement, reconstruction of damaged or injured tissue.

**REGENERATIVE MEDICINE
 IN ORTHOPEDICS**

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ADIPOSE – DERIVED MSCs
DO YOU KNOW WHAT YOU'RE PREPARING & INJECTING?
Definition: ...Resized Fat.



**REGENERATIVE MEDICINE
 IN ORTHOPEDICS**

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ADIPOSE – DERIVED MSCs

World J Stem Cells, 2014 Jul 26; 6(3): 312-321. PMID: PMC4131273
 Published online 2014 Jul 26. doi: 10.4252/wjsc.v6.i3.312 PMID: 25126381

Adipose-derived stem cells: Implications in tissue regeneration
Wakako Tsuji, J Peter Rubin, and Kacey G Marra

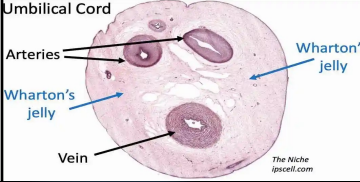
Cell Count >>> BM-Derived MSCs
 Harvest "Less" Invasive than BM MSCs
 "Live" Cells
 Exosomes, Growth Factors, AI Cytokines

▶ **PROLIFERATION
 REPAIR
 REGENERATION**

**REGENERATIVE MEDICINE
 IN ORTHOPEDICS**

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UMBILICAL CORD MSCs



Passage	MM Cells
3	~120
4	~250
5	~400
6	~400
7	~400

REGENERATIVE MEDICINE IN ORTHOPEDICS

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UMBILICAL CORD MSCs


Received 2 March 2023 | Accepted 17 April 2023
DOI: 10.1002/jbm.b.15404

REVIEW ARTICLE

WILEY

Regenerative potential of Wharton's jelly-derived mesenchymal stem cells: A new horizon of stem cell therapy

Hassan Alkawasbi^{1,2} | Farzad Ghobas^{1,2} | Mubt Darashah^{1,2} | Ali Akbar Mousavizadeh^{1,2} | Mehdi Yousefi^{1,2} | Mahdi Talebi^{1,2} | Karim Shamsaei^{1,2}



PROLIFERATION
REPAIR
REGENERATION

Cell Count >>> Adipose or BM-Derived MSCs
Harvest Least Invasive than BM or Live Cells
Exosomes, Growth Factors, AI Cytokines

REGENERATIVE MEDICINE IN ORTHOPEDICS

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Sources of MSCs

MSC's	Source		Markers	
	Bone Marrow		CD73, CD90, CD105, STRO-1	
	Gingival Tissue		CD 29, CD44, CD90, CD105	
	Adipose Tissue		CD13, CD29, CD44, CD73, CD90, CD105, CD165, STRO-1	
	Dermis		CD44, CD73, CD90, CD105, SDF-1, Vimentin	
	Placenta		CD29, CD73, CD90, CD105	
	Umbilical Cord	Umbilical Cord Blood		CD 29, CD 44, CD51, CD73, CD105
		WJ		CD73, CD90, CD105
	Amniotic Fluid		CD29, CD44, CD90, CD105, SH-2, SH-3	
Blood		CD44, CD90, HLA-BE		

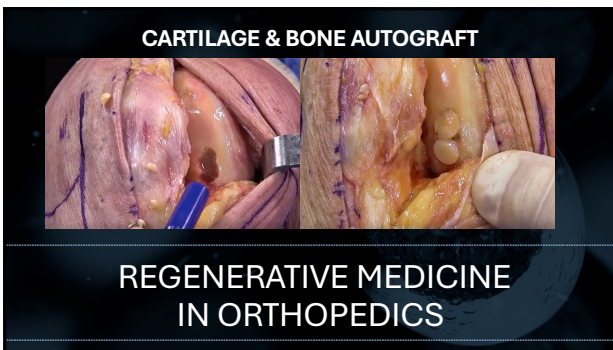
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MSC COMPARISON

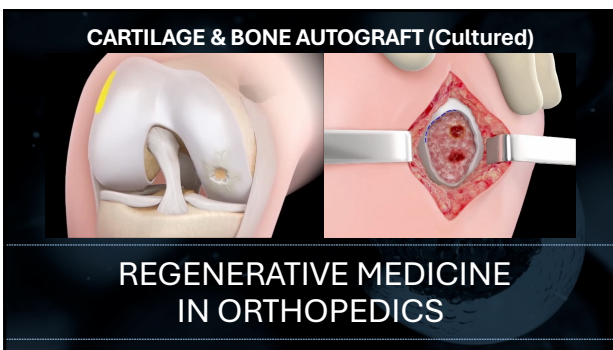
	AVAILABILITY	COST	RESEARCH	INVASIVE	COUNT	PURITY	POTENCY
BONE MARROW - DERIVED	✓✓✓	\$	✓✓✓	↑	#	—	↑
ADIPOSE - DERIVED	✓✓✓	\$	✓✓✓	↑	#	—	↑
UMBILICAL CORD - DERIVED	✓	\$\$\$	✓✓✓	—	###	↑↑↑	↑↑↑

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

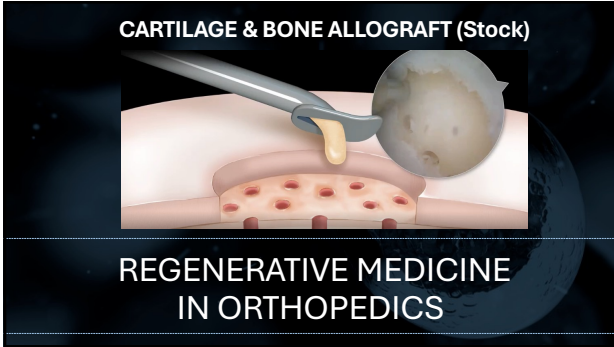
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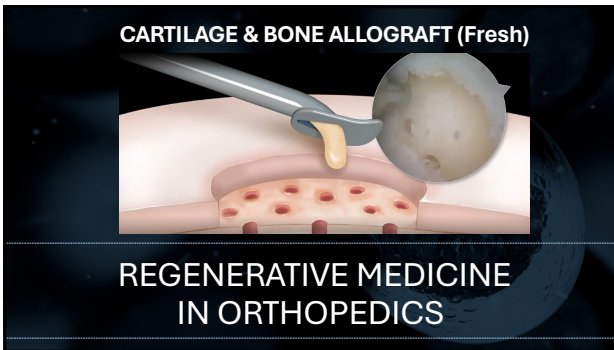
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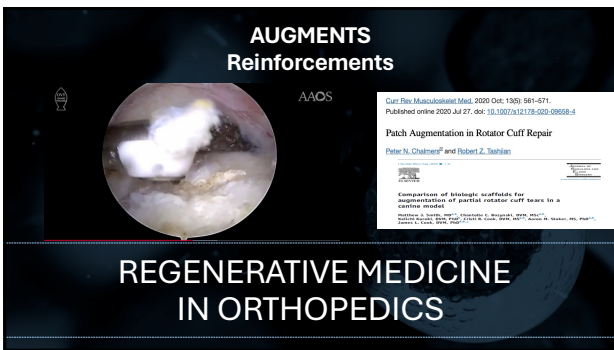
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AUGMENTS - ALLOGRAFT

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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AUGMENTS – ACELLULAR DERMAL MATRIX

Review | Orthop Clin North Am. 2015 Jul;46(3):377-86, x. doi: 10.1016/j.ocl.2015.02.006. Epub 2015 Apr 15.

Orthopedic applications of acellular human dermal allograft for shoulder and elbow surgery

Daniel C. Acaveiro¹, Brett Shore², Raffy Mirzayan²

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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AUGMENTS – AMNION SCAFFOLD

Review | Open access | Published: 10 January 2022

Applications of the amniotic membrane in tissue engineering and regeneration: the hundred-year challenge

Foad El-Hemary, Azza El-Dorbi, Mohamed Abd Elkhouas, Radwa A. Salah, Ahmed Lutfy A. Nassar El-Hady^{1*}

Open Cell Researched & Thorax 13, Article number: 6 (2022) | Cite this article

**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

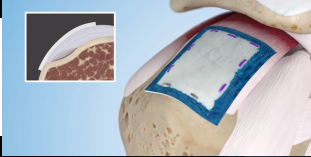
39

AUGMENTS – XENOGRIFT

Am J Sports Med. 2019 Jul;47(18):1901-1908. doi: 10.1177/0363546819850795. Epub 2019 May 31.

Evaluation of Healing Rates and Safety With a Bioinductive Collagen Patch for Large and Massive Rotator Cuff Tears: 2-Year Safety and Clinical Outcomes

Stephen G Thon¹, Larry O'Malley 2nd², Michael J O'Brien³, Felix H Svardle 3rd³



**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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AUGMENTS – BIOENGINEERED

J Biomed Mater Res A. Author manuscript; available in PMC 2020 Apr 1. PMCID: PMC7020941


Published in final edited form as: NIHMSID: NIHMS1068050

J Biomed Mater Res A. 2020 Apr; 108(4): 872-883. PMID: 31895482

Published online 2020 Jan 12; doi: 10.1002/jbm.b.36874

Current advances in biodegradable synthetic polymer based cardiac patches


Sara McMahan¹, Alan Taylor², Katherine M. Coombs¹, Zui Pan², Jun Liao², and Yi Hong¹



**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

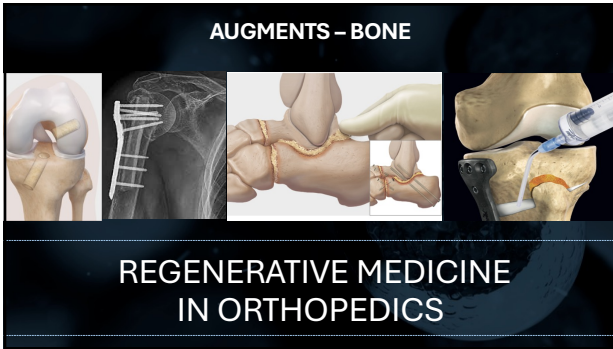
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AUGMENTS – BONE



**REGENERATIVE MEDICINE
IN ORTHOPEDICS**

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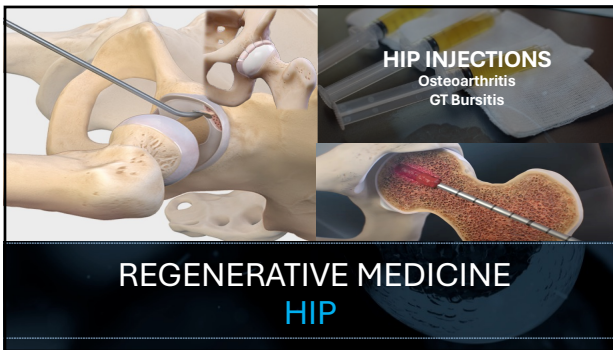
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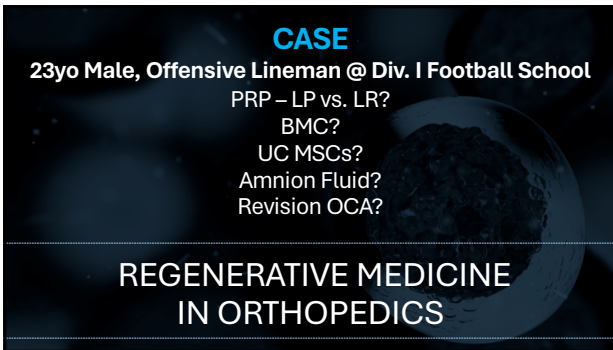
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