

The essence of nature in expert hands

naturesque

» REGENERATION LINE



Competence and synergy



[Parrot] synonymous with creativity, communication, and originality

From deep down inside, we create power and might. To produce something new, sometimes the mind's eye has to turn outwards so that creativity and cleverness can shine like brilliant plumage. The most powerful tool for sharing ideas, knowledge, experience, and stories with one another is language. It is what makes humans unique. It opens a door for us to inspire each other to greater flights of fancy.

With a mutual appreciation of value and open communication, we create the foundation for successful partnerships in which new ideas are generated and we grow beyond the average.

Universal solutions will never satisfy all requirements

For years we at BEGO Implant Systems have implemented the system concept in the area of implant dentistry. For this reason, BEGO Implant Systems works together with partners in certain areas so that we are always able to offer products at the peak of dental technology.

Our procedure in the area of regeneration materials is called OWN Brand Distribution Label—an expression for us of partnerships that are full of synergies between manufacturers with established expertise in innovative regenerative biomaterials and our expertise as a developer, manufacturer, and distributor of dental implants.

BEGO Implant Systems will stake out a stronger position in the area of regenerative materials in implant dentistry with the naturesQue product line because we perfectly combine the established with the innovative.

The framework conditions and rules of the game in the area of medical devices

Our naturesQue product line is synonymous with modern and successful regenerative materials. In light of increasing regulatory requirements, this is simply not enough. For BEGO Implant Systems and our partners this means that our approach and the implementation of regulatory frameworks have to be implemented conscientiously, precisely, reliably, and practicably.



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REGENERATION



[Duck] synonymous with empathy, trust, and respect

Nature is that which humans have not created. Beyond intellectual speculations, we sense, feel, and know that the exceptional abilities and fantastic mechanisms found in nature contain far more than is apparent to us at first glance. Whoever makes use of the opportunities found in nature must act with this in mind. Inspiration from nature based on solid foundations of respect and understanding can lead to outstanding developments.



naturesQue regenerative materials

The melodious and wonderfully expansive name of our new regenerative product line naturesQue is based on the French adjective *naturalesque* and means *a faithful recreation of nature and being as true as possible to the natural details*.

The name naturesQue is for us an expression of our respect for the exceptional abilities and fantastic mechanisms seen in nature and for the skill of modern science and technology to use these properties to produce exceptional medical devices. These are

the cornerstones of the new naturesQue product line. The naturesQue regenerative materials combine the strengths of the natural origin of the material with scientific and clinical expertise for tissue regeneration.

BONE SUBSTITUTE MATERIALS

1. an innovative xenohybrid bone substitute material derived from **bovine bone**, coated with a **co-polymer mix** and **collagen fragments**
2. an established xenogeneic bone substitute material derived from **porcine cancellous bone**

COLLAGEN PRODUCTS

1. a stable **porcine barrier membrane** to protect the augmentation material
2. **a microfibrillar bovine collagen** that forms a highly viscous gel after exudate uptake and has intrinsic hemostatic properties
3. **a porcine collagen fleece** that retains its 3D structure and stabilizes the blood clot



[Rhino] synonymous with certainty, calm, and power

Those who embrace ancient knowledge and exude self-confidence are able to intuitively access their abilities to implement their desires—against resistance, without fear. In a fast world, superior force and wisdom do not always prevail. In striving for security and success, demand outstrips feasibility and opportunities are passed by unused. And yet—when the power of nature inspires the (natural) sciences, outstanding medical devices are developed in which the innovative and the established unite.

Xenogeneic bone substitute materials

The exceptional ability of bone tissue to regenerate is fascinating. This complex tissue heals almost without forming scars and recovers its original structure and functionality. The *jumping distance* that osteoblasts can bridge and the dimensions of the *critical size defects* that are used in study models impressively demonstrate not the limits but rather the potential of bone for regeneration.

The essential factors for bone regeneration are an adequate blood supply, mechanical support in the form of a guiding structure, and rest. Bone substitute materials are used for the regeneration of bone where the human body is not able to heal the bones itself. Along with the requirements for an ideal bone

substitute material, it is a generally accepted paradigm that bone substitute materials should mimic human cancellous bone as closely as possible ^[1].

The natural origin of xenogeneic bone substitute material gives it an optimal design. Porosity, pore distribution, and pore size correspond largely to those of human bone and are suitable to achieve bone formation, maturation, and remodeling. However, the purification of animal bone leads to a reduction in mechanical strength and biological potency, because cells and proteins have to be removed to eliminate the risk of transmitting disease and of rejection.

The xenohybrid bone substitute material naturesQue *SemOss B* is one of the new generation of regenerative nature-based regeneration materials. The combination of different material classes compensates for the limitations of the individual elements and amplifies their positive properties. The established inorganic bone mineral naturesQue *MaxOss P* is obtained from porcine cancellous bone. The matrix is very porous and also provides ample space for new bone apposition and the remodeling processes during bone maturation.

Properties of xenogeneic bone substitute materials

Porous, interconnecting structure with adequate pore size ($\geq 100 \mu\text{m}$)

Surface characteristics

Adequate mechanical strength and elasticity

Controlled biodegradation



Function and use in bone regeneration

Diffusion and migration of cells, nutrients, and exchange of metabolic products throughout the entire material

Allows cell adhesion, migration, and proliferation of osteoblasts

Enables the absorption of applied force into the surrounding hard and soft tissues in non-self-retaining defects

Resorption during the tissue remodeling process with the volume being retained to allow bony ingrowth in the defect

naturesQue SemOss B



naturesQue SemOss B is a xenohybrid bone substitute material with a coating of a co-polymer mix and collagen fragments.

The combination of different material classes compensates for the limitations of the individual elements and amplifies their positive properties. This combination produces a resorbable bovine bone substitute material. To apply the material, the granules are moistened with blood so that the positive properties of the coating can develop effectively.



Safety

naturesQue SemOss B is a safe bone substitute material and satisfies the requirements of Directive 93/42/EEC Annex 2 Section 4 and Regulation 722/2012.



Bovine bone matrix

- Femoral heads with a high proportion of cancellous bone
- Porous raw material with naturally perfect design features for osseointegration and remodeling



Chemical purification procedure

- Removal of organic components
- Unchanged crystalline structure in the bone matrix



Finishing procedure to enhance the matrix properties

- Enhances the elastic mechanical properties
- Increases colonization by cells in the bone matrix



ORIGIN

- Bovine bone
- Co-polymer mix
- Porcine collagen

COMPOSITION

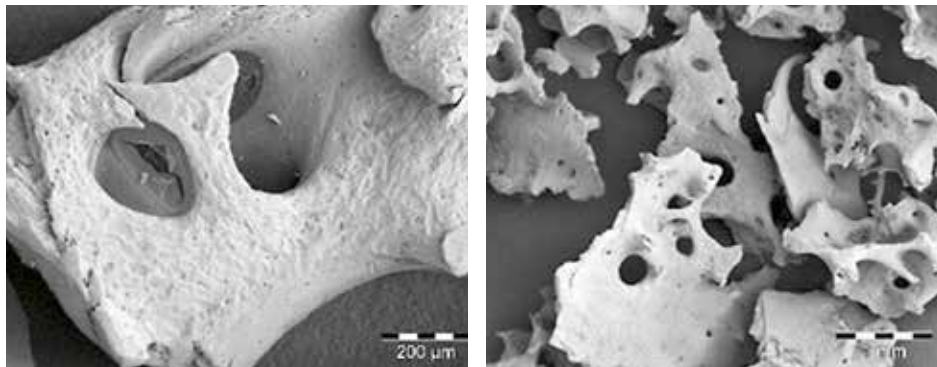
- Mineral phase of the cancellous bone
- Poly(L-lactide) and poly(ε-caprolactone)
- Porcine collagen fragments

PROCESSING

- Removal of the organic phase
- Reinforcement/Finishing treatment: Application of the co-polymer mix and the collagen fragments
- Screening, packaging, sterilization

Structure and design

The porosity of naturesQue *SemOss B* is determined by the large spaces in the cancellous bone. The trabecular architecture is retained and creates the perfect design for the migration of osteoblasts, the growth of blood vessels, and remodeling.



Scanning electron microscopy image of naturesQue *SemOss B* granules.

Application—The recommended rehydration with (patient) blood



Blood

The bovine bone matrix of naturesQue *SemOss B* is reinforced by a surface coating. Denatured collagen fragments create an environment suitable for cell colonization. The first weeks are characterized by cell migration and colonization of the surface of naturesQue *SemOss B*. At the same time the co-polymer mix is degraded, making the mineral bone matrix fully accessible.



Saline

For the positive properties of the surface coating of naturesQue *SemOss B* to develop, naturesQue *SemOss B* must be moistened with blood. This ensures that important biological molecules from the blood bind to the surface and contribute to formation of new bone in direct contact with the bone substitute material.

APPLICATION

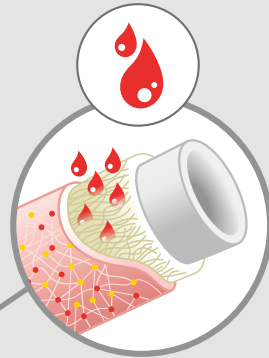
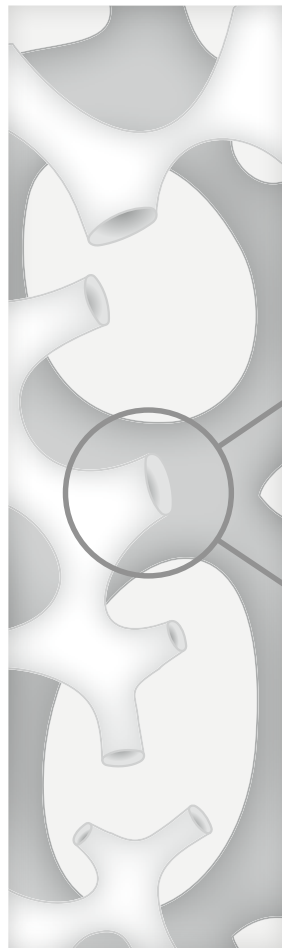
- Mix with patient blood
- Insert into the defect using sterile instruments
- Avoid mixing with aqueous solutions (NaCl, saline)

CONSISTENCY/FEEL

- Dry: hard and solid
- Moistened with blood: slightly plastic, can be modeled because the granules adhere to one another

RESORPTION

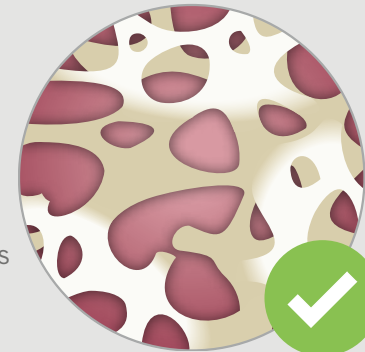
- Resorbable; resorption profile depends on the individual condition of the patient
- Mechanical load in the augmentation area after 6 months at the earliest



Apply: Hydration with blood

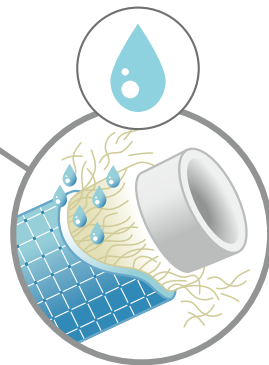
Binding of biological molecules to the surface

- + Surface conditioning with the serum components of the blood
- + Very good cell adhesion to the RGD motifs of the denatured collagen fragments
- + Stable bone bed



Biological conditioning

The hydration with blood develops the positive properties of the coating. The bone substitute material is permeated by blood in the defect. Local microcoagulation of the blood in the augmentation material initiates a signal cascade and creates the conditions for the integration of naturesQue SemOss B.



Avoid: Hydration with saline

Extraction of the denatured collagen fragments from the co-polymer film

- Missing binding sites for cells as a result of the extraction of the denatured collagen fragments from the co-polymer film
- Connective tissue boundary layer between new bone and bone substitute material
- Insufficient stability in the bone bed



CLOSE UP

CO-POLYMER MIX OF POLY (L-LACTIDE) & POLY (ε-CAPROLACTONE)

- Increased resistance of naturesQue SemOss B
- Protects the mineral bone matrix against premature resorption during the inflammatory phase after the surgical procedure
- Gives naturesQue SemOss B plastic properties for outstanding handling

PORCINE DENATURED COLLAGEN FRAGMENTS

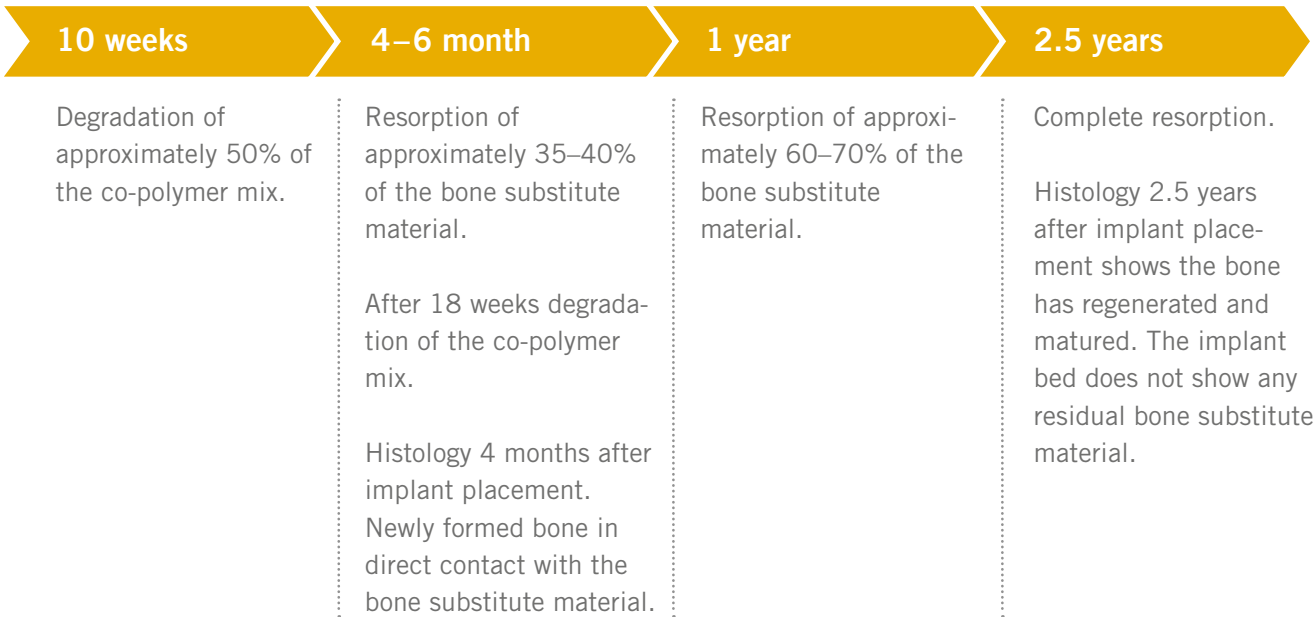
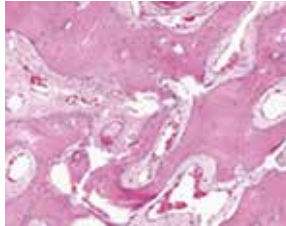
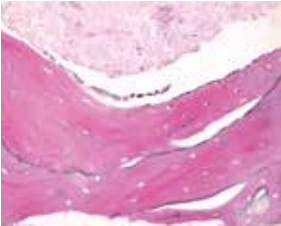
- Immobilized short biomolecules
- Contain the RGD sequence (Arg-Gly-Asp) that promotes cell adhesion and forces the start of bone formation

Resorption profile

As a result of the natural crystalline structure of the bone mineral that is left after processing, the xenogeneic bone matrix of *naturesQue SemOss B* is completely resorbable.

The finishing treatment with a co-polymer mix protects the bone matrix against premature resorption and improves its elastic mechanical properties. The collagen fragments are an attractive substrate for cellular adhesion and encourage the wettability of the surface of *naturesQue SemOss B*.

naturesQue SemOss B is completely resorbed within 1–2 years as part of the remodeling and replaced by the patient's own bone. The co-polymer mix in the finishing coating of *naturesQue SemOss B* is degraded over an average of 18 weeks, an optimal time frame during which good bone formation and tissue integration can be expected.



RESORBABLE BOVINE BONE SUBSTITUTE MATERIAL

- The mineral structure of the bovine bone matrix remains unchanged during production. The natural crystalline network can thus be completely degraded during remodeling by osteoclasts

RADIOPACITY

- After application, *naturesQue SemOss B* is less opaque due to the low density and very open, porous structure. During bone healing and remodeling the opacity increases as new mineralized bone is formed in the defect region

naturesQue MaxOss P



naturesQue MaxOss P is obtained from porcine cancellous bone and has a large and open porosity thanks to the fine and complex trabecular structure. The free spaces are connected to one another and provide plenty of room for bone regeneration, maturation, and remodeling. The large internal surface area provides enormous potential for the adhesion of cells.

Light and airy—why large cavities are so important for bone substitute materials

Porosity is one of the most important properties of a bone substitute material. Cells can migrate into the bone substitute material through the pores and newly formed blood vessels can connect to the vascular network so that the new bone in the regeneration area is supplied with oxygen and nutrients.



Osteoblasts prefer large pore diameters⁽²⁾; the macropores of naturesQue MaxOss P are between 100 and 1000 µm in size and are therefore perfectly suited for the migration of osteoblasts. After bony integration, remodeling and adaptation of the bone to applied force need plenty of space, which is available in the highly porous structure of naturesQue MaxOss P.

ORIGIN	COMPOSITION	PROCESSING
<ul style="list-style-type: none"> • Porcine cancellous bone 	<ul style="list-style-type: none"> • Mineral phase of the cancellous bone • Preservation of the natural content of carbonate apatite 	<ul style="list-style-type: none"> • Porcine bone • Cleaning and removal of proteins (deproteinization) using high heat • Washing with buffer solution • Measurement, screening, packaging, and sterilization • QA control

Structure and design

The trabecular network is an anatomic and architectural masterpiece. The arrangement of the bony struts and rods means that bone can achieve a high degree of stability with minimal use of substance. This produces a structure that has a very high surface area.

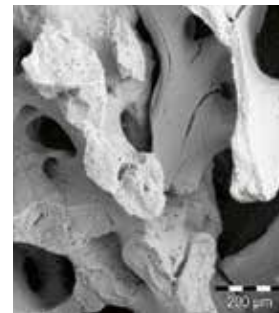
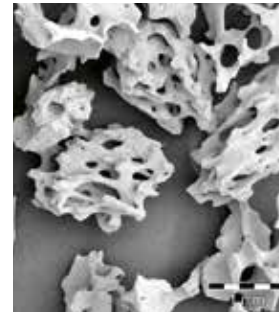
When producing xenogeneic cancellous bone substitute materials, medical technology makes use of these properties. When processing the porcine bone tissue the natural trabecular network is preserved and the structure of the carbonate apatite crystals is retained in the mineral phase. Carbonate apatite crystals support the activities of the cells in the various stages of bone healing.

Analytical measurements (IR spectrum, X-ray diffraction) reveal the similarity in the mineral phase and crystalline structure between *naturesQue MaxOss P* and mature native bone tissue.



Safety

naturesQue MaxOss P is a safe bone substitute material and satisfies the requirements in Directive 93/42/EEC



Scanning electron microscopy image of *naturesQue MaxOss P*

naturesQue MaxOss P and bone—a permanent bond

Plenty of space for the bone—the design of *naturesQue MaxOss P* is derived from the trabecular network of the bone: a complex framework made up of narrow struts and rods and large interconnected spaces. This creates a large surface area onto which the osteoblasts adhere and are able to deposit the new bone matrix. In the large pores the vascularization and the remodeling of the newly formed bone can proceed undisturbed. Thus, a stable and permanent bond is formed between *naturesQue MaxOss P* and the new bone.

APPLICATION

- Mixing with autologous bone preparations, patient blood, or saline is possible
- Only place in direct contact with well vascularized local bone
- Cortical bone should be manually perforated

CONSISTENCY/FEEL

- Granules are highly porous, so avoid placing pressure on the granules to prevent the fragile trabecular structure being crushed

RESORPTION

- Integration into the newly formed bone
- Slow course of resorption, superficial traces of resorption
- Stable framework for the bone



[Chameleon] synonymous with adaptability, change, and transformation

To exist in a changeable environment, the ability to adapt is prized. The talent to be in the center of events without being noticed makes it possible to acquire and manifest knowledge and aptitude. In this way, we learn to balance on a narrow beam without losing our equilibrium.

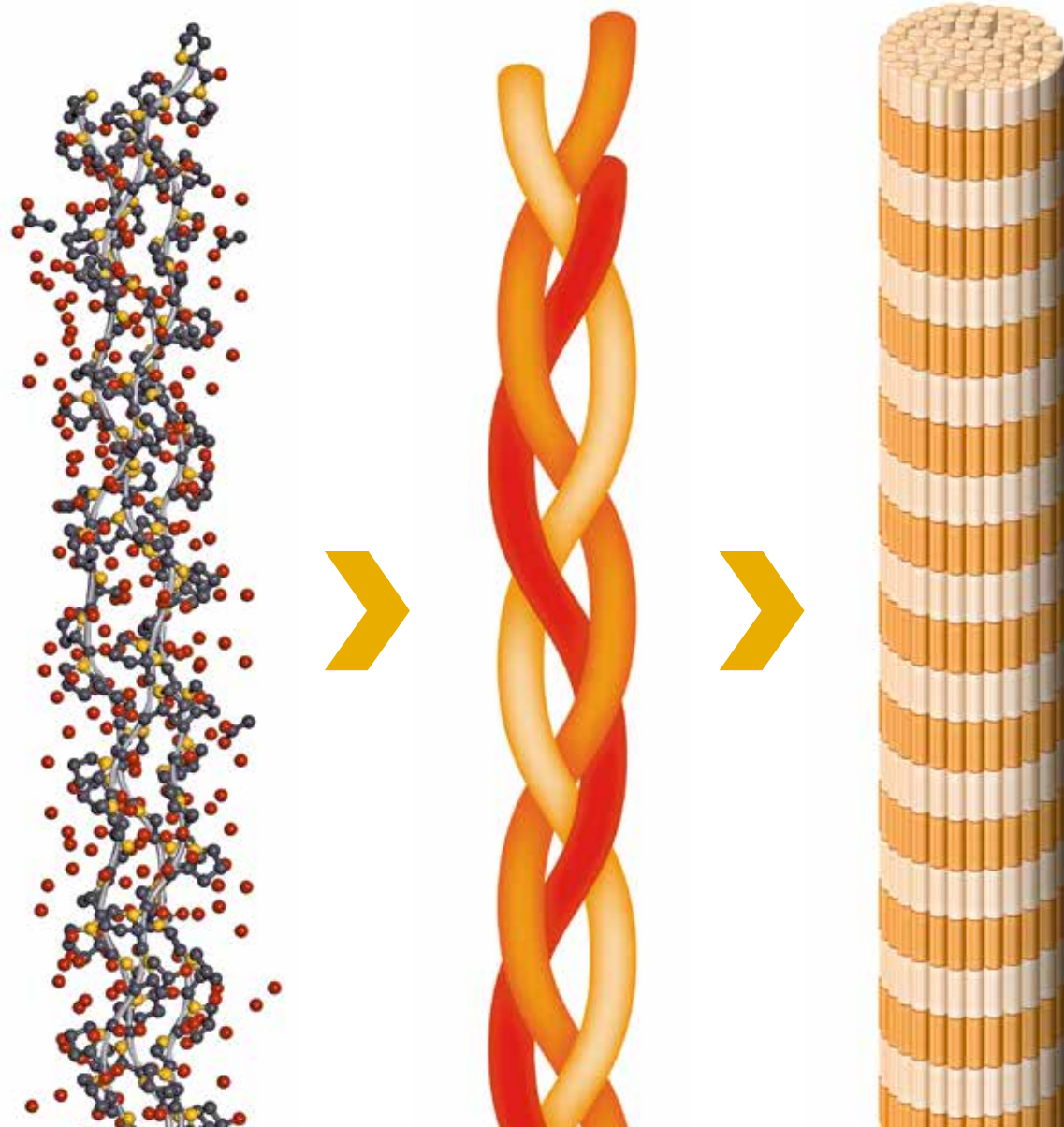
Always having a precise 360° view of what's going on and the amazing talent to adapt to changing circumstances promises protection and security in times of change and transformation.

Xenogeneic collagen products

Collagen is highly conserved throughout evolution, meaning that xenogeneic collagen is very similar to that of humans and generally tolerated exceptionally well. Along with the donor species and the tissue used, there are a number of other factors that are critical for the properties of collagenous medical devices, with the procedures used during harvesting playing a role in which characteristics are highlighted in the product. Modern medicine is inconceivable without collagens and their use is one of many important therapeutic concepts.

Fibrillar collagens are proteins with a high tensile strength that are essential for structure formation and biomechanics in tissues.

Collagen has positive effects in healing. In the early phases, it has intrinsic hemostatic properties while also being able to absorb large volumes of fluid, thus helping to create a moist wound environment that encourages healing^[3].



[3] Kujath P, Michelsen A. Wounds – From Physiology to Wound Dressing. Deutsches Ärzteblatt International Dtsch Arztebl Int (2008) 105;13: 239–4

Properties of xenogeneic collagens

Conserved throughout evolution

Intrinsic hemostatic properties

Ability to integrate into the surrounding tissue

Adaptable properties resulting from the processing method



Function and use in regeneration

Significant similarity between human and xenogeneic collagens leads to outstanding tolerance of xenogeneic collagens

Collagen can act as a substrate for platelet binding^[4]

Thanks to the good tolerance of xenogeneic collagens, they are generally integrated into the surrounding tissue and broken down by physiological catabolic processes.

Tear-resistant fibrillar collagen can be processed to produce a number of sophisticated medical devices with different properties—including:

- Non-adherent thin barrier membranes
- Porous collagen sponges having intrinsic hemostatic properties to control minor bleeding
- In fibrillar form as an absorbent agent in the wound area because large volumes of fluid can be absorbed

[4] D. Rothamel, F. Schwarz, V. Stoldt, M. Herten, C. Kotthaus, J. Becker. In-vitro-Testung der Thrombozytenaggregation an zahnärztlich verwendeten kollagenen Hämostyptika. Mund- Kiefer- und Gesichtschirurgie 10(3):148-54 · May 2006

naturesQue ColTect P

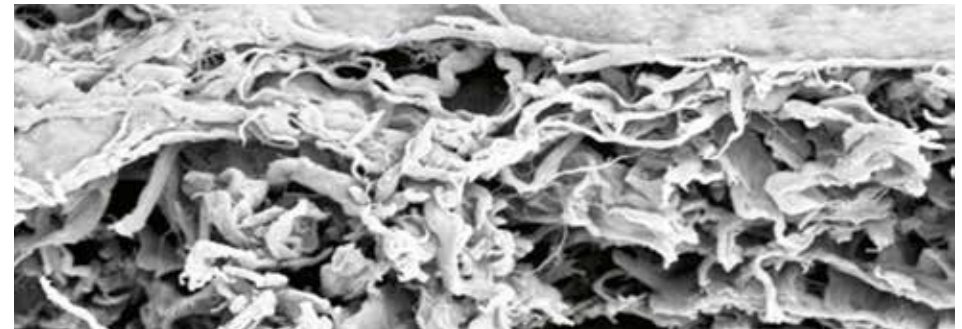


Assuming that the clinical requirements for a barrier membrane are satisfied, individual preferences for the handling properties play a major role in the choice of collagen membranes. The easy handling of naturesQue ColTect P enables diverse applications in therapeutic concepts that include the use of regenerative measures.

Structure, design, and stability

naturesQue ColTect P is manufactured from purified collagen-rich tissue. Using a gentle method, the collagen is minimally crosslinked to give the membrane a predictable resorption profile with maximum tissue tolerability. A crosslinked structure prevents premature enzymatic cleavage of the collagen fibers and gives naturesQue ColTect P a reproducible and reliable barrier function that is adapted to the time profile of bone healing.

This produces a highly versatile and strong membrane with comfortable handling properties. naturesQue ColTect P is made up of a layer of intact collagen fibers. The membrane is not side specific.



ORIGIN

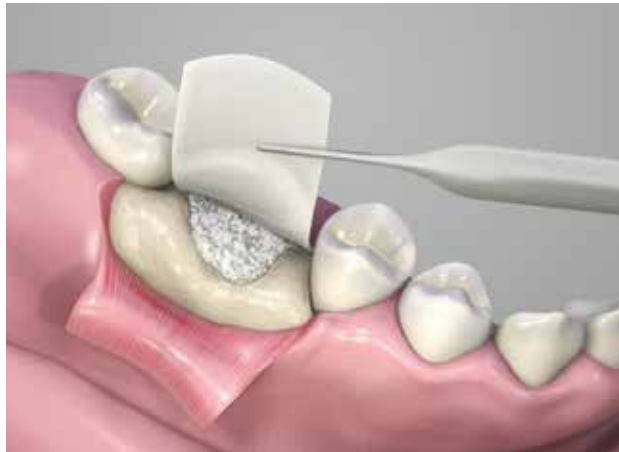
- Porcine peritoneum

COMPOSITION

- Intact collagen fibers
- Stabilized by reliable minimal crosslinking

PROCESSING

- Collagen-rich peritoneum
- Cleaning and removal of non-collagenous proteins
- Stabilization of the collagen fibers using minimal crosslinking
- Washing, rinsing, and drying
- Measurement, packaging, and sterilization
- Quality Control



Requirements profile for a collagen membrane

Collagen membranes alone do not have sufficient mechanical stability to shape and protect defect contours. For this reason *naturesQue ColTect P* is used together with bone substitute materials such as *naturesQue SemOss B* or *naturesQue MaxOss P*. The use of bone substitute materials creates a volumizing framework in the defect space that is used by the osteoblasts as a substrate for bone deposition.

A barrier membrane protects the spaces in the bone defect and prevents the ingrowth of soft tissues. The job of the membrane is to establish and maintain a barrier that is permeable to nutrients between the bone and soft tissue. The membrane also stabilizes the augmentation material by covering the bone defect. The barrier function of *naturesQue ColTect P* lasts about 3 months, which is sufficiently long to ensure adequate bone healing.

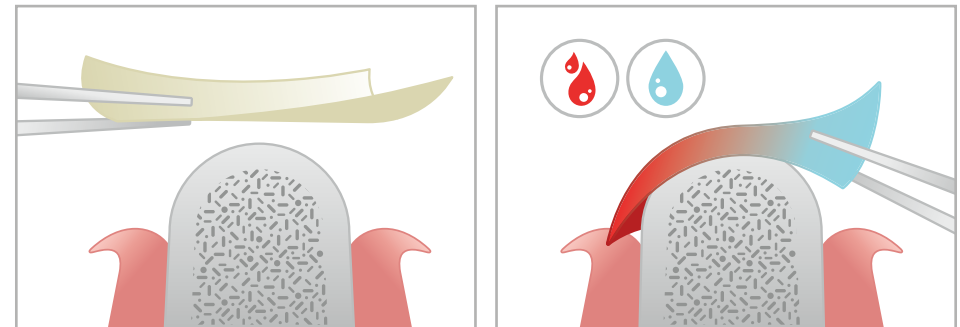
Handling and feel

The *naturesQue ColTect P* membrane can be applied wet or dry. The membrane is cut to size so that the piece overlaps the margin of the defect by about 2 mm. When dry, *naturesQue ColTect P* is a sturdy, stable membrane. Wetting the membrane with saline or blood makes *naturesQue ColTect P* flexible, enabling it to be adapted to the defect contours.

It is not usually necessary to fix *naturesQue ColTect P* because the membrane can be easily wetted and adheres to the bone walls.

Nevertheless, *naturesQue ColTect P* can be repositioned should this be necessary.

If needed, *naturesQue ColTect P* can be sutured or fixed with pins.



APPLICATION

- Remove with sterile instruments
- Processed wet or dry
- Adapt to the size of the defect, overlapping by about 2 mm
- Closed healing is recommended
- No specific side for positioning
- Can be repositioned

CONSISTENCY/FEEL

- Dry: Stable and rigid, sturdy
- Wet: Can be draped, sturdy, adhesive, not sticky
- Does not stretch
- Tear resistant

RESORPTION

- Resorption time between 12 and 16 weeks

naturesQue ColAid B



When applied as microfibrils the bovine collagen of naturesQue ColAid B has an extremely diverse range of uses. naturesQue ColAid B has the familiar intrinsic hemostatic properties of collagen and can be used to manage various indications. These include dental wounds and ulcers (not infected) and periodontal, surgical, and traumatic wounds.



Regeneration and the influence of the surrounding environment

An essential component of collagen is water—it makes up to 60% of the weight of collagen. In the physiological state the water molecules integrate seamlessly into the collagen molecule and follow its helical structure. naturesQue ColAid B is made up of purified, dried collagen that absorbs fluids and can form a viscous gel. This creates a moist wound environment that manages healing in which the wound space and the new tissue are protected.

Easy and comfortable to use

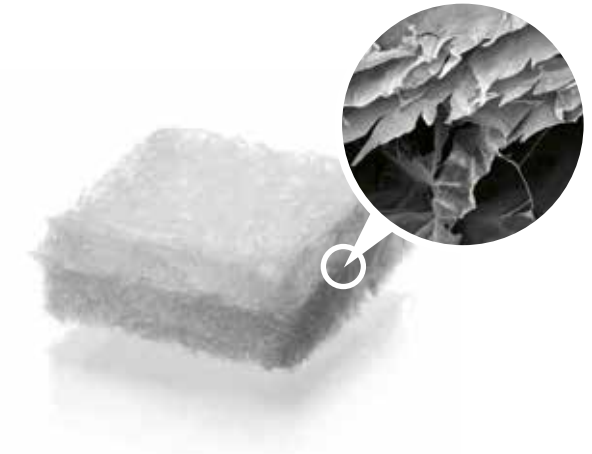
The bovine collagen microfibrils are available in single tubes in a storage box. It is easy to remove the microfibrils from the tube using forceps. naturesQue ColAid B is applied dry directly to the wound bed where it immediately absorbs fluid and transforms to a highly viscous gel.

ORIGIN/COMPOSITION	APPLICATION	CONSISTENCY/FEEL	RESORPTION
<ul style="list-style-type: none">• Bovine tissue• Purified microfibrillar collagen	<ul style="list-style-type: none">• Apply dry to the wound bed	<ul style="list-style-type: none">• The microfibrils are fluffy when dry and form a highly viscous gel when wetted	<ul style="list-style-type: none">• After about 2 weeks

naturesQue ColAid P



The formation of a stable blood clot is important for wound healing. When an open-pored collagen sponge is used, the outstanding hemostatic properties of collagen are at the forefront. Modern collagen sponges act as an initial matrix for tissue healing over the course of healing. The blood clot is stabilized in the defect and the subsequent steps in wound healing can proceed undisturbed.



Versatile and easy to use

Collagen sponges are suitable for a wide range of applications in both the treatment of soft tissue wounds and in small bony defects such as intact extraction sockets or after root tip resection. Collagen sponges can also be used to protect the sinus membrane during sinus floor elevation. The stable, open-pored sponge is cut to size and applied when dry.

Dimensions and regeneration

The special feature of sponge-like collagen products is their ability to absorb many times their own weight in fluid without changing their spatial dimensions. This means that they do not create any pressure or swelling in the defect. The delicately interwoven collagen fleece preserves and stabilizes the blood clot, acts as a matrix for migrating cells, and supports the generation of new tissue.

ORIGIN/COMPOSITION	APPLICATION	CONSISTENCY/FEEL	RESORPTION
<ul style="list-style-type: none"> • Porcine dermis • Purified collagen 	<ul style="list-style-type: none"> • Apply dry to the wound bed 	<ul style="list-style-type: none"> • When dry, the collagen fleece has a stable and porous spongy structure. • Wetted, it forms a pressure-sensitive 3D gel 	<ul style="list-style-type: none"> • Enzymatic after about 2–4 weeks

OVERVIEW OF REGENERATIVE MATERIALS

Art. No.	Product	Specification	Weight	Volume	Packages
naturesQue <i>SemOss B</i> • xenohybrid bovine bone substitute material					
58500	<i>SemOss B</i>	0.25–1.0 mm	0.25 g	0.5 ml	Vial
58501	<i>SemOss B</i>	0.25–1.0 mm	0.50 g	1.0 ml	Vial
58502	<i>SemOss B</i>	0.25–1.0 mm	1.00 g	2.0 ml	Vial
58503	<i>SemOss B</i>	0.25–1.0 mm	2.00 g	4.0 ml	Vial
58504	<i>SemOss B</i>	1.0–2.0 mm	0.50 g	1.0 ml	Vial
58505	<i>SemOss B</i>	1.0–2.0 mm	1.00 g	2.0 ml	Vial
58506	<i>SemOss B</i>	1.0–2.0 mm	2.00 g	4.0 ml	Vial
naturesQue <i>MaxOss P</i> • porcine bone substitute material					
58488	<i>MaxOss P</i>	0.25–1.0 mm	0.18 g	0.5 ml	Jar
58489	<i>MaxOss P</i>	0.25–1.0 mm	0.35 g	1.0 ml	Jar
58490	<i>MaxOss P</i>	0.25–1.0 mm	0.70 g	2.0 ml	Jar
58491	<i>MaxOss P</i>	0.25–1.0 mm	1.40 g	4.0 ml	Jar
58492	<i>MaxOss P</i>	1.0–2.0 mm	0.23 g	1.0 ml	Jar
58493	<i>MaxOss P</i>	1.0–2.0 mm	0.46 g	2.0 ml	Jar
58494	<i>MaxOss P</i>	0.25–1.0 mm	0.09 g	0.25 ml	Syringe
58495	<i>MaxOss P</i>	0.25–1.0 mm	0.18 g	0.5 ml	Syringe
naturesQue <i>ColTect P</i> • porcine barrier membrane					
58496	<i>ColTect P</i>	15×20 mm		1	Piece
58497	<i>ColTect P</i>	20×30 mm		1	Piece
58498	<i>ColTect P</i>	30×40 mm		1	Piece
naturesQue <i>ColAid B</i> • bovine collagen microfibrils					
58499	<i>ColAid B</i>		0.10 g	15	Vial
naturesQue <i>ColAid P</i> • porcine collagen fleece					
58507	<i>ColAid P</i>	20×20 mm		10	Piece



Hands become beautiful animals! Our regeneration products are represented by so-called „handimals“: These are animal paintings made with human hands. Created by the Milan artist Guido Daniele, they symbolize our credo: „The essence of nature in expert hands“.

Not all products of the naturesQue regeneration line are available throughout the world, depending on authorities' approvals. For more information, please consult your local BEGO Implant Systems sales partner.



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