HYPRO-OSS & HYPRO-SORB

Innovative Bovine Biomaterials for Implantology, Periodontology and Maxillofacial Surgery

bioimplon Biotech Innovation Pioneers

Letter from the General Manager

Dear clinical user,

Bioimplon's focus is to develop, manufacture and market unique native bovine products in the cutting edge field of regenerative medicine. Our extensive product offerings cover the fields of bone and tissue regeneration, tissue engineering and wound healing for dental, spinal, orthopaedic and dermatologic applications. They are used by oral and maxillofacial surgeons, periodontists and dental implantologists as well as by orthopaedic and spinal surgeons.

Patient safety, ease of use, reliable and predictable treatment results are our first priorities. Our products have proven their success in safety, efficacy, reliability and superior handling characteristics in clinical studies and documented cases as well as in the daily clinical work with many hundred thousands of patients worldwide.

In addition to our Hypro-Sorb® membranes, matrices and cones as well as Hypro-Oss® bovine bone substitution and regeneration material, the company has developed a future-oriented product pipeline. These products contain moldable bone graft blocks an injectable gel forms that we will launch in the near future.

We thank our customers worldwide for positive feedback and invite you to share with us your experiences and suggestions for improvements.

Dr. med. Sami Watad

General Manager
Bioimplon GmbH

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Bioimplon

Bovine biomaterials for your needs

Bioimplon GmbH is one of the leaders in the development, manufacture, and distribution of innovative regenerative biomaterials for the medical and dental fields. Our product portfolio includes:

- Bone substitute material
- Membranes for guided bone and tissue regeneration (GBR / GTR)
- Collagen matrices for GBR / GTR and haemostasis
- Haemostatic sponges and cones

Our biomaterials are indicated for use in the following dental fields:

Implantology

Maxillofacial Surgery

Periodontology

We continuously invest in research and development and trust in our qualified and specialized employees.

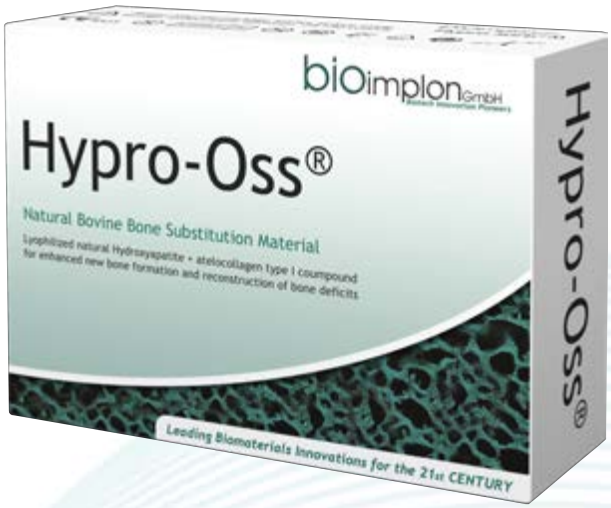
All our products contain Atelo-Collagen Type I of bovine origin. Our membranes, matrices, and sponges are made entirely of this modified, non-immunogenic collagen.

HYPRO-OSS®: The patented bone graft innovation was developed by scientific teams of Bioimplon GmbH and Hypro s.r.o. It is the first native bovine bone substitute material that is composed of about 30% Atelo-Collagen Type I integrated within the hydroxyapatite particles of each bone granule structure. The bone graft is manufactured using a lyophilization processing technology, atelopeptidized, and biocompatible. It has been histologically proven that Hypro-Oss completes a high quality new bone formation within a very short period of time.

HYPRO-SORB®: The range of our Atelo-Collagen Type I - portfolio includes a large variety of shapes and sizes for a diverse field of applications. All Hypro-Sorb products consist of 99.9% pure Atelo-Collagen Type I – a biocompatible, non-immunogenic collagen free of telopeptides. The source of the Atelo-Collagen Type I is the bovine Achilles tendon. Atelo-Collagen Type I is the most effective haemostatic product with bacteriostatic effect. The Hypro-Sorb portfolio is the result of many years of experience and an intensive research cooperation between Bioimplon and Hypro s.r.o.

Hypro-Oss®

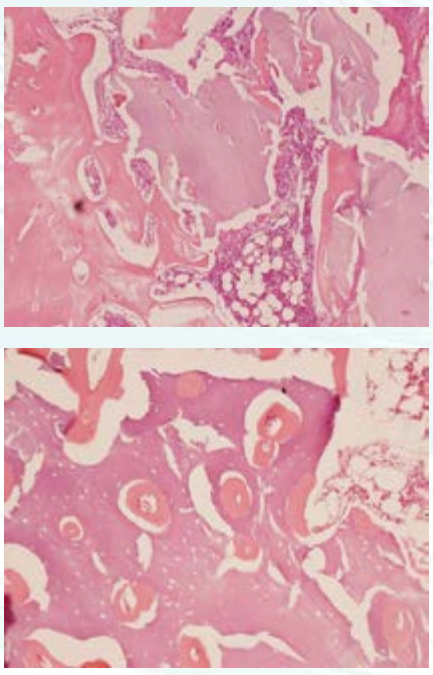
Hypro-Oss® is a natural bovine bone substitute material with incorporated Atelo-Collagen Type I. It is used for the permanent filling or reconstruction of antiseptic bone defects.



Hypro-Oss
Properties and advantages

Hypro-Oss is produced with our patented atelopeptidation and lyophilization technologies. These result in the following important characteristics:

- Native bovine bone graft composite for enhanced new bone formation
- Telopeptide-free collagen components; non-immunogenic peptide
- Acceleration of physiological tissue healing process
- Protects grafting site from infection (bacteriostatic effect of Atelo-Collagen Type I)
- Hydrophilic property: optimal cell adhesion and blood absorption
- Capability to carry medication to the surgical site
- Highest biocompatibility: absence of any foreign body response
- Natural structure of collagen and hydroxyapatite due to lyophilization processing
- Osteopromotive Atelo-Collagen Type I components and osteoconductive hydroxyapatite components
- Native crystalline structure guarantees long-term dimensional stability
- Powerful haemostatic effect of the Atelo-Collagen Type I averts heamatoma formation after surgical procedures
- Consistent availability and safety
- Reliable clinical results
- No need for autograft harvesting
- Lyophilized bovine bone has a very similar composition to human



Hypro-Oss intraosseous implantation in beagle dogs – Histology after 14 weeks

These characteristics allow enhanced and consistent new bone formation, and persistent integration between mature new formed bone and existing bone materials.

Bovine bone substitute

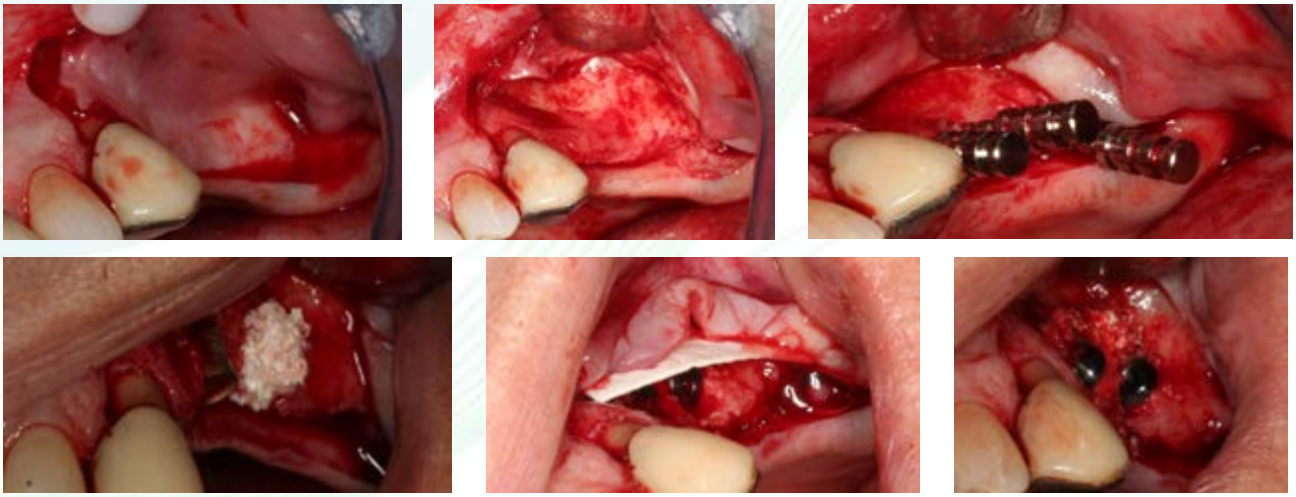
Hypro-Oss grain size: 1.0 - 2.0 mm

Hypro-Oss grain size: 0.5 - 1.0 mm

Hypro-Oss

Indications in implantology, periodontology and maxillofacial surgery:

- Sinus lift
- Vertical and horizontal augmentation
- Intraosseous defects
- Peri-implant defects
- Extraction sockets
- Furcation defects
- Filling of cysts
- Periodontal defects



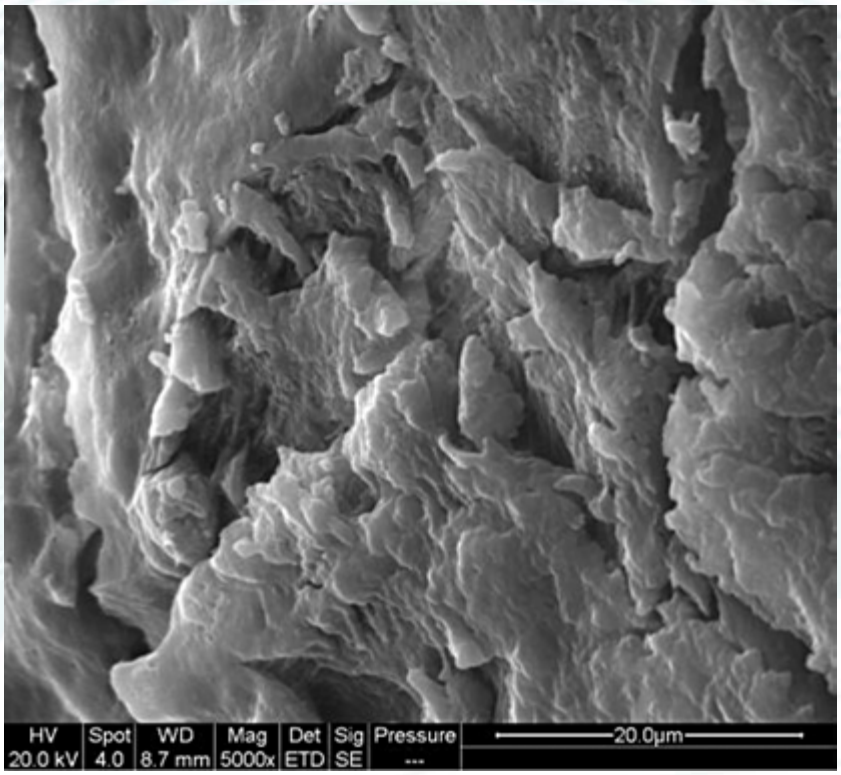
Hypro-Oss used together with Hypro-Sorb F. Images courtesy of Dr. Amir Gazmawe DMD Prosthodontist

Hypro-Oss
Composition

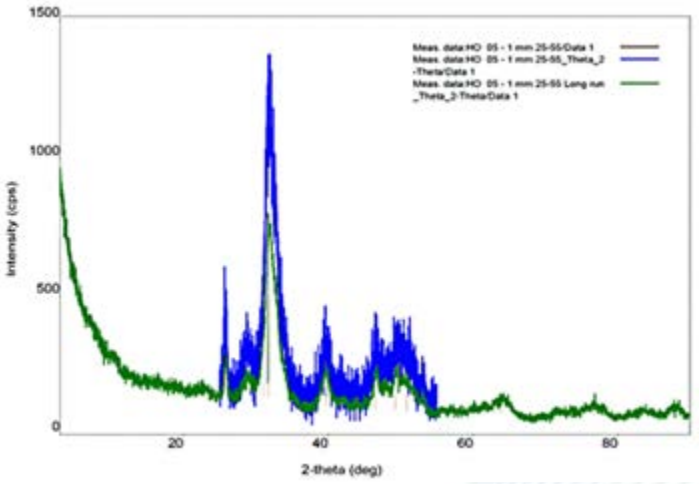
Hypro-Oss is a natural bovine bone graft. Each granule consists of approximately 70% hydroxyapatite and 30% Atelo-Collagen Type I. It is sterile and safe.

Readings	Human (%)	CI*95%	Bovine (%)	CI*95%
Fat	0.06	0.1	0.1	0.1
Nitrogen	4.3	0.1	4.3	0.1
Proteins	27.5	0.2	27.2	0.2
Phosphorus	11.9	0.1	11.9	0.2
Total P205	27.1	0.2	27.2	0.7
Calcium	24.6	0.7	23.7	0.6
Total Sodium	0.57	0.01	0.46	0.01
Ashes	64.8	0.6	64.3	0.1
Chlorides	1.3	0.06	1.3	0.2
Water	7.93	-	7.75	-
Ca/P	2.06	-	1.99	-

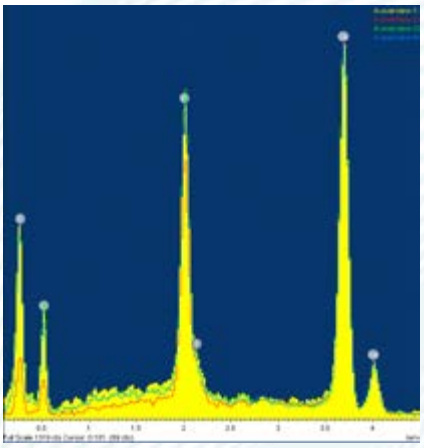
Chemical composition: Human bone in comparison to lyophilized bovine bone



Hypro-Oss – Electron microscopy



Hypro-Oss – X-ray diffraction



Hypro-Oss – Energy dispersive spectoscropy (EDS)

Hypro-Oss

Available sizes and volumes

Product Name / Description	Cat. No.	Granule Size	Volume
Hypro-Oss Natural bovine bone graft with incorporated Atelo-Collagen Type I	070	0.5 – 1.0 mm	0.5 ml
	071		1.0 ml
	072		3.0 ml
	073		5.0 ml
	090		25 ml
	074	1.0 – 2.0 mm	0.5 ml
	075		1.0 ml
	076		3.0 ml
	077		5.0 ml
	091		25 ml

Storage conditions

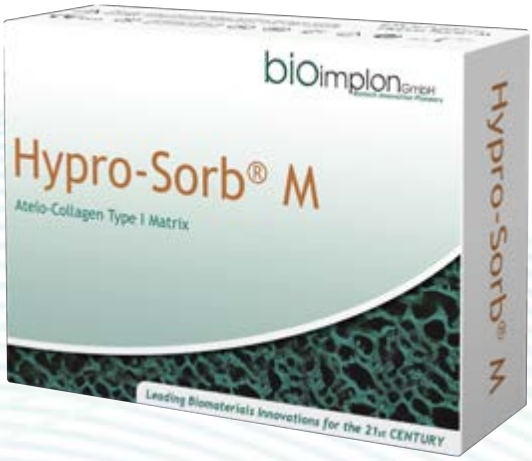
Hypro-Oss must be stored in a dry place at room temperature. Hypro-Oss is not damaged by temperatures from 0°C to +50°C. It needs to avoid sources of heat and direct sunlight.

Hypro-Oss is a sterile medical device class III, ISO and CE certified.

Hypro-Sorb® M Matrix

Our multilayer Atelo-Collagen Type I matrix for guided tissue regeneration in periodontology and maxillofacial surgery

The Hypro-Sorb® M Matrix is a multilayer tissue matrix of pure, crystalline Atelo-Collagen Type I (telopeptide-free collagen) derived from the bovine Achilles tendon. The Hypro-Sorb M Matrix supports neovascularization and controlled soft tissue integration and is a safe alternative to the patients' own soft tissue grafting material. In addition, it has an excellent barrier function due to the solid collagen structure and long resorption time of six months. The Hypro-Sorb M Matrix was conceived and developed by researchers of Bioimplon GmbH and Hypro s.r.o.



multilayer, native, resorbable

Mechanism of regeneration and remodeling kinetics

After placement, the patient's blood infiltrates the Hypro-Sorb M Matrix graft through the three-dimensional multilayer soft tissue structure, bringing host cells to the soft tissue graft surface and starting the neovascularization process. Significant neovascularization can begin after implantation depending on the patient's health condition.

Regeneration is a heterogeneous process occurring at the interface of solid Atelo-Collagen Type I and fluid (blood, wound exudate). The kinetics of the heterogeneous processes depends primarily on the interface area and – as a consequence – on the correlation with the internal surface area of the Atelo-Collagen Type I Matrix. The internal surface area of the Hypro-Sorb M Matrix exceeds 150,000 cm^2/cm^2, which is one of the highest known values among similar products worldwide

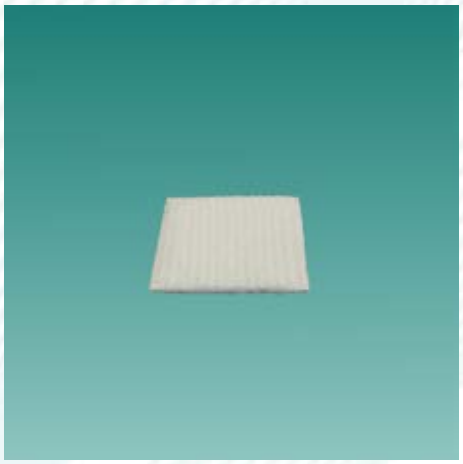
The natural specific affinity of Atelo-Collagen Type I to thrombocytes results in the release of agglutination factors and growth factors such as IGF I, TGF-beta, PDGF, which in combination with blood plasma factors promote the regeneration of the soft tissue. In addition, Atelo-Collagen Type I inhibits the serine proteinase of exudate and promotes granulation and epithelisation.

Moreover, the implanted Hypro-Sorb M Matrix is absorbed within six months. Read more about the resorption process in *Resorption of Atelo-Collagen Type I* on page 19.

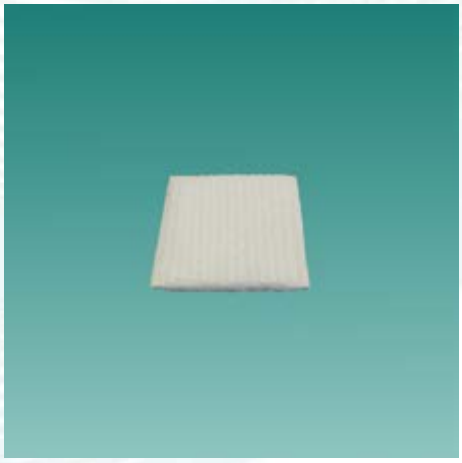
Guided tissue regeneration

Hypro-Sorb M Matrix
Advantages

- Consistent availability and safety
- No need for autograft harvesting
- High patient acceptance
- Reliable clinical results
- Cost effective



Hypro-Sorb M Matrix – 20 x 25 x 2 mm



Hypro-Sorb M Matrix – 25 x 25 x 2 mm

Hypro-Sorb M Matrix
Properties

- Biocompatible pure, crystalline Atelo-Collagen Type I - free of antigenic telopeptides
  (for more information on etelocollagen, see the chapter *About Atelo-Collagen Type I)*
- Multilayer soft tissue structure
- Rapid neovascularization and integration
- Accelerates soft tissue replacement without the need for autograft harvesting
- Complete remodeling into patients' own tissue
- Excellent barrier function
- Resorption time of approximately six months
- Easy handling, can be easily applied and fixed
- Can be cut to shape for specific procedures
- Sterile for five years, safe and resorbable

Hypro-Sorb M Matrix

Indications

- Maxillofacial and periodontal surgery
- Treatment of gingival recession
- Sinus lifting
- Segmental growing of the alveolar tissue
- Periimplantitis
- Furcation treatment
- Vertical and segmental augmentation
- Cleft lip and palate

Hypro-Sorb M Matrix – 25 x 50 x 2 mm

Hypro-Sorb M Matrix

Handling instructions

1. Trim the matrix to the size you need using scissors.
2. The matrix should overlap the walls of the defect by at least 2-3 mm in order to achieve complete coverage of the bone and thus prevent lateral ingrowth of gingival tissue.
3. The defect cavity is then filled loosely with bone substitute material such as Hypro-Oss.
4. The matrix is applied over the defect with its smooth side turned towards the soft tissue and held in place with moderate pressure. The saturation of the matrix with blood and exudate permits perfect adaptation to the bone surface. Additional stabilization by pins may be indicated for complex defects.
5. The flaps are closely sutured over the matrix and should be free of tension. The wound should, whenever possible, be completely closed.
6. During the healing phase, stress in the wound area from prosthetic pressure or palpation should be avoided. Intensive mechanical oral hygiene should be replaced by antibacterial rinsing (e.g. with chlorhexidine) for the first three weeks. Antibiotic therapy is prescribed at the discretion of the clinician.

Hypro-Sorb M Matrix

Available sizes

Product Name / Description	Cat. No.	Product Size	Pieces / Package
Hypro-Sorb M Matrix Bovine Atelo-Collagen Type I matrix	039	20 x 25 x 2 mm	6
	040	25 x 25 x 2 mm	1
	041	25 x 50 x 2 mm	1

Composition

Natural pure (99.9%), crystalline, multilayer Atelo-Collagen Type I tissue structure of bovine Achilles tendon.

Storage conditions

The Hypro-Sorb M Matrix must be stored in a dry place at room temperature. It is not damaged by temperatures between -25°C to +50°C. It must be protected from direct sunlight and heat. The product is sterile for five years.

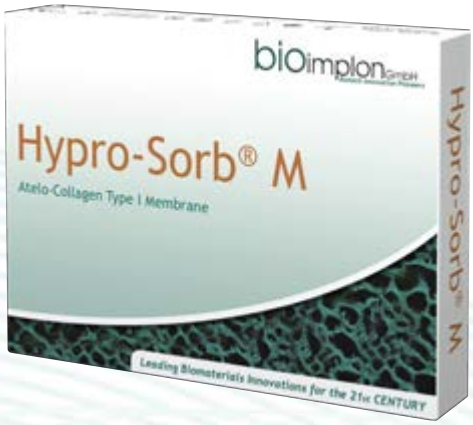
Hypro-Sorb M is a medical device class III, ISO and CE certified.

Hypro-Sorb® M and F

Our natural Atelo-Collagen Type I membranes for guided tissue and bone regeneration in maxillofacial surgery and implantology

Hypro-Sorb® M membranes are biphasic, bilayer membranes of pure, crystalline Atelo-Collagen Type I of bovine origin. They come in three different sizes and two convenient thicknesses.

The membranes differ with regards to their handling: The 0.8 mm thick Hypro-Sorb M membrane is soft, whereas the 0.3 mm thick Hypro-Sorb M membrane is medium rigid. Due to the special processing of the collagen fibers it is not necessary to soak these membranes with saline or the patient's blood before application.



biphasic, native, resorbable

bilayer, native, resorbable

Hypro-Sorb®F is rigid, bilayer membrane of pure, crystalline Atelo-Collagen Type I derived from the bovine Achilles tendon. It is the most rigid membrane in our portfolio and comes in three different sizes.

Hypro-Sorb F is 0.2 mm thick with high tensile and bending stength due to densely packed collagen fibers. Therefore, it is recommended to soak the membrane with saline or the patient's blood for at least 1 minute before application to facilitate handling.

The membranes are the result of many years of experience and an intensive research collaboration between scientific teams of Hypro s.r.o. and Bioimplon GmbH.

Membranes

Guided tissue and bone regeneration

Hypro-Sorb M and F Membranes

Properties and advantages

As all our membranes consist of Atelo-Collagen Type I and have been lyophilized, they share the following characteristics:

- Pure, crystalline Atelo-Collagen Type I – free of telopeptides
- Highest degree of tissue biocompatibility with excellent wound healing characteristics
- Quick adaptation to the defect due to its potent hydrophilic properties
- Reduced risk of dehiscence formation due to the texture and mild bacteriostatic effect of Atelo-Collagen Type I
- Can be attached with pins and suturing material
- Sufficiently long barrier function – membranes stay intact for the first six weeks
- Naturally resorbable within six months
- Long shelf life – safe and sterile for five years after production
- Consistent availability and safety
- Reliable clinical results
- Unmistakable rough and smooth sides

Rough side of Hypro-Sorb M

Hypro-Sorb M and F Membranes

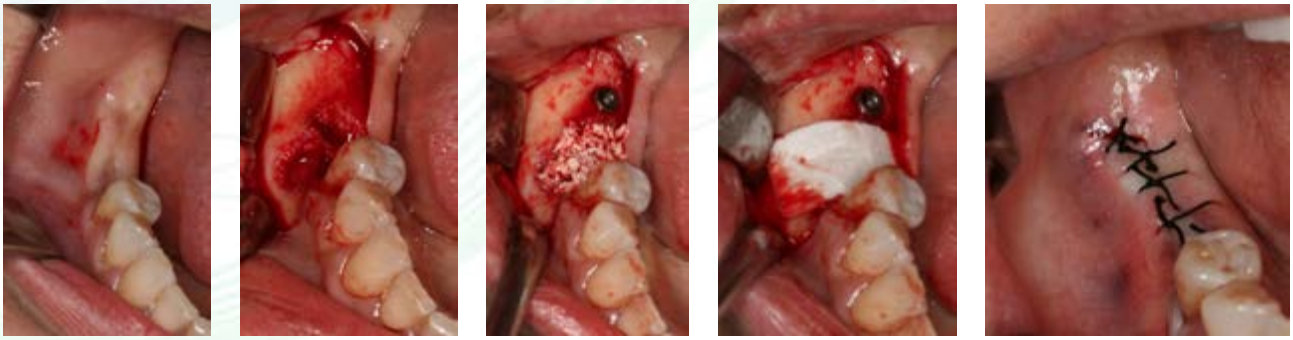
Indications

Smooth side of Hypro-Sorb M

All our membranes can be used for the following indications:

- Sinus Lifting
- Segmental growing of the alveolar tissue
- Periimplantitis
- Furcation treatment
- Vertical and segmental augmentation
- Cystectomy
- Maxillofacial and Periodontal surgery
- Cleft lip and palate

However, periodontists tend to prefer Hypro-Sorb M, whereas Hypro-Sorb F is often favoured by maxillofacial surgeons.

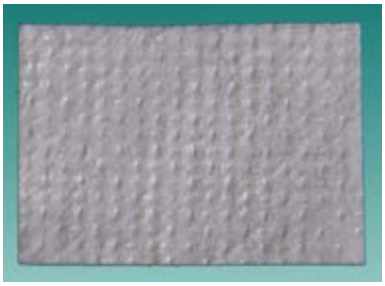


Application of Hypro-Sorb® M and Hypro-Oss® – Images courtesy of Dr. Labazanov Ashab, Maxillofacial Surgeon, Moscow, Russia

Hypro-Sorb M and F Membranes

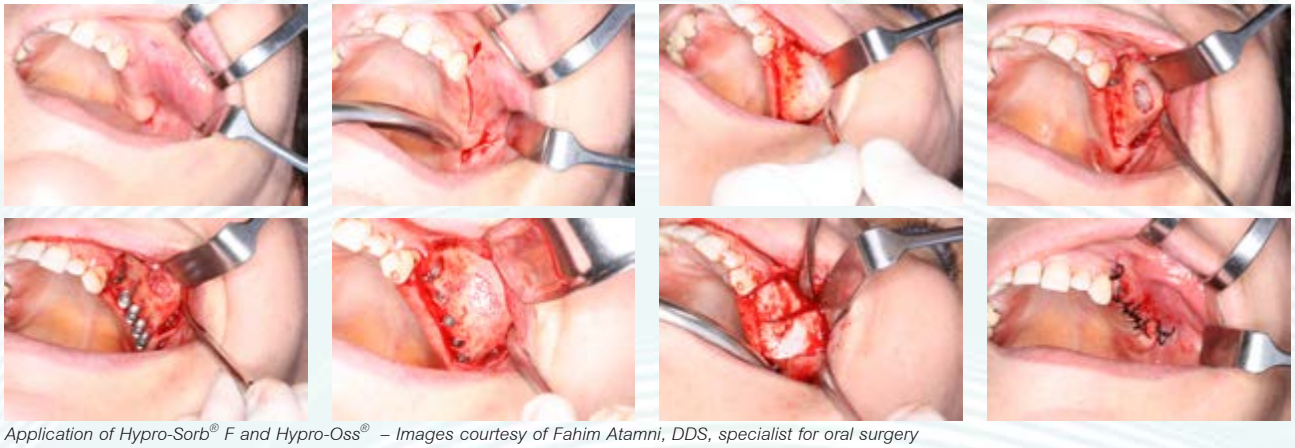
Handling instructions

1. Trim the membrane to the size you need using scissors.
2. The membrane should overlap the walls of the defect by at least 2-3 mm in order to achieve complete coverage of the bone and thus prevent lateral ingrowth of gingival tissue.
3. The defect cavity is then filled loosely with bone substitute material such as Hypro-Oss.
4. The membrane is applied over the defect with its smooth side turned towards the soft tissue and held in place with moderate pressure. The saturation of the membrane with blood and exudate permits perfect adaptation to the bone surface. Additional stabilization by pins may be indicated for complex defects.
5. The flaps are closely sutured over the membrane and should be free of tension. The wound should, whenever possible, be completely closed.
6. During the healing phase, stress in the wound area from prosthetic pressure or palpation should be avoided. Intensive mechanical oral hygiene should be replaced by antibacterial rinsing (e.g. with chlorhexidine) for the first three weeks. Antibiotic therapy is prescribed at the discretion of the clinician.



Rough side of Hypro-Sorb F

Smooth side of Hypro-Sorb F



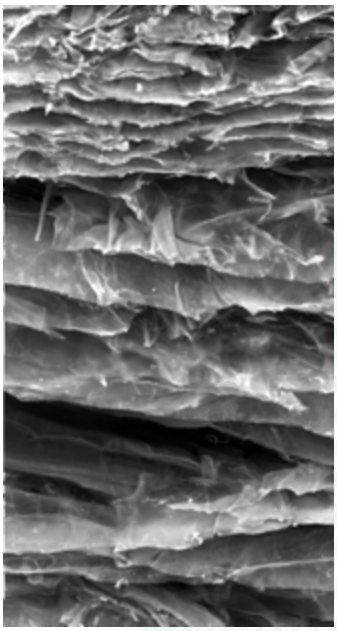
Application of Hypro-Sorb® F and Hypro-Oss® – Images courtesy of Fahim Atamni, DDS, specialist for oral surgery

Postoperative care

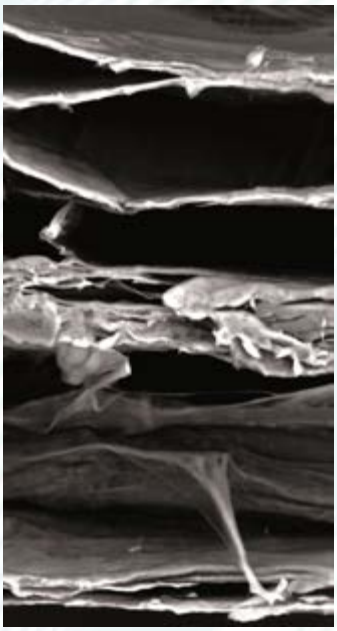
In case of wound dehiscence with membrane exposure, the usual antimicrobial precautions are recommended. Removal of the membrane is not necessary. The resorption time may be accelerated by external influences such as saliva, etc. The properties of collagen may favour a rapid healing of the wound dehiscence.

Composition

Natural pure (99.9%), crystalline Atelo-Collagen Type I tissue structure of bovine Achilles tendon.



Hypro-Sorb M: Electron microscope image



Hypro-Sorb F: Electron microscope image

Hypro-Sorb M and F Membranes

Available sizes

Product Name / Description	Cat. No.	Product Size	Pieces / Package
Hypro-Sorb F Bovine Atelo-Collagen Type I membrane (rigid)	023	15 x 20 x 0.2 mm	1
	024	20 x 30 x 0.2 mm	1
	025	30 x 40 x 0.2 mm	1
Hypro-Sorb M Bovine Atelo-Collagen Type I membrane (medium-rigid)	035	16 x 20 x 0.3 mm	1
	036	22 x 32 x 0.3 mm	1
	037	32 x 42 x 0.3 mm	1
Hypro-Sorb M Bovine Atelo-Collagen Type I membrane (soft)	030	16 x 20 x 0.8 mm	1
	031	22 x 32 x 0.8 mm	1
	032	32 x 42 x 0.8 mm	1

Storage conditions

Hypro-Sorb M and F must be stored in a dry place at room temperature. They are not damaged by temperatures between -25°C to +50°C. It must be protected from direct sunlight and heat. The product is sterile for five years.

Hypro-Sorb M and F are medical devices class III, ISO and CE certified.

Hypro-Sorb® R

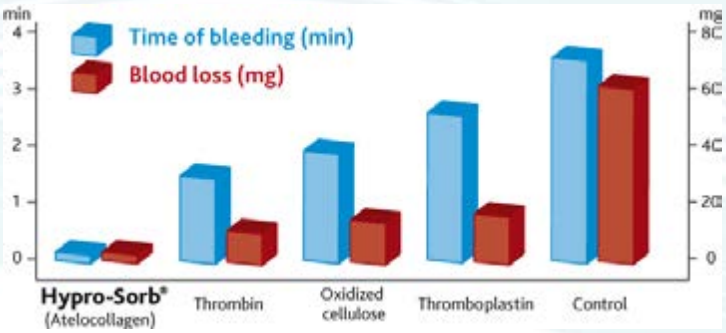
Our natural Atelo-Collagen Type I sponge for an effective haemostasis and wound regeneration

Hypro-Sorb R® is a range of bioabsorbable haemostatic sponges of pure, crystalline Atelo-Collagen Type I of bovine origin (for more information on Atelo-Collagen Type I in general and how it induces haemostasis in particular, see the chapter *About Atelo-Collagen Type I*).

Hypro-Sorb R

Properties and advantages

- Haemostatic sponge of pure, crystalline Atelo-Collagen Type I of bovine origin – free of antigenic telopeptides
- Highest degree of tissue biocompatibility and safety with excellent wound-healing characteristics
- Most effective haemostatic material with bacteriostatic effect
- Usable in infected wounds or with medically compromised patients
- Can be cut to size without loss of haemostatic properties
- Resorbs spontaneously within two to four weeks
- Available in a large variety of shapes and sizes
- Long shelf life – safe and sterile for five years



Atelo-Collagen Type I haemostatics are fastest in helping achieve haemostasis and reduce blood loss substantially better than other haemostatic materials, when stopping parenchymatous bleeding from surgically cut liver.

Hypro-Sorb R

Indications

Hypro-Sorb R is indicated for the control of capillary and parenchymatous bleeding in maxillofacial surgery. It can also be used as resorbable cyst filling in surgery, stomatology and traumatology.

Haemostatic sponges

Hypro-Sorb R
Handling instructions

1. Hypro-Sorb R is applied usually with its smooth side into the wound surface, softly pressed down and left on the wound until the fibrin adhesion develops.
2. Bleeding usually stops in two to five minutes; it lasts longer in haemophiliacs.
3. Usually it is used in dry state but it may also be moistened with sterile saline solution.
4. It should be used in amounts which fully cover the wounded surface. It is recommended that the surgeon remove the excess felt before closing the wound or leave only the minimum amount in the tissue because it slightly swells and it could exert pressure on the vicinity of the wound.

Hypro-Sorb R
Available sizes

Product Name / Description	Cat. No.	Product Size	Pieces / Package
Hypro-Sorb R Pure crystalline bovine Atelo-Collagen Type I fleece for haemostasis	003	20 x 25 x 4 mm	6
	013	50 x 50 x 4 mm	1
	006	10 x 10 x 10 mm	10

Hypro-Sorb R 20 x 25 x 4 mm

Hypro-Sorb R 10 x 10 x 10 mm

Hypro-Sorb R 50 x 50 x 4 mm

Composition

Natural pure (99.9%), crystalline Atelo-Collagen Type I tissue structure of bovine Achilles tendon.

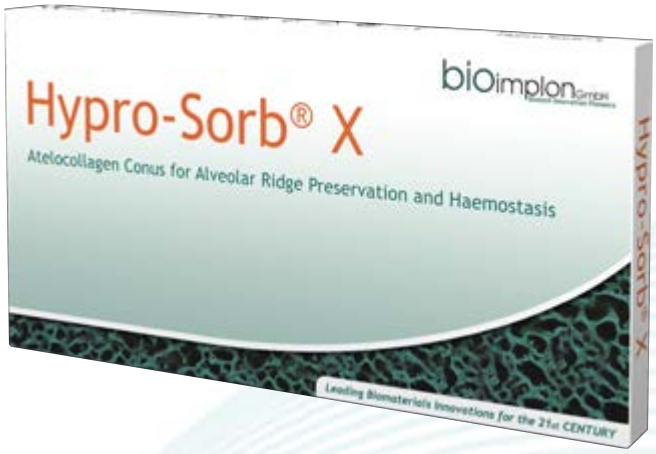
Storage conditions

Hypro-Sorb R must be stored in a dry place at room temperature. It is not damaged by temperatures between -25°C to +50°C. It must be protected from direct sunlight and heat. The product is sterile for five years.

Hypro-Sorb R is a medical device class III, ISO and CE certified.

Hypro-Sorb® X and Z

Our natural Atelo-Collagen Type I cones for the preservation of the alveolar ridge and an effective haemostasis



Hypro-Sorb® X and Z are root-shaped cones of pure, crystalline, bovine Atelo-Collagen Type I that are indicated to stop the bleeding after tooth extraction and to help preserve the alveolar ridge (for more information on Atelo-Collagen Type I in general and how it induces haemostasis in particular, see the chapter *About Atelo - Collagen Type I*).

Hypro-Sorb X and Z

Properties and advantages

- Haemostatic cones of pure, crystalline Atelo- Collagen Type I of bovine origin - free of antigenic telopeptides
- Highest degree of tissue biocompatibility and safaty with exellent wound-healing characteristics
- Usable in infected wounds or with medically compromised patients
- The special shape of the cones (Ø6mm x 20 mm x Ø10mm, and Ø3mm x 15mm x Ø6mm respectively) is an excellent matrix for the bone formation after tooth extraction
- Accelerated soft tissue healing
- Potent haemostatic effect
- Can be cut to size without loss of haemostatic property
- Resorbed within two to four weeks
- Long shelf-life, sterile and safe for five years after production

Hypro-Sorb X

Hypro-Sorb X and Z

Indications

- Control of capillary and parenchymatous bleeding
- Haemostasis after tooth extraction in stomatology
- Closure of extraction sites
- Alveolar ridge preservation
- Control of bleeding in extraction sockets or biopsy site

Alveolar ridge preservation and haemostasis

Hypro-Sorb X and Z

Handling instructions

1. Hypro-Sorb X and Z are applied usually with the smooth side onto the wound surface, softly pressed down and left on the wound until the fibrin adhesion develops.
2. Bleeding usually stops in two to five minutes; it lasts longer in haemophiliacs.
3. Usually it is used in dry state but it may also be moistened with sterile saline solution.
4. The cones should be used in amounts which fully cover the wounded surface. It is recommended that the surgeon remove the excess felt before closing the wound or leave only the minimum amount in the tissue because it slightly swells and it could exert pressure on the vicinity of the wound.

Hypro-Sorb Z

Hypro-Sorb X and Z

Available sizes

Product Name / Description	Cat. No.	Product Size	Pieces / Package
Hypro-Sorb X Atelo-Collagen Type I conus for alveolar ridge preservation and heamostasis	014	Ø6 x 20 x Ø10 mm	10
Hypro-Sorb Z Atelo-Collagen Type I mini-conus for alveolar ridge preservation and heamostasis	009	Ø3 x 15 x Ø6 mm	10

Composition

Natural pure (99.9%), crystalline Atelo-Collagen Type I tissue structure of bovine Achilles tendon.

Storage conditions

Hypro-Sorb X and Z must be stored in a dry place at room temperature. They are not damaged by temperatures between -25°C to +50°C. They must be protected from direct sunlight and heat. The product is sterile for five years.

Hypro-Sorb X and Z are medical devices class III, ISO and CE certified.

Dental portfolio

	Product Name	Cat. No.	Granule Size	Volume
Bone Regeneration	**Hypro-Oss** Natural bovine bone graft with incorporated Atelo-Collagen Type I indicated for - dental and - maxillofacial surgery	70	0.5 – 1.0 mm	0.5 ml
		71		1.0 ml
		72		3.0 ml
		73		5.0 ml
		90		25 ml
		74	1.0 – 2.0 mm	0.5 ml
		75		1.0 ml
		76		3.0 ml
		77		5.0 ml
		91		25 ml

	Product Name / Description	Cat. No.	Product Size	Pcs. per Package
Membranes for GBR/GTR in Dental and Maxillofacial Surgery	**Hypro-Sorb F** Bovine Atelo-Collagen Type I memebrane (rigid)	23	15 x 20 x 0.2 mm	1
		24	20 x 30 x 0.2 mm	1
		25	30 x 40 x 0.2 mm	1
	Hypro-Sorb M Bovine Atelo-Collagen Type I membrane (medium-rigid)	35	16 x 20 x 0.3 mm	1
		36	22 x 32 x 0.3 mm	1
		37	32 x 42 x 0.3 mm	1
	Hypro-Sorb M Bovine Atelo-Collagen Type I membrane (soft)	30	16 x 20 x 0.8 mm	1
		31	22 x 32 x 0.8 mm	1
		32	32 x 42 x 0.8 mm	1

	Product Name / Description	Cat. No.	Product Size	Pcs. per Package
Matrix for GTR in Periodontal and Maxillofacial Surgery	**Hypro-Sorb M Matrix** Bovine Atelo-Collagen Type I matrix	39	20 x 25 x 2 mm	6
		40	25 x 25 x 2 mm	1
		41	25 x 50 x 2 mm	1

	Product Name / Description	Cat. No.	Product Size	Pcs. per Package
Haemostatic Biomaterials	**Hypro-Sorb R** Pure crystalline bovine Atelo-Collagen Type I fleece for haemostasis in - maxillofacial and - dental surgery	3	20 x 25 x 4 mm	6
		13	50 x 50 x 4 mm	1
		6	10 x 10 x 10 mm	10
	Hypro-Sorb X Atelo-Collagen Type I conus for alveolar ridge preservation and haemostasis	14	Ø6 x 20 x Ø10 mm	10
	Hypro-Sorb Z Atelo-Collagen Type I mini-conus for alveolar ridge preservation and Haemostasis	9	Ø3 x 15 x Ø6 mm	10

About Atelo-Collagen Type I

What is Atelo-Collagen Type I?

Atelo-Collagen Type I is a specifically modified type of collagen that has been freed from immunogenic telopeptides during the process of atelopetidation.

Pure, crystalline Atelo-Collagen Type I structure

What is atelopeptidation?

Atelopeptidation is a term that describes the physicochemical deletion of the immunogenic/antigenic terminal peptide sequence (telopeptide) in a collagen molecule. The resulting modified collagen is called an Atelo-Collagen Type I, a safe non-immunogenic collagen that can be implanted in patients without any adverse reactions. Our patented biological technology (registered patent no. 276891) allows us to physicochemically delete the antigenic peptide segment within the bone or membrane compound, and therefore preserve the native collagen matrix structure inside the granules, membranes, sponges and cones, making them biocompatible.

Moreover, thanks to the unique lyophilization processing technology implemented, the crystalline molecular structure of the collagen is preserved without alteration. In our bone graft – Hypro-Oss® – the same is true for the molecular structure of the natural hydroxyapatite.

In contrast to the manufacturing processes implemented by other manufacturers, heat (thermal processing) was not used in processing Hypro-Oss. It is well known that heating bone materials negatively affects the natural crystalline micro-structure of hydroxyapatite, causing bone ceramization, in addition to destroying collagen components.

What is lyophilization?

Lyophilization is a process of freeze-drying that removes water from the material by sublimation – i.e. by directly converting ice to water vapor, without passing through the intermediary stage of a liquid. Freeze-dried materials become highly absorbent and can be stored at room temperature.

Properties of Atelo-Collagen Type I

- Highest degree of tissue biocompatibility and safety
- Very weak – if any – inflammatory response
- No support of microbial growth
- Excellent wound healing characteristics
- Strong hydrophilicity results in optimal cell adhesion and blood absorption
- Release of clotting and growth factors (IGF 1, TGF-beta, PDGF) by thrombocytes
- Inhibition of the collagenolytic activity of wound excretions
- Promotion of soft tissue healing and guided tissue regeneration through the supported granulation and epithelisation
- Powerful haemostatic effect of the Atelo-Collagen Type I averts haematoma formation after surgical procedures
- Capability to induce differentiation of mesenchymal osteoprogenitor stem cells into osteoblasts
- Significantly enhanced proliferation rate of osteoblasts in association with a scaffold of natural hydroxyapatite

Resorption of Atelo-Collagen Type I

The mechanism of absorption and biotransformation is initiated through the activity of specific enzymes – latent collagenases – which are activated in the tissues during injuries and healing. Collagenases are also present in lysosomes, granulocytes and other cell structures near the wound.

Preclinical tests have shown that the process is apyrogenic (without inflammatory reaction) and the presence of macrophages (inflammation cells) is irrelevant to the resorption of the Atelo-Collagen Type I. The absorption process results in slow hydrolysis of the collagen protein to give soluble peptides and amino acids, which are metabolized by the tissue cells and so promote the regeneration process and remodeling into the patients' own tissue. The Atelo-Collagen Type I is tolerated by human tissues without any immune reaction and is metabolized through a mechanism similar to that of the tissue's own collagen.

Haemostasis with Atelo-Collagen Type I

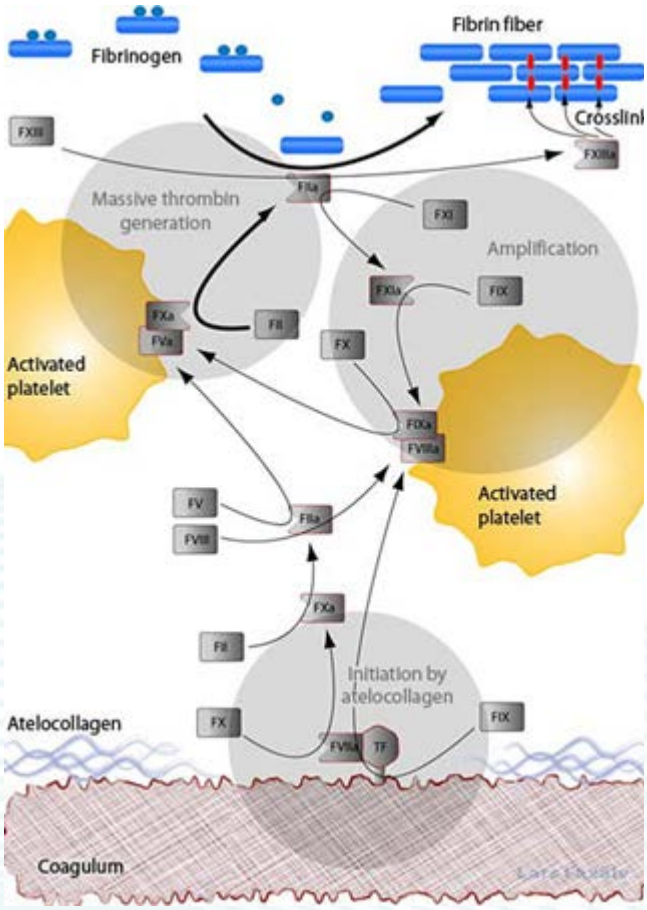
Haemostasis is triggered by a protein called collagen, which is present in the walls of the blood vessels. It is normally isolated from direct contact with the blood by the internal endothelium. However, if a blood vessel wall is damaged by an injury or contusion, collagen comes into contact with the blood, whereby haemostasis is induced so as to minimize blood loss.

The activation of haemostasis by drying materials of Atelo-Collagen Type I occurs in a heterogeneous system consisting of a liquid phase – blood – and a solid phase – Atelo-Collagen Type I. The rate, or reaction kinetics, of such reactions is mainly determined by the interface area, i.e., the surface area of the solid phase which is in contact with the liquid.

The larger this interface area is, the faster the process of stopping the bleeding is activated. The interface area is determined by what is called the internal area of the solid phase and also by the moistening ability of the liquid in contact with it. Thus, the porosity and hydrophilic nature of the surface are very important, not only pertaining to the drying process but also regarding haemostasis.

Atelo-Collagen Type I is a naturally hydrophilic peptide. The enormously porous matrix of non-immunogenic collagen in our products is achieved by lyophilization and is highly hydrophilic. Thus, huge interstitial space as well as the hydrophilicity of the collagen matrix provides a big surface area for thrombocytes to adhere on, followed by quick release of coagulation factors, which explains the immense hemostatic effect of Hypro-Sorb products.

During the initial phase of blood coagulation, fibrinogen is hydrolyzed enzymatically and fibers of fibrin are formed. The fibers form agglomerates under the effect of the surface charge, forming soft coagulate. This is converted to hard coagulate by crosslinking under the effect of transglutaminase FXIIIa, which forms new amidic bonds. Serine proteinase, which catalyzes fibrinogen hydrolysis, is called thrombin. It is released from its precursor, prothrombin, on the action of another proteinase whose activity is controlled by the factor FVIII complex.



Atelo-Collagen Type I activates a cascade of coagulation steps, as a result of which a blood clot is formed and bleeding is stopped. The picture was modifiec Courtesy Lars Faxälv, www.haemostasis.se.

Safety information

BSE prevention regulations

The safety of our products is of the utmost importance to us. This is why the manufacturer, Hypro s.r.o., only uses material of cows/oxen from countries that have established strict regulations for the protection against BSE. E.g. the compulsory notification of BSE, and that all slaughtered animals are subject to an obligatory examination based on the Notices of the Department of Agriculture no. 286/1999, Coll. of Laws, DOA no. 399/2001, Coll. of Laws, and DOA no. 400/2001, Coll. of Laws. The manufacturer monitors and reacts to current requirements or directives issued by the European Union, including the OIE notice Terrestrial Animal Health Code.

Deactivation and removal of infectious agents

The method of collagen treatment includes several repeated extractions that are employed to remove non-collagen globular proteins from the connective tissue, since prion (the infectious agent of BSE) belongs to the category of globular proteins. The extraction process is an additional safeguarding procedure that results in reduced prion content, in case there is any in the tissue.

Another technological process that is appropriate in view of deactivation of prions is the action of a saturated calcium hydroxide solution with pH-value of 12.5. The prion protein (globular protein) contains an elongated conformation of the beta-pleated sheet type that changes to a physiologically normal conformation (non-infectious) through the action of hydrotropic substances (saturated calcium hydroxides with PH 12.5). The action of hydroxides is recommended in the WHO Document CPMPaCVMP EMEA/410/01, Rev. 2 as an effective measure to reduce the risk of TSE transfer through medical devices.

These procedures induce structural changes such as decrystallization of prion protein (sensitive to proteolysis), which results in irreversible, non-toxic conformation of the prion protein. Collagen treated this way is used in the production of Hypro-Oss and Hypro-Sorb. It consists of prion-free tissues, which are fully safe as TSE is concerned.

Sterilization method

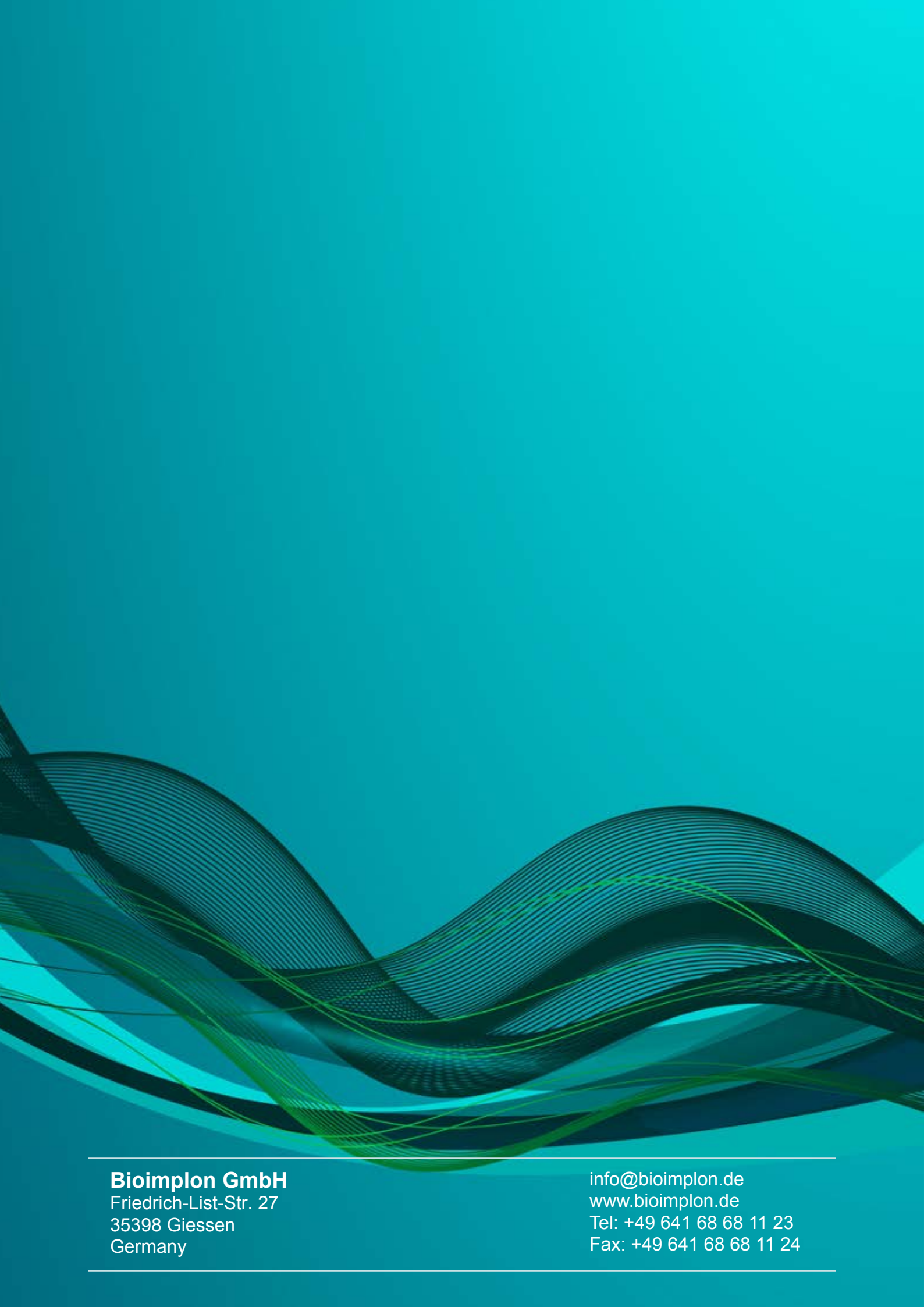
After being packed in a double blister packaging, our biomaterials undergo Gamma Irradiation as the final sterilization step. Gamma irradiation sterilization is a process that effectively kills or eliminates almost all microorganisms like fungi, bacteria, viruses and spore forms. Gamma irradiation is a physical means of decontamination, because it kills bacteria by breaking down bacterial DNA, thus inhibiting bacterial division.

The products fulfill the following regulatory requirements:

- DIR 93/42/EEC: 2007 Council Directive concerning medical devices
- DIR 2003/32/EC Commission Directive on medical devices manufactured utilizing tissues of animal origin
- CSN EN ISO 14971:2009 Medical devices – Application of risk management on medical devices
- CSN EN ISO 22442:2008 Medical devices utilizing animal tissues and their derivatives
- CSN EN ISO 10993-1:2010 Biological evaluation of medical devices – Evaluation and testing
- CSN EN ISO 10993-5:2010 Biological evaluation of medical devices – Tests for in vitro cytotoxicity
- CSN EN ISO 10993-6:2009 Biological evaluation of medical devices – Tests for local effects after implantation
- CSN EN ISO 10993-10:2011 Biological evaluation of medical devices – Tests for irritation and skin sensitization
- CSN EN ISO 11137:2012 Sterilization of health care products – Sterilization by radiation

Hypro-Sorb & Hypro-Oss – CERTIFICATIONS

- EC Certificate No. 13 0049 QS/NB attesting that the products are manufactured under conditions meeting the requirements of the quality system in accordance with Annex II, Sections 3.3.and 5, of the Directive 93/42/EEC, Notified Body No.1023.
- EC Design-Examination Certificate No. 13 0050 CN/NB certifying that the products comply with the essential requirements specified in Article 4 of Annex II to Council Directive 93/42/EEC, Notified Body No.1023.



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