Summary of safety and clinical performance SmartBone® microchips / granules

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device SmartBone®.
The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

THE FOLLOWING INFORMATION IS INTENDED FOR USERS/HEALTHCARE PROFESSIONALS

1. Device identification and general information

1.1. Device trade name

SmartBone®.

1.2. Manufacturer's name and address:

Industrie Biomediche Insubri SA,
Via Cantonale 67,
6805 Mezzovico-Vira,
Switzerland.

1.3. Manufacturer's single registration number (SRN)

CH-MF-000049165

1.4. Basic UDI-DI

SmartBone® microchips/granules: 764017868P900401DGRSH

1.5. Medical device nomenclature description

EMDN P900402 - RESORBABLE FILLING AND RECONSTRUCTION DEVICES

1.6. Class of device (according to MDR 2017/745 Annex VIII)

Class III

1.7. Year when the first certificate (CE) was issued covering the device

2012

1.8. Authorised representative

MedEnvoy Global BV
33 Prinses Margrietplantsoen
2595 AM The Hague
Netherlands

SRN: NL-AR-000024028

1.9. NB's name and the NB's single identification number

Eurofins Product Testing Srl, 0477.

2. Intended use of the device

2.1. Intended purpose

SmartBone® is intended for use for bone regeneration in dental applications.

2.2. Indications and target populations

SmartBone® is intended for use for bone regeneration dental applications, in the following indications:

- Regeneration of periodontal bone defects;
- Regeneration of extraction alveoli;
- Regeneration of cavities between the alveolar wall and immediate implants;
- Horizontal alveolar ridge augmentation;
- Sinus lift floor elevation;
- Alveolar ridge augmentation at implant sites with sufficient residual bone and a good blood supply.

Target population: Smartbone® is intended to be used in patients who require surgical interventions aiming for bone regeneration in dental applications. Data on the use of the product during pregnancy or lactation, or in subjects who have not reached skeletal maturity, are not available. Women who are pregnant or breastfeeding and subjects who have not reached skeletal maturity should not be treated with SmartBone®.

2.3. Contraindications

Do not use SmartBone® in patients with known allergies to collagen and its derivatives.
Do not use SmartBone® where there are infected wounds or in case of acute or chronic infections at/near the surgical site (i.e. osteomyelitis).
As a matter of experience from clinical practice and similarly to any bone grafting procedures, surgeons and dentists should be restrained in using SmartBone® in the following cases, due to higher risks for complications and side-effects:

- systemic infections;
- uncontrolled metabolic diseases, such as diabetes, thyroid dysfunctions;
- severe kidney or liver diseases;
- bone metabolic diseases, such as osteomalacia and any medications that negatively influence bone
- healing (such as the use of bisphosphonates to treat osteoporosis);
- on-going treatment with gluco- and mineralcorticoids and with agents affecting calcium metabolism (e.g. calcitonin);
- autoimmune diseases;
- immunosuppressive therapy;
- scleroderma;
- local radiotherapy;
- heavy smokers;
- high LDL or low HDL cholesterol level;
- low blood levels of Vitamin D;
- abnormal uncontrolled blood pressure (high or low) or impaired microcirculation.

There is insufficient data on use of the product in pregnant or lactating women. As a safety precaution, do not treat pregnant or lactating women with SmartBone®.
There is no experimental data on the safety and efficacy of SmartBone® in children who have not reached skeletal maturity. As a safety precaution, do not treat subjects who have not reached skeletal maturity with SmartBone®.

3. Device description

3.1. Description of the device

SmartBone® is a composite bone substitute, composed of bovine-bone- derived porous mineral matrix, reinforced with a blend of collagen fragments of porcine origin (in the form of hydrolysed gelatine) and biodegradable synthetic polymers (i.e. resorbable aliphatic block-co-polyesters).
SmartBone® is a long-term implantable, resorbable, sterile, single-use medical device, which is supplied in different shapes and dimensions to best match surgical needs. From big (15 x 30 x 60 mm3) solid blocks to granulates (2-4 mm) to fine microchips (0.25-1 mm and 1-2 mm).
The sterilization processes are validated and different sterilization methods are used: ethylene oxide is used for all products packaged in double pouch, while Beta-rays for products packaged in vial, as specified on the product labels.
SmartBone® is a composite material, made by combining 3 different components:

- a bovine bone derived matrix (as starting material), as per 98 + 0,5 % in final weight (mass);
- being reinforced with medical grade polylactide-co-ε-caprolactone biopolymers (PLA-CL), as per 1 + 0,2 % in final weight (mass);
- added with porcine derived medical grade gelatine, as per 0,5 + 0,1 % in final weight (mass).

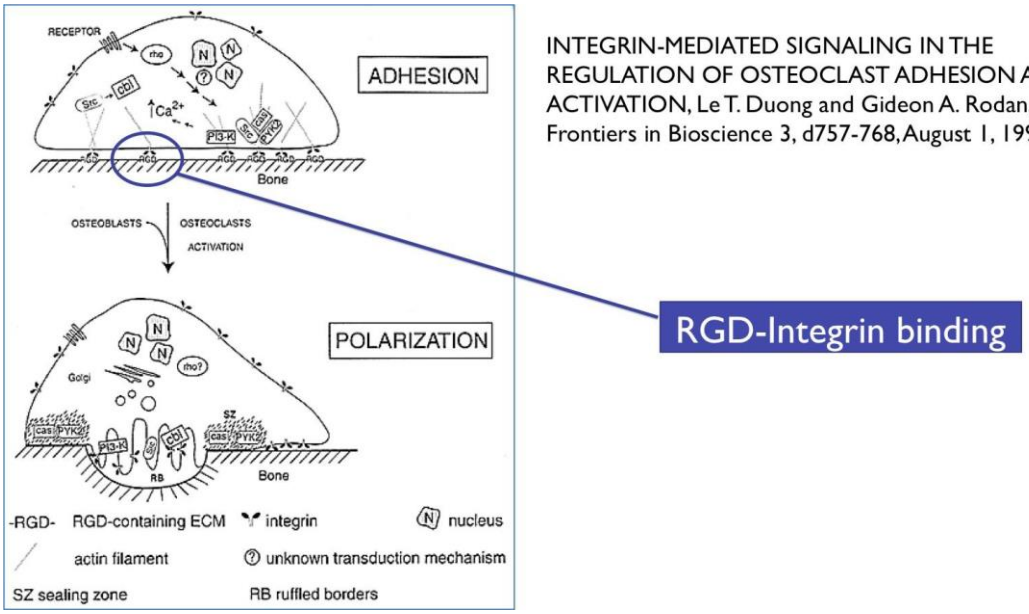
Residual water might be present, both from animal tissues and process, but only up to 0,5 % of final weight (mass).

The key features of SmartBone® are thus the following:

- mimicking human bone microstructure (i.e. adequate-sized open porosity);
- high mechanical performances, close to human healthy bone (i.e. rigid-elastic behaviour, adequate elastic modulus, proper load bearing resistance, dust and debris free shaping, ability to be precisely shaped, tenacity to fixation screws, hammering and heavy surgical manoeuvring resistance, etc.);
- high hydrophilicity and thus high capability to absorb and retain blood once in situ;
- high tissue integration in order to support the regenerative process with a proper timing.

SmartBone® integration into the natural bone and hence its resorption is driven by its being progressively substituted with healthy living bone from host. This is a key feature of SmartBone® and one of its major innovative claims. Here, moreover, lies one of the keys to understanding the mechanism of action of SmartBone®.
The SmartBone® graft soaks up blood, thus starting microcoagulation to occur inside the graft itself and hence enhancing graft integration. The first weeks are then needed for cellular colonization of the graft, which is also enhanced by the presence of gelatine that offers a viable environment for cells to spread onto; meanwhile, this time lag is also necessary for the degradation of the thin polymeric film, which progressively fades away leaving mineral structure for cells to consolidate and promoting the formation of new living bone (also by means of formation of new vessels); the following couple of months are needed for the integration of the graft with the native patient bone, thanks also to vascularization and new bone formation inside the graft.
Based on the collected evidence the coating of SmartBone® with poly(l-lactide-co-ε-caprolactone)

(PLCL) and gelatin promoted an increased proliferation of mesenchymal stem cells and bone formation when compared to un-treated bovine bone grafts.
In particular, histological analysis was obtained evaluating samples harvested in clinical practice and from in vitro and in vivo studies, supplying strong evidence of the mechanism of action of SmartBone® as a scaffold that is transformed by the osteoclasts and by the osteoblasts stimulating the bone remodelling of native bone tissue, in the direction of obtaining new bone formation.



3.2. Description of any accessories which are intended to be used in combination with the device.

No accessory is required for the use of SmartBone®.

3.3. Description of any other devices and products which are intended to be used in combination with the device.

Devices such as membranes, screws, sutures, surgical instruments, dental implants can be used along with SmartBone® following the standard clinical practice.

4. Risks and warnings

4.1. Residual risks and undesirable effects

Potential risks have been controlled and managed in the frame of a risk management process performed according to the provisions of ISO 14971. The risks related to the Medical Device and the production process have been analyzed to the best of the manufacturer's possibility.
The overall residual risk is deemed ACCEPTABLE, and the manufacturer has implemented procedures for the management of production and post-production information according to the current version of ISO 13485 and European Regulation 2017/745.
Based on the clinical experience with the SmartBone® the following risks and safety events are known (expected) for SmartBone®.
As indicated in the SmartBone® IFU (IBI-IFU025), possible complications that can occur in any surgery include:

- swelling of the operative site
- flap necrosis

- bleeding
- local inflammation
- bone loss
- infection
- pain
- lack or incomplete osteointegration
- partial or complete graft resorption
- partial or complete loss of mechanical performances of graft
- dehiscence.

4.2. Warnings and precautions

- Do not use if the packaging is damaged or open.
- Do not use if the bone graft is damaged.
- Do not use in the case of impurities/contaminations inside the primary packaging.
- Do not use after the expiration date indicated on the label.
- This is a single use medical device; any attempt to reuse the medical device is strictly forbidden; improper reuse of the device carries a very high risk of infection and/or incorrect tissue regeneration and can cause failure of the implant.
- Do not re-sterilize the product. The use of the product if removed from the packaging in advance can carry serious risks of infection.
- Remove the product from the packaging only immediately prior to its use and only in a controlled environment (such as for example operating room).
- SmartBone® must not be mixed/used with other bone substitutes other than patient's autograft.
- Do not mix SmartBone® with any saline solution or saline based preparations or suspensions or any other salty liquid.
- Cover SmartBone® with periosteum or with a protective membrane if in direct contact with non-bony tissues, e.g. connective tissue. Indeed, non-bony tissue in contact with the product does not promote the new bone formation but it supports its resorption.

To ensure bone tissue regeneration, SmartBone® must be implanted exclusively in presence of viable bone tissue and in direct contact with the bone in the receiving site (it is recommended to perform micro-channeling in the cortical bone to support the blood flow and bone graft vascularization).
In case of extensive defects, the addition of autologous trabecular bone or bone marrow can promote the regeneration process.
According to oral surgery experience, implant placement must be correctly evaluated case-by-case, using the radiological images available (suggested the CBCT scans). Contextual positioning (implant + graft) is not suggested even if possible. In general, the correct moment for insertion of the implant depends on the residual bone volume in the site and also it generally depends on patient's health condition, gender, age and grafting site. In augmented sites a mechanical load should not be applied without a primary stability evaluation. 6 months are generally a minimum waiting time before implant placement.
Based on Local National Regulations, patients who have received SmartBone®, that is a xenograft, cannot be blood nor organ donors.
The clinician should inform the patient about the animal origin of the device.

4.3. Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN)

In 2025, one Field Safety Notice has been issued to inform the Competent Authorities of Turkey and Switzerland that a suspect counterfeit device was found on the Turkish market.

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1. Summary of clinical data from conducted investigations of the device before the CE-marking

The first pre-market clinical investigation was performed with the aim of obtaining CE mark in conformity to the Medical Device Directives 93/42/EEC.
The study was a single-centre, non-randomized, comparative one, at a University site, following Helsinki Declaration indications, under ethical committee approval and it had the aim to obtain the experimental assessment of efficacy of SmartBone® in the bone regeneration of edentulous areas.
Beside all technical, scientific and safety requirements, the clinical trial on SmartBone® was performed for 3 main reasons and, hence, the 3 main endpoints were the following:

- regulatory compulsory assessment of complete biocompatibility in humans, hence providing experimental confirmation to all deductive statements made during product development and strengthened by previous investigations concerning product safety;
- experimental assessment of efficacy and also claimed superior features, particularly with respect to other commercially available bone substitutes (SmartBone® has very high mechanical performances and can, hence, easily withstand heavy surgical manoeuvres; furthermore, SmartBone® has a high capability to soak up blood and finally allows to obtain a good and fast tissue integration thanks to its osteoinduction and conduction);
- running a detailed study on best surgical procedures to follow in order to allow SmartBone® to best perform once in situ (SmartBone® mechanical characteristics are tremendously different, better and higher, from all other substitutes available on the market, hence a fully dedicated and careful surgical approach is needed to use this graft).

A comparative study was hence performed, using the CE-marked Tutobone®, as control material, where 5 patients were enrolled, all having important edentulous areas and willing to be treated with the best available methodology (the implant-prosthetic treatment). In total 8 sites were treated: two sinus lifts and five augmentations.

Clinical protocol required collection of all details of each single patient:

- preclinical data and enrolment information;
- detailed case description, including case aims;
- pre-surgical X-ray images and photographs of intervention sites;
- surgical report, including detailed surgery protocol description, used materials and photos;
- post-surgical follow-up report;
- mid time point report (9 weeks after surgery);
- end time point report (>4 months after surgery, at implant procedure);
- histological analysis.

The clinical results were assessed through both radiological and histological evaluation of the regenerated bone.
Overall, this study had proven key feedback on product, allowing the CE-granting.
Biocompatibility was widely and very satisfactorily proven, confirming preclinical evidence.
Surgical interventions proved and strongly confirmed SmartBone® high mechanical performances and capability to easily withstand heavy surgical manoeuvres that others grafts cannot (in many cases it showed all its advantages allowing easy and precise shaping and allowing the use of few fixation devices, thus making surgery much simpler and faster; furthermore, in some circumstances, control grafts had not been used because of lack of adequate mechanical performances and SmartBone® was hence used providing to absolutely fit the needs and being applicable also there where other substitutes fail).

Osteointegration and remodelling capabilities were proven by histological analyses performed on harvested samples during implant placement procedures (at month >4 post-surgery): SmartBone® grafts strongly supported native bone growth, which progressively replaced the grafted material, resulting in a fully integrated region of new bone.
Overall, clinical data and histological analysis allowed stating that SmartBone® is a successful bone graft, having shown osteoconduction (guiding the reparative growth of the natural bone) and osteoinduction (encouraging undifferentiated cells to become active osteoblasts) and being finally reabsorbed and replaced as the natural bone heals over a few months' time (physiological remodelling).

5.2. Summary of clinical data from other sources

After obtaining the CE mark, IBI had continued the surveillance of the product on the market with the aim to have a constant verification and confirmation of clinical performance and safety of SmartBone®. The clinical data were collected from the following activities:

- clinical investigations;
- clinical literature review;
- clinical experiences collection from users.

Thanks to the literature review the following studies were included in the post-market clinical follow-up.

- Pertici G. et al; "Composite Polymer Coated Mineral Scaffolds for Bone Regeneration: from Material Characterization to Human Studies"; J Biol Regul Homeost Agents, Jul-Sep;29(3S1):136-48, 2015.
- Poonia N., Morales H., Lanka M.: "Management of a Failed Implant Site with Guided Bone Regeneration, Reimplantation, and Root Submergence Technique", International Journal of Oral Implantology and Clinical Research, May-August 2016;7(2):1-3.
- Zollino I., Carusi G., Carinci F., Perale G.; "Positioning of a contextual implant along with a sinus with SmartBone MicroChips of Composite heterologous-synthetic Bone"; Indian Journal Stomatology, 2016.
- Lanka M., Devich A.S., Sagrika S.: " Socket Preservation Using a Small Particulate Xenograft: A Case Report", The Journal of Implant & Advanced Clinical Dentistry, Vol. 9, No. 4, 12-17, May/June 2017.
- D'Alessandro D, Perale G, Milazzo M, Moscato S, Stefanini C, Pertici G, Danti S. Bovine bone matrix/poly(l-lactic-co-ε-caprolactone)/gelatin hybrid scaffold (SmartBone®) for maxillary sinus augmentation: A histologic study on bone regeneration. Int J Pharm. 2017 May 25;523(2):534-544. doi: 10.1016/j.ijpharm.2016.10.036. Epub 2016 Oct 18. PMID: 27769886.
- Secondo F, Grottoli CF, Zollino I, Perale G, Lauritano D. Positioning of a contextual implant along with a sinus lift anchored with a block of heterologous bone. Oral Implantol (Rome). 2017 Jan 21;10(4):457-467. doi: 10.11138/orl/2017.10.4.457. PMID: 29682263; PMCID: PMC5892665.
- Spinato S, Galindo-Moreno P, Bernardello F, Zaffe D. Minimum Abutment Height to Eliminate Bone Loss: Influence of Implant Neck Design and Platform Switching. Int J Oral Maxillofac Implants. 2018 March/April;33(2):405–411. doi: 10.11607/jomi.5604. Epub 2017 Aug 17. PMID: 28817742.
- Mandelli F, Perale G, Danti S, D'Alessandro D, Ghensi P: "Clinical and histological evaluation of socket preservation using SmartBone®, a novel heterologous bone substitute: a case series study", Oral & Implantology – Anno XI – N. 2/2018.
- Stacchi C, Lombardi T, Ottonelli R, Berton F, Perinetti G, Traini T. New bone formation after transcrestal sinus floor elevation was influenced by sinus cavity dimensions: A prospective histologic and histomorphometric study. Clin Oral Implants Res. 2018 May;29(5):465-479. doi: 10.1111/clr.13144. Epub 2018 Mar 23. PMID: 29569763.

- Grottoli, C.F. & Ferracini, Riccardo & Compagno, Mara & Tombolesi, Alessandro & Rampado, Osvaldo & Pilone, Lucrezia & Bistolfi, Alessandro & Borrè, Alda & Cingolani, Alberto & Perale, Giuseppe. (2019). A Radiological Approach to Evaluate Bone Graft Integration in Reconstructive Surgeries. Applied Sciences (Switzerland). 9. 10.3390/app9071469.
- Ghiretti, Roberto, Carlo F. Grottoli, Alberto Cingolani, and Giuseppe Perale. 2020. "Clinical Case Employing Two Different Biomaterials in Bone Regeneration" Applied Sciences 10, no. 13: 4516. https://doi.org/10.3390/app10134516.
- Taschieri S, Ofer M, Corbella S, Testori T, Dellavia C, Nemcovsky C, Canciani E, Francetti L, Del Fabbro M, Tartaglia G. The Influence of Residual Alveolar Bone Height on Graft Composition after Maxillary Sinus Augmentation Using Two Different Xenografts: A Histomorphometric Comparative Study. Materials (Basel). 2020 Nov 11;13(22):5093. doi: 10.3390/ma13225093. PMID: 33187350; PMCID: PMC7697912.
- Ghiretti, Roberto, Carlo F. Grottoli, Alberto Cingolani, and Giuseppe Perale. 2020. "Clinical Case Employing Two Different Biomaterials in Bone Regeneration" Applied Sciences 10, no. 13: 4516. https://doi.org/10.3390/app10134516
- Taschieri S., Ofer Moses, Claudia Dellavia, Elena Canciani, Carlos Nemcovsky, Luca Francetti, Stefano Corbella. Comparative Study of Deproteinized Bovine Bone Mineral and Bovine Bone Mineral Enriched with a Polymer and Gelatin in Maxillary Sinus Floor Elevation Procedures. Int J Periodontics Restorative Dent. Jul-Aug 2021;41(4):579-586.
- Azab, Mostafa; Diaa, Mohammed; EL-Beialy, Waleed; and Ghanem, Amr Amin (2021) "Three-Dimensional Maxillary Alveolar Ridge Augmentation Using Modified Cortical Shell Technique and Composite Bone Graft," Future Dental Journal: Vol. 7 : Iss. 1 , Article 2.
- Available at: https://digitalcommons.aaru.edu.jo/fdj/vol7/iss1/2
- Mandelli F., Traini T., Ghensi P. Customized-3D zirconia barriers for guided bone regeneration (GBR): clinical and histological findings from a proof-of-concept case series. Journal of Dentistry, https://doi.org/10.1016/j.jdent.2021.103780

5.3. An overall summary of the clinical performance and safety

The clinical benefit of SmartBone® is due to its osteo-conduction, -induction and -integration capability into the natural bone, promoting the bone tissue regeneration. SmartBone® stimulates the bone remodelling of native bone tissue in the direction of obtaining new bone formation.
Thanks to its composition and microstructure, SmartBone® has the following characteristics:

- high mechanical performances (hence high capability to withstand heavy surgical manoeuvres) and high volumetric stability due to the presence of biopolymers;
- high capability to soak up blood (deriving from its hydrophilicity) due to the presence of gelatine, hence ability to spark the biochemical cascade of events sustaining graft integration.

The device safety has confirmed based on the information collected in a meaningful observation period of almost 10 years passed since first market introduction to present date.
Based on all clinical evidence collected, SmartBone® recorded a failure rate in the range of ca.1%, according to indications and surgical procedures.
The collected clinical data underline and confirm also the long-term safety and performance of SmartBone®, from surgery to follow-up, till final prosthesis as a bone substitute that contributes to guarantee successful implantology treatments also when it’s needed to manage complex cases.
Considering long-term follow-up, SmartBone® allows to have satisfactory results thanks to grafted volume stability and implant stability.
Histological analysis evidenced the osteoconduction (guiding the reparative growth of the natural bone) and osteoinduction (encouraging undifferentiated cells to become active osteoblasts) of SmartBone® that is reabsorbed and replaced as the natural bone heals over a few months’ time (physiological remodeling). Histological analysis provided further confirmation on the integration mechanism of SmartBone® which underlies a complete remodeling process that occurs from the

outer part of the graft to the most inner, within a timeframe of av. 12 months in the average dental graft.
Overall clinical data confirmed the safety of SmartBone® as well as performance in a wide range of indications as claimed. The data supports the claims of SmartBone® as an osteoconductive material for bone regeneration.

All risks that were identified were mitigated such that the individual and global residual risk was judged acceptable and such that no new risks emerged from mitigations.
After review and appraisal of the available safety and performance data no further need was identified for adaptations of the existing product, as no new and unacceptable clinical risks were identified which might negatively impact the safety or performance of SmartBone®.
The residual known clinical risks are deemed acceptable and the measures for their avoidance and risk mitigation are described in the information materials supplied with SmartBone®.
The results of the data collected to date, confirmed the safe performance of the SmartBone® device when used in accordance with the instructions for use. Based on the clinical evaluation, IBI concluded that the overall profile of benefits versus risk of the SmartBone® continues to be favourable.

5.4. Ongoing or planned post-market clinical follow-up

Based on its post-market clinical follow-up plan, IBI has defined the following activities for the collection of information on the quality, performance and safety of the device placed on the market:

- the clinical investigation “comparison of xenograft and autogenous bone block grafts for treatment of horizontal bone deficiency in the maxilla”, a co-sponsored study conducted in Turkey.

Up to date, no emerging risks, unpredictable complications or unexpected device failures have been detected.

6. Possible therapeutic alternatives

Possible therapeutic alternatives can be divided into 6 main categories:

Autografts
Autologous bone grafts are the predominantly considered osteoconductive materials for bone replacement. Multiple clinical concerns, however, have largely limited the transfer of autografts, including the possibility of surgical complications and pain associated with the donor site morbidities associated with the harvest site, amount of available graft material, short-term viability and unpredictable graft resorption.

Allografts
Allografts derived from both living donors’ and cadavers’ bone duly sterilized.
Types of available bone include fresh, fresh-frozen, freeze-dried, and demineralized types of bone.
Their limitations are related to the quality of the regenerated bone tissue that is not always predictable due to its limited osteoinduction, in addition to requiring costly and laborious processing to eliminate its antigenic capacity.
The fundamental problems of this grafting material are antigenicity and the potential for infectious agent transmission (such as HIV, hepatitis B, hepatitis C, and human T-lymphotropic virus), which is a major consideration that is in fact minimized by recent strategies associated with tissue processing including sterilization and freezing. However, these procedures in turn decrease graft properties with regard to osteoinduction, osteoconduction and mechanical strength, and indeed, real and perceived risks of disease transmission still exist.

Naturally derived biomaterials
Natural polymers benefit from a low immunological potential but one of the major limitations is their weak physical property and mechanical instability, making them unsuitable for load-bearing applications.

Synthetic scaffolds
Synthetic bone grafts are a wide group and the main types are bio-ceramics, bioactive glass, metallic materials and polymer organic synthetic materials.
Synthetic biomaterials have better controlled physical and mechanical properties, but poor biocompatibility compared against naturally occurring biomaterials.

Xenografts, i.e., bone segments taken from animal bones, duly acellularized and sterilized
Xenografts currently are mainly harvested from bovine or equine sources.
The xenografts are processed to remove all of the organic constituents of the material. The remaining material is composed of only the mineral constituents.
A distinctive advantage of this bone graft is that it has an abundance of availability, and the material cost is far lower than that of allogenic bone.
Often xenograft is mixed with autogenous graft to augment the volume of autograft. The osteoinductive and osteogenic properties of autogenous bone combined with the osteoconductive properties of xenograft makes for a successful regeneration of substantial volume of bone.

Composite materials
The composite biomaterials combine advantages of the other types of scaffolds and show good mechanical hardness and load-bearing capabilities as well as ideal biocompatibility.
Different strategies were implemented to improve bone regeneration using a different combination of bone sources, biomaterials, or biomolecules.

7. Suggested profile and training for users

SmartBone® is intended for professional use only. *It should only be used by licensed dentists or physicians familiar with bone regeneration procedures.*
The user must ensure that the general rules of Good Clinical Practice for handling medical devices under aseptic conditions are observed when using SmartBone®.
The product is to be used in a controlled environment (operation room). The general principles of sterile handling, using sterile surgical instruments and patient medication must be followed when using SmartBone®.

8. Reference to any harmonised standards and CS applied

- MDR 2017/745 - Regulation (EU) of the European Parliament and of the Council on medical device.
- MEDDEV 2.12 rev.2 - Post Market Clinical Follow-Up Studies.
- MEDDEV 2.7.1/ rev 4 Clinical Evaluation of clinical data: A guide for manufacturers and notified bodies, June 2016;
- ISO 13485:2016 - Medical devices — Quality management systems — Requirements for regulatory purposes.
- MDCG 2020-5 – Clinical Evaluation – Equivalence.
- MDCG 2020-6 - Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC.

- MDCG 2020-7 - Post-market clinical follow-up (PMCF) Plan Template.
- MDCG 2020-8 - Post-market clinical follow-up (PMCF) Evaluation Report Template.
- MDCG 2020-13 - Clinical evaluation assessment report template.
- EN ISO 14971:2019 Medical devices – Application of risk management to medical devices.

9. Revision history

Revision	Date	Description	
0	30.03.2022	Document creation	
1	11.11.2025	Update to address findings from Notified Body Split SSCP for healthcare professionals and patients	