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.
The SSCP is not intended to replace the Instructions for Use (IFU) 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. Following this information there is a summary intended for patients.

1. Device identification and general information

1.1. Trade name

INNOTERE 3D Scaffold

1.2. Manufacturer's name and address

INNOTERE GmbH
Meissner Str. 191, 01445 Radebeul, Germany
Tel: +49 351 259994-20
Fax: +49 351 259994-29
email: contact@innotere.de
Website: www.innotere.de

1.3. Manufacturer's single registration number (SRN)

DE-MF-000006515

1.4. Basic UDI-DI

++EINNCPFK9C

1.5. European Medical Device Nomenclature (EMDN)

P900402 - Resorbable filling and reconstruction device

1.6. Class of device

Class III, according to Rule 8, number 3 of the EU Regulation (MDR) 2017/745, Annex VIII, chapter III

1.7. Year of first certificate (CE)

2023, year of first CE-mark under MDR 2017/745
2017, year of first CE-mark under MDD 93/427EEC

1.8. Authorised representative

N/A

1.9. Notified Body and single identification number

TÜV Rheinland LGA Products GmbH
No. 0197

2. Intended use of the device

2.1. Intended purpose

INNOTERE 3D Scaffold is a synthetic, porous bone substitute material for filling non-infected bone defects.

2.2. Indication(s) and target population(s)

INNOTERE 3D Scaffold is intended for filling or reconstructing non-load-bearing bone defects or for filling bone defects that have been sufficiently stabilised by appropriate means.

Particular indications are:

- metaphyseal defect fractures, e.g. fractures of the tibia, radius, humerus
- osteotomy
- bone defects after removal or replacement of osteosynthesis implants

Intended patient population: Adults
To date, there are no studies with children, pregnant or breastfeeding women. As a safety measure, the use of INNOTERE 3D Scaffold in children and women during pregnancy and breastfeeding is not recommended.

2.3. Contraindications and limitations

INNOTERE 3D Scaffold must not be used in case of:

- acute or chronic infections at the implantation site, e.g. osteomyelitis
- bone defects due to malignant tumours
- bone defects in the area of open epiphyseal plates
- known disturbance of calcium metabolism, e.g. hypercalcaemia
- pregnant or breastfeeding women

INNOTERE 3D Scaffold must be used only after carefully weighing the risks and benefits in the case of:

- bone metabolism disorders
- endocrinopathies
- immunosuppressive therapy
- simultaneous treatment with medication that has an effect on bone metabolism

3. Device description

3.1. Description of the device

INNOTERE 3D Scaffold is a synthetic, porous, biocompatible, osteoconductive and bioresorbable bone substitute material for filling non-load-bearing bone defects. INNOTERE 3D Scaffold is available in the form of blocks, cylinders and wedges. See table below. INNOTERE 3D Scaffold is a porous, mineral bone substitute material of synthetic calcium and phosphate salts with a calcium-to-phosphate ratio of around 1.5. The calcium phosphates are present with a microcrystalline, calcium-deficient hydroxyapatite (CDHA) and alpha-tricalcium phosphate (α-TCP), which are the main phase. The minor phase consists of monetite and calcite. INNOTERE 3D Scaffold has an interconnecting pore system with pore sizes of around 100 – 1000 µm.

INNOTERE 3D Scaffold does not contain any medicinal substances, tissue, cells or their derivates of human origin and/or animal origin.
INNOTERE 3D Scaffold is resorbed by biological processes and replaced by the body's own bone. Depending on the implantation conditions and the metabolic activity at the implantation site, INNOTERE 3D Scaffold can also remain permanently in the body as an osseous integrated material.
INNOTERE 3D Scaffold may contain residual amounts of polyoxyl-35-castor oil, for which very rare cases of allergic reactions and anaphylactic shock have been described in the literature.

INNOTERE 3D Scaffold is a sterile medical device. It is sterilised using gamma radiation. Due to the risk of infection transmission and/or the potential impairment of product performance, INNOTERE 3D Scaffold must not be cleaned or resterilised. INNOTERE 3D Scaffold is intended for use on a single person for a single procedure.

3.2. Product variants and reference to previous variants

INNOTERE 3D Scaffold is the modified device of the previously CE marked device under the Medical Device Directive 93/42/EEC (MDD) and marketed by INNOTERE for the same intended purpose under the same trade name (legacy device MDD). CP-Scaffold has the same design and technological characteristics of the legacy device. There is no change in the materials, design, manufacture, packaging or sterilization method or other features of the design of the device compared to the legacy device. The main difference between the legacy device and CP-Scaffold is related to the changes not safety related; streamlining of the product portfolio and the deletion of medical indications. The legacy device is considered equivalent to the modified device as it shares the same technical, biological and clinical characteristics. The benefit-risk ratio of the device remains unchanged.

Article number	Product name
121TS1	INNOTERE 3D Scaffold (Block 10x10x5mm, 2 pieces)
141TS2	INNOTERE 3D Scaffold (Block, 10x5x5mm, 4 pieces)

Article number	Product name
111TS3	INNOTERE 3D Scaffold (Block, 20x10x10mm, 1 piece)
811TS3	INNOTERE 3D Scaffold (Block 3x3x3mm, 10cc)
811TS4	INNOTERE 3D Scaffold (Block 4x4x4mm, 10cc)
811TS5	INNOTERE 3D Scaffold (Block 5x5x5mm, 10cc)
321TS1	INNOTERE 3D Scaffold (Cylinder 20x10mm, 2 pieces)
321TS2	INNOTERE 3D Scaffold (Cylinder, 16x10mm, 2 pieces)
321TS3	INNOTERE 3D Scaffold (Cylinder, 12x10mm, 2 pieces)
721TS1	INNOTERE 3D Scaffold (Wedge 7x3x30x12mm, 1 piece)
721TS2	INNOTERE 3D Scaffold (Wedge, 10x3x30x12mm, 1 piece)
721TS3	INNOTERE 3D Scaffold (Wedge, 12x3x35x15mm, 1 piece)
721TS4	INNOTERE 3D Scaffold (Wedge, 15x3x35x15mm, 1 piece)

3.3. Description of accessories
N/A

3.4. Other devices used in combination with the device
Intra-operative adaptation to the geometry of the defect is possible using the usual surgical instruments (e.g. scalpel).

4. Risks and warnings
4.1. Residual risks and undesirable effects
Product and treatment related: Swelling, seroma and hematoma formation, fever, allergic reaction, pain, device mechanical failure, wound healing disorders, rejection reaction, infection, delayed and non-union (pseudarthrosis).

4.2. Warnings and precautions
The use of INNOTERE 3D Scaffold is restricted to health care specialists who are familiar with handling bone substitute materials, the appropriate surgical techniques and the treatment of bone defects from their training.

INNOTERE 3D Scaffold is intended for use on a single person for a single procedure
A subsequent reoperation may be required because of undesirable side-effects of the original surgery.
Patients with a weakened immune system (e.g. those suffering from rheumatism or diabetes), in addition to smoking and alcohol abuse increase the risk of infections and implant failure. These patients must be informed by medical staff of the possible risks before surgery.
The treatment of post-operative infections may be hampered by the presence of an implanted foreign body and it may prove necessary to remove the implanted material.

INNOTERE 3D Scaffold may contain very small amounts of polyoxyl-35-castor oil, for which very rare cases of allergic reactions and anaphylactic shock have been described in the literature.
INNOTERE 3D Scaffold must only be implanted after sufficient debridement of the bone defect in order to ensure a vital bone site. The defect must be completely filled in order to establish direct osseous contact between INNOTERE 3D Scaffold and the surrounding bone. If a complete defect filling with INNOTERE 3D Scaffold alone is not be possible, the remaining defect sites should be filled with autologous bone or allogeneic materials.

Due to its mechanical properties, INNOTERE 3D Scaffold can support the stabilisation of bone defects, but the actual stabilisation must be ensured by other means.
INNOTERE 3D Scaffold can be combined intra-operatively with autologous or allogeneic materials, particularly blood, blood-based products, bone marrow aspirate or autologous cancellous bone. In these cases, special care must be taken to maintain aseptic conditions.
INNOTERE 3D Scaffold is resorbed by biological processes and replaced by the body's own bone. Depending on the implantation conditions and the metabolic activity at the implantation site, INNOTERE 3D Scaffold can also remain permanently in the body as an osseous integrated material.
Any unused content of opened or damaged packages must not be used for further operations and must be discarded. Particles produced due to intra-operative shaping of the scaffold must not be reused.

4.3. Other safety relevant aspects
There were no field safety corrective actions (FSCA) since CE-marking (2017).

5. Summary of clinical evaluation and post-market clinical follow-up (PMCF)
5.1. Summary of clinical data related to equivalent device
INNOTERE conducted a PMCF study with INNOTERE 3D Scaffold in opening wedge high tibial osteotomy (OWHTO) to confirm the clinical benefit and the acceptability of the benefit-risk ratio of the device. The retrospective study including 71 patients evaluated the clinical outcomes bone healing, osseointegration and resorption (mode of action) in a non-inferiority trial between INNOTERE 3D Scaffold and the comparator device OSferion®. Non-inferiority of INNOTERE 3D Scaffold is concluded for bone healing (p=0.00868). None of the patients experienced non-union (non-union rate 0%). INNOTERE 3D Scaffold is not inferior to the comparator device for mode of action; both test device and comparator device achieve 100% osseointegration. Non-inferiority of INNOTERE 3D Scaffold is concluded for resorption (p=0.0081).

Complications reported for INNOTERE 3D Scaffold included four adverse events (pain, device fracture, hinge fracture, wound healing disorder), and one serious adverse event (infection) with no causal correlation to the device. No new risks were identified for CP-Scaffold. The results of PMCF show that the non-union rate of 0% is below the specified threshold acceptance criterion of 1.1%; furthermore the occurrence of the reported adverse events are within the specified threshold acceptance criteria of risk management, and identified residual risks remain acceptable. The PMCF study with INNOTERE 3D Scaffold when used as intended confirms the clinical performance and safety of the device including its clinical benefit for the expected lifetime of the device outweighing any residual risks. The benefit-risk ratio is acceptable.

5.2. Summary of clinical data before CE-marking
N/A

5.3. Summary of clinical data from SOTA
Despite the profound clinical and economic impact, the management of bone defects remains controversial which is in part related to the size of the defect and how to determine whether the defect is critical sized. What constitutes a ''critical-sized defect'' varies with the anatomic location of the defect as well as the state of the soft tissues surrounding it. Bone defects that do not heal spontaneously can develop into atrophic non-unions because of the nature of the fracture, with impaired vascularity and soft tissue injury.

Alternative treatment options in bone replacement include the use of autologous bone grafts (autograft); bone grafts of other human individuals (allograft) or animal origin (xenograft), synthetic bone grafts substitutes (BGS), or a combination of any of these options. Major disadvantages of autografts (persistent pain at the harvest site, limited availability), allografts and xenografts (residual risks of infection or disease transmission) have encouraged the development of synthetic BGS, particularly calcium phosphate (CaP)-based compounds in pure form (α-TCP, ß-TCP) or in biphasic combinations (BCP) because of their physiochemical properties (similarity to bone composition, biocompatible, osteoconductive, bioresorption). Structural properties such as pore size and their spatial arrangement leading to the formation of an interconnected network facilitating the ingrowth of new bone.

CaP based BGS are used both in adults and in children but the majority of cases are reported in adults with favourable outcomes. There is few clinical data available for children and no data for pregnant and lactating women to draw conclusions.

The majority of clinical outcomes with CaP grafts in bone replacement confirm the excellent biocompatibility, minimal side effects and good bone substitute integration. Functional outcome was improved in many cases but not correlated to bone integration. Histological examinations confirm active bone turnover with new bone formation in the implanted area. Bone ingrowth and resorption was related to structural features of the graft. Other factors reported influencing the clinical outcome are size and location of the defect, physiological environment and health status of the patient.

The use of CaP grafts for osteosynthesis emerged as an ancillary therapy as it avoids the use of autogenous bone grafting procedures while shortening the surgical time, reducing donor site morbidities associated with harvesting of donor bone. A combination of CaP graft with alternative medical options

such as autologous bone and e.g. platelet rich plasma (PRP) did not show further improvement of the bone healing and regeneration process. In general, the use of CaP eliminates donor site morbidity without compromising the outcome. Morbidity was minimal when CaP grafts were used for backfilling of donor harvest site.

Undesirable side-effects are reported to be very low or practically non-existent when using Ca/P BGS. Major complications such as non-union requiring revision, infection and foreign-body reaction were rare in the majority of studies. Results from a comparative opening wedge high tibial osteotomy (OWHTO) study including the use of a fixation plate and different types of bone grafts/substitutes (autologous bone and synthetic CaP BGS) versus no use of graft detected a difference between the rate of non-union and type of bone graft used, favourable for CaP. The protrusion of CaP BGS in OWHTO with medial knee osteoarthritis (OA) had no adverse effects. Incomplete resorption of the CaP graft (wedge) in OWHTO was reported up to 8 years post-surgery but showed a low incidence of complications and satisfactory conversion to total knee arthroplasty (TKA); delayed unions and wedge fracture did not cause complications or impact on clinical outcome.

There is a wealth of clinical data available showing the wide use of synthetic CaP based BGS as alternative treatment to autologous bone grafts, allografts and xenografts or a combination with them for filling of bone defects and fractures in a series of orthopaedic, trauma and surgery conditions. Although management of bone defects remains controversial particularly in terms of critical defect size and anatomic location, other factors such as health status and underlying conditions of the patient may justify the use of BGS also in non-critical size defects after careful evaluation. The clinical, radiological and histological data reported in the literature for CaP graft confirm the material properties supporting the bone healing, remodelling and regeneration process; the low allergy potential and excellent biocompatibility make a CaP a reliable alternative to medical treatment options. For a limited amount of bone loss, whenever there is good contact between the BGS and the surrounding bone tissue and/or a stabilization can be realised, CaP graft represents an effective and safe treatment of bone defects and fractures with good functional recovery and no inflammatory reactions.

5.4. Overall summary of clinical performance and safety

Clinical data and clinical evidence for INNOTERE 3D Scaffold is identified, collected and appraised through systematic PMS including PMCF throughout the expected lifetime of the device. The clinical data is used for the analysis of clinical safety and performance of the device including clinical benefit to demonstrate conformity with GSPR, the reassessment of the benefit-risk ratio and risk acceptability and for identifying and initiating appropriate measures including corrective actions. Data identification, collection and appraisal follow established methods and procedures according to the PMS-Plan.

During the PSUR reporting period from 01/2017-02/2022, INNOTERE processed 1 complaint. No risks were identified that required appropriate measures and no CAPA or FSCA were initiated for the device within the period of the evaluation. Results from FSCA database search did not reveal any findings as no relevant adverse events and safety reports were extracted for INNOTERE 3D Scaffold over the course of four years. At the same time, INNOTERE did not identify a systematic misuse or off-label use of the device. There were no incidents or medical device reporting by INNOTERE for the device; hence no trends can be derived for any of these PMS activities.

INNOTERE conducted a PMCF study with INNOTERE 3D Scaffold in opening wedge high tibial osteotomy (OWHTO) to confirm the clinical benefit and the acceptability of the benefit-risk ratio of the device. The retrospective study including 71 patients evaluated the clinical outcomes bone healing, osseointegration and resorption (mode of action) in a non-inferiority trial between INNOTERE 3D Scaffold and the comparator device OSferion®. Non-inferiority of INNOTERE 3D Scaffold is concluded for bone healing ($p=0.00868$). None of the patients experienced non-union (non-union rate 0%). INNOTERE 3D Scaffold is not inferior to the comparator device for mode of action; both test device and comparator device achieve 100% osseointegration. Non-inferiority of INNOTERE 3D Scaffold is concluded for resorption ($p=0.0081$). Complications reported for INNOTERE 3D Scaffold included four adverse events (pain, device fracture, hinge fracture, wound healing disorder), and one serious adverse event (infection) with no causal correlation to the device. No new risks were identified for CP-Scaffold. The results of PMCF show that the non-union rate of 0% is below the specified threshold acceptance criterion of 1.1%; furthermore the occurrence of the reported adverse events are within the specified threshold acceptance criteria of risk management, and identified residual risks remain acceptable. The PMCF study with INNOTERE 3D Scaffold when used as intended confirms the clinical performance and safety of the device including its

clinical benefit for the expected lifetime of the device outweighing any residual risks. The benefit-risk ratio is acceptable. The results from the PMS including PMCF provide relevant clinical data and clinical evidence for the analysis of the clinical safety and clinical performance including clinical benefit of CP-Scaffold in addition to the benefit-risk determination.

5.5. Ongoing PMCF

Ongoing activities comprise:

- Collection of feedback from distributors and customers through questionnaires on clinical safety and performance aspects
- Evaluation of complaints and vigilance data, if applicable

Following the completion of the PMCF study (2022-02), no new PMCF study is currently planned.

6. Possible diagnostic or therapeutic alternatives

Managing of bone defects is controversial particularly in terms of critical defect size and anatomic location and other factors such as health status and underlying conditions of the patient that may justify the use of BGS also in non-critical size defects after careful evaluation.
There are various bone substitute materials on the market, each of which has specific advantages and disadvantages that the surgeon has to consider. There are three main groups of bone substitutes available to date such as autologous bone, allografts and synthetic materials.

- Autologous bone is considered the gold standard among bone graft substitutes due to its osteogenic, osteoinductive, and osteoconductive properties. However, a major disadvantage is harvesting morbidity, resulting in persistent pain at the graft harvest site, and their limited availability.
- Allograft grafts offer osteoconductive properties but carry the potential for residual infection risks (viral transmission).
- Synthetic materials (alloplasts) are also osteoconductive and are offered in a variety of geometries that allow high accuracy in defect filling and ease of use for the surgeon.

No use of any bone graft substitute is a treatment alternative in defect sizes (non-critical) that will heal spontaneously without medical intervention.

7. Suggested profile and training for users

The use of INNOTERE 3D Scaffold is restricted to health care specialists who are familiar with handling bone substitute materials, the appropriate surgical techniques and the treatment of bone defects from their training. The use of INNOTERE 3D Scaffold does not require a device-specific training before its use.

8. Reference of applied harmonised standards and guidance documents

DIN EN 556-1:2002+ Cor 2006, DIN EN ISO 10993-3:2015, DIN EN ISO 10993-5:2009, DIN EN ISO 10993-6:2017, DIN EN ISO 10993-9:2022, DIN EN ISO 10993-10:2023, DIN EN ISO 10993-11:2018, DIN EN ISO 10993-12: 2021, DIN EN ISO 10993-14:2009, DIN EN ISO 10993-17:2024, DIN EN ISO 10993-23:2021, DIN EN ISO 11137-1:2020, DIN EN ISO 11137-2:2023, DIN EN ISO 11737-1:2021, DIN EN ISO 11737-2:2020, DIN EN ISO 13485:2021, DIN EN ISO 14602:2012, DIN EN ISO 14630:2013, DIN EN ISO 14971:2022, DIN EN ISO 15223-1:2022