Summary of Safety and Clinical Performance

Clouz OneKnot Polyester

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1 Purpose

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 Clouz OneKnot Polyester.

The SSCP is not intended to replace the Instructions For Use (IFU) [1] 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.

2 Scope

The following information is intended for users/healthcare professionals of Clouz OneKnot Polyester.

3 Definitions and Abbreviations

DEFINITIONS	
Name	**Definition**
Residual risk	Risk remaining after risk control measures have been taken.
ABBREVIATIONS	
Name	**Definition**
SSCP	Summary of Safety and Clinical Performance
SRN	Single Registration Number
IFU	Instructions for use
MDR	Medical Device Regulation
UDI-DI	Unique Device Identification – device identifier
CS	Common Specification

4 Related Documents

No.	Document ID	Document Title
[1]	CLZ.PAR.5.001.01.	Instructions for Use
[2]	CLZ.DEV.2.001.01.	Intended Use
[3]	CLZ.DEV.5.003.01.	Hazard Traceability Matrix
[4]	CLZ.CLI.1.008.01.	Post Market Clinical Follow Up Plan
[5]	CLZ.CLI.1.001.01.	Clinical Evaluation Plan
[6]	CLZ.CLI.2.001.01.	Clinical Evaluation Report
[7]		MDCG 2019-9 rev 1
[8]		Megas et Al., “A propensity score matched analysis of ventral-TAPP revealed it was less painful and costly than laparoscopic IPOM repair for small and mid-sized ventral hernias,” 2021.
[9]		MEDDEV 2.7.1 Rev. 4
[10]	CLZ.CLI.2.005.01.	Biocompatibility Assessment Report
[11]	CLZ.DEV.4.007.01.	Knot Verification Test Protocol and Report
[12]	CLZ.DEV.6.001.01.	Usability_Engineering_File
[13]	CLZ.DEV.5.004.01.	Risk Management Report

5 SSCP versions and revision history

5.1 SSCP language versions

The first SSCP version has been established in English. The first market entry for Clouz OneKnot is foreseen to be Germany. A German translation of the IFU for Clouz OneKnot is available.

5.2 Revision History

SSCP document number incl. revision number	**Language**	**Change Description**	**Revision validated by the Notified Body***
CLZ.CLI.2.004.01. Summary_of_Safety_and_Clinical_Performance.211207	English	First version	[ ] Yes [x] No

**class IIb implantable WET devices shall be validated by a NB as per MDCG 2019-9 Summary of safety and clinical performance A guide for manufacturers and notified bodies) **"No" is only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB.*

6 Device identification and general information

Device trade name(s)	Clouz OneKnot Polyester
Manufacturer's name and address	Clouz GmbH Schinkestr. 9 12047 Berlin Germany
Manufacturer's single registration number (SRN)	DE-MF-000007330
Basic UDI-DI	426074624clz1kUB
Medical device nomenclature description/ CND code	H010201
Class of device	class IIb according to MDR 2017/745, Rule 8 (Annex VIII)
Year when the first certificate (CE) was issued covering the device	Expected EU market approval in 2024
Authorized representative if applicable; name and the SRN	N/A
Name of the Notified Body (NB) that will validate the SSCP	DQS MED
Single Identification Number of the NB	0297

7 Intended use of the device

7.1 Intended purpose

Clouz OneKnot Polyester is intended for use in general soft tissue approximation and/or ligation, excluding use in cardiovascular, ophthalmic, and neurological procedures. Clouz OneKnot delivers a single knot and is intended for single patient use only [2].

7.2 Indication(s) and target population(s)

Clouz OneKnot was developed for the fast and secure placement of knots in surgical procedures. The non-absorbable suture may be removed upon healing or left indefinitely. The users of Clouz OneKnot Polyester are surgeons of any experience level.

7.3 Contraindications and/or limitations

Use of Clouz OneKnot Polyester is contraindicated in patients with known sensitivities or allergies to polyester and/or silicone.

8 Device description

8.1 Description of the device

Clouz OneKnot Polyester is a pre-tied non-closed knot for performance of a single knot.
Clouz OneKnot Polyester consists of the following components:

- Suture cartridge and pre-tied knot holder
- Needle and needle holder
- Non-absorbable polyester suture

Each suture cartridge, including the suture, needle and needle holder is packed within a single pouch, which is fitted into a dispenser box of 12e.a. products and sterilized by ethylene oxide (EtO).

8.2 A reference to previous generation(s) or variants if such exist, and a description of the differences

Not Applicable

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

Not Applicable

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

Not Applicable

9 Risks and warnings

9.1 Residual risks and undesirable effects

Adverse reactions associated with the use of non-absorbable polyester sutures include minimal initial inflammatory tissue reaction and transient local irritation at the wound site.

All identified risks have been mitigated as recorded in the Hazard Traceability Matrix document [3]. The remaining risks after risk reduction actions have been implemented are low because the risk of harm is unlikely, and would be slight, so all residual risks are considered acceptable.

9.2 Warnings and precautions

Users should be familiar with surgical procedures and techniques involving non-absorbable sutures prior to employing Clouz OneKnot. Misuse of this suture, like any other suture, can result in severe injury or death to the patient. When handling the suture, care should be taken to avoid any damage of the material due to application of surgical instruments, such as forceps or needle holders.

Care should be taken when handling surgical needles. Grasp the needle at approximately ¾ distance away from the pointed end in order to avoid bending or breakage of the needle. Users should exercise caution to prevent needle-stick injury. Used needles should be discarded in sharps containers. Do not re-sterilize or reuse the device.

9.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN), if applicable

Not Applicable

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

The aim of the clinical evaluation for Clouz OneKnot Polyester was to review the clinical performance and safety of the device and to evaluate its benefit-risk profile according to MEDDEV 2.7.1 Rev. 4 [9]. The results from the Clinical Evaluation are presented in the Clinical Evaluation Report [6], and summarized within this section of the SSCP. Clouz OneKnot Polyester is intended for fixation, tissue approximation and/or ligation where the use on non-absorbable sutures is appropriate, including minimally invasive surgery, excluding use in cardiovascular, ophthalmic and neurological procedures. Based on the analysis of clinical data from the literature review, and on the results of the risk analysis and preclinical testing of the device [11], as well as clinical data from the use of the manually tied Fikatas knot [8], which is identical to the pre-tied Clouz OneKnot Polyester, it is concluded that Clouz OneKnot Polyester provided by Clouz GmbH is able to fulfill its intended use as claimed by Clouz GmbH and raises no further questions regarding safety. Clouz OneKnot Polyester meets the General Safety and Performance Requirements as stipulated in MDR 2017/745, Chapter I. A systematic literature search in PubMed, Scopus, and free internet pages was conducted to give evidence and compile this clinical evaluation.
Moreover, it has been shown within this clinical evaluation that sutures represent the current state of the art in tissue approximation. Proofs of the performance and safety of the device under

evaluation was brought using published literature [6]. Risk reduction measures conducted by Clouz GmbH are adequate [13]. Usability aspects have been considered during the development of the device [12]. The performance of Clouz OneKnot Polyester is demonstrated by preliminary clinical data on the use of the manually tied Fikatas knot.
Known risk and side effects are outlined in the IFU [1], which contains all the important information to reduce the risk of use errors, on residual risks and their management. No unacceptable risks remain after implementation of the risk mitigation measures. All seven risks that were identified as not acceptable in the initial review, were mitigated to acceptable levels, and will be addressed in PMS activities/are foreseen to be followed-up in PMCF studies. Additional risks of Clouz OneKnot Polyester were not detected.
There are no concerns related to the performance and safety of the product under discussion. The performance and safety of the device under consideration can be regarded as demonstrated and in compliance with MDR GSPR I and GSPR II. The identified side-effects were acceptable when compared to product benefits and are compliant with the MDR GSPR III. The benefit outweighs the potential risks of the product and the benefit-risk profile according to the state of the art in the medical fields concerned, and according to available medical alternatives used under normal conditions of use, is compatible with a high level of protection of health and safety and in compliance with the MDR GSPR III.
Overall, sufficient evidence was available to support and demonstrate every intended performance and safety claim. From a clinical perspective, the general safety and performance requirements of the Medical Device Regulation 2017/745 applicable to Clouz OneKnot Polyester are fulfilled.

10.1 Summary of clinical data related to equivalent device, if applicable

Not Applicable

10.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

Not Applicable

10.3 Summary of clinical data from other sources, if applicable

General Surgeon Dr. med. Panagiotis Fikatas developed a modification of the surgical laparoscopic procedure for the repair of hernias in the abdominal wall, ‘ventral Transabdominal Preperitoneal Patch Plasty’ (ventral-TAPP). The primary objective was to develop an alternative to a well-established technique referred to as ‘laparoscopic intraperitoneal onlay mesh’ repair (lap. IPOM), which is associated with severe adverse events, including abdominal adhesions, and associated postoperative pain (Loit et al., 2017; Sharma A, et al., 2018). The latter is believed to be due to the fixation of a mesh with the posterior fascia with absorbable staples (Securestrap™, Ethicon) using a double crown technique. This approach is known to create tension in the tissue and irritate nerves with the protruding tips of the tacks/staples. The procedure developed by Dr. Fikatas and colleagues has two innovative steps. The first step is to close the hernia defect with an extracorporeally tied sliding knot (‘Fikatas knot’) which allows placement of knots in laparoscopic surgery only within the fascia layer close to the defect. In a second step, the mesh may be gently positioned in the preperitoneal space without further fixation yet held in place between tissue layers. Together, these measures reduce tissue tension beyond the fascia layer, eliminating the need for tacking and thus associated pain.

In a manuscript submitted for publication in the journal 'Surgical Endoscopy', the team report a clinical study of 180 patients with abdominal wall hernias which were either repaired with the lap. IPOM or modified ventral-TAPP procedures (*Megas, I-F, Benzing, C., Winter, A., Raakow, J., Chopra, S., Pratschke, J., and P. Fikatas, A propensity score matched analysis of ventral-TAPP repair with primary defect closure with a novel sliding knot, in comparison to laparoscopic IPOM for small and mid-sized ventral hernias. (2021) Surgical Endoscopy, submitted*) [8].

In this clinical study, 34 patients with abdominal hernias of ~ 5cm were treated with a modified ventral-TAPP procedure that utilized the Fikatas knot. Approximately ~4-6 interrupted non-absorbable/polyester sutures (Ethibond™, USP 0) with the Fikatas' knot were used to close each hernia. As such ~140-204 Fikatas knots were used in this clinical study. None of these 34 patients experienced hernia recurrence. Moreover, they had significantly less pain and shorter hospital stays, due to the procedure. These data also indicate that the use of the extracorporeally tied Fikatas sliding surgical knot to close the hernia, followed by the insertion of a mesh in the preperitoneal space without further fixation, is a safe combination.
The Fikatas knot has a locking function that allows for the secure approximation of tissues without cumbersome use of intracorporeal laparoscopic knot tying with e.g. multiple half-hitches which generally fail to secure tissue under such tension as peritoneum. Importantly, although the Fikatas knot used in this study was hand-tied, it has an identical conformation and loop structure to the pre-tied Clouz OneKnot device, albeit the latter is tied with a semi-automated machine and loaded onto a paper holder before sterilization.

10.4 An overall summary of the clinical performance and safety

Proofs of the performance and safety of the device under evaluation was brought using published literature. Risk reduction measures conducted by Clouz GmbH are adequate. Usability aspects have been considered during the development of the device. The performance of Clouz OneKnot Polyester is demonstrated by preliminary clinical data on the use of the manually tied Fikatas knot [8].
Known risk and side effects are outlined in the IFU [1], which contains all the important information to reduce the risk of use errors, on residual risks and their management. No unacceptable risks remain after implementation of the risk mitigation measures. All seven risks that were identified as not acceptable in the initial review, were mitigated to acceptable levels, and will be addressed in PMS activities/are foreseen to be followed-up in PMCF studies. Additional risks of Clouz OneKnot Polyester were not detected.
There are no concerns related to the performance and safety of the product under discussion. The performance and safety of the device under consideration can be regarded as demonstrated and in compliance with MDR GSPR I and GSPR II. The identified side-effects were acceptable when compared to product benefits and are compliant with the MDR GSPR III. The benefit outweighs the potential risks of the product and the benefit-risk profile according to the state of the art in the medical fields concerned, and according to available medical alternatives used under normal conditions of use, is compatible with a high level of protection of health and safety and in compliance with the MDR GSPR III.
Overall, sufficient evidence was available to support and demonstrate every intended performance and safety claim. From a clinical perspective, the general safety and performance requirements of the Medical Device Regulation 2017/745 applicable to Clouz OneKnot Polyester are fulfilled.
Clouz OneKnot Polyester is a class IIb, suture assistance device based on Well-Established Technology (WET). The conformance route chosen includes a full technical documentation, and Quality Management system review, but due to its particular status of WET technology, it is exempt from the requirement of clinical data (MDR, Article 52).

Numerous prospective and/or randomized controlled trials found have evaluated the use of extracorporeally pre-tied knots in open and laparoscopic surgery[6]. Results from these trials have demonstrated that these knots are advantageous due to their ease of deployment, and efficiency in holding the tissue edges together I.e. sufficient holding strength. Similarly, a major benefit of Clouz OneKnot Polyester is its ease of use and its holding strength, which have been demonstrated in usability testing and verification studies, as well as supported through clinical data from use of the manually tied Fikatas knot [8].
It can be stated that existing clinical data from the use of other extracorporeally pretied knots, and clinical data from the use of a manually tied extracorporeal Fikatas knot has demonstrated the performance of Clouz OneKnot Polyester in the context of tissue approximation in surgery. It is concluded that the performance of the Clouz OneKnot Polyester is in compliance with the MDR GSPR 1.

All clinically relevant safety information including precautions and training requirements is provided to the user in the Instructions for Use. Available data on the State of the Art and similar devices in literature and adverse events databases have been thoroughly evaluated. Clinical data regarding the use of extracorporeally, pre-tied sliding knots in laparoscopy emphasize the safety of placing pretied knots as opposed to manually, intracorporeally tied knots.
In conjunction with the successful clinical use of the Fikatas knot in the last years, it can be concluded that the benefit/risk ratio is positive when at least moderate benefits through the use of the Clouz OneKnot Polyester are expected by the responsible physician.
Clinical data from similar devices clearly indicate an acceptable level of safety. With regards to the product under evaluation, there are no special design features that pose specific safety concerns. A comprehensive risk analysis for the product under evaluation has been performed by the manufacturer. Thereby, potential risks have been addressed and discussed.
Silicon coating of sutures is described as biocompatible in the Biocompatibility Assessment Report [10].
Inherent risks associated with the use of pre-tied extracorporeal knots (i.e. procedure-related risks) have been detailed during the risk analysis in the Hazard Traceability Matrix [3]. These risks apply for the device under evaluation and similar devices. In the risk analysis, hazards and their clinical consequences have been characterized according to the putative harm for patients and probability of occurrence. Main potential risks listed in the risk analysis include:

- Knot placement failure
- Over-tightening of the knot causing tissue damage
- User/assistant-user needle-stick injury
- Wrong suture or needle size selected for the specific surgical need
- Use in a patient with allergy to the product materials
- Use of suture for a different use than intended

Risk-diminishing measures have been taken. For more detailed information, reference is made to the technical, biological, and clinical point of view. The residual risks for clinical use of the product under evaluation is tolerable after implementation of risk-minimizing measures.
The post-market surveillance will ascertain that Clouz OneKnot Polyester is a safe treatment option that comprises benefits including ease of use, appropriate strength, and knot locking that avoids knot loosening. The treating expert should make their patients aware of the risk of patients' allergy to polyester or silicon.
In the course of the present clinical evaluation, no new or unknown complications or risks associated with the use of Clouz OneKnot Polyester could be revealed. From a clinical point of view the clinical

use of the Clouz OneKnot Polyester (Clouz GmbH) for the treatment of tissue approximation during surgery, can be evaluated as a safe treatment option.
In conclusion, sufficient evidence is available to support and demonstrate the safety of Clouz OneKnot Polyester, in compliance with GSPR2 of the MDR.
The patient population for this device includes all patients undergoing surgery. The likelihood of benefit (reduced risk of knot loosening and failure of tissue approximation/wound opening) is high. A reduced risk of suture loosening in turn reduces the risk of repeated surgery and patient injury. An additional benefit in laparoscopic surgery is the reduction in surgery time, which has impact on the individual patient recovery as well as the time and cost of surgery. Further benefits include ease of use, in particular for surgeons with limited experience.
The risks of using Clouz OneKnot Polyester were determined to be the same as for using manually tied extracorporeal sliding knots in terms of knot security and knot strength, as well as in terms of sterility for the suture (which is equivalent), and the method of knot placement [8].

10.5 Ongoing or planned post-market clinical follow-up

Following the market approval of Clouz OneKnot Polyester, a PMCF study and a survey will be performed to confirm the safety of the device. These are detailed in the PMCF Plan [4]. The study will determine if there are any infections, serious bleedings, death-events, or any other non-anticipated reactions. Non-anticipated reactions will also be observed immediately during use of Clouz OneKnot or shortly after surgery.
In addition, a survey will be performed in order to get feedback from users (surgeons). Feedback will be collected proactively from healthcare professionals in clinics. Users surveyed will be selected to ensure varied regional and clinical representation. Finally, a literature search and review of case reports will be performed to reveal misuse or off-label use.
Justification for approach: polyester sutures are very common in surgery and similar products have therefore been in use for this purpose for decades. Surgeons are accustomed to handling sutures and surgical knots, and as such able to assess the effectiveness of the product both during and post-surgery. The survey will thus provide useful data on device usage and the PMCF study will provide data on patient outcome.

11 Possible diagnostic or therapeutic alternatives

The need for more efficient and user-friendly devices for implant fixation, and wound closure in restricted spaces is well documented, leading initially to the development of extracorporeally hand-tied sliding knots that could be utilized during laparoscopic surgeries. This need has driven innovation in several directions. These include laparoscopic instruments such as staplers (e.g. <www.medtronic.com> or <www.jnjmedicaldevices.com>), clips (<www.bbraun.de>), as well as assistance devices (OverStitch, Apollo Medical; EndoStitch, Medtronic; Eagle Claw VII, Olympus Medical Systems Corp), which allows for suturing deep within the cavities of the body (Göpel et al. 2011; Chiu et al., 2008; Halvax et al., 2015). Moreover, the development of barbed suture materials (Lin et al., 2017), such as V-Loc (<www.medtronic.com>), Stratafix (<www.jnjmedicaldevices.com>) or Quill (<www.bbraun.de>) (Gingras et al., 2012) allow for continuous suturing. These technologies are further enhanced when loaded e.g. into the EndoStitch or SILS (Single Incision Laparoscopic Surgery) suturing devices (<www.medtronic.com>). Routinely, these solutions are compared to more classical, manual suturing with both absorbable and nonabsorbable materials. Although most of these more sophisticated devices are functionally equivalent to manual knot placement and can be used to save time, they are quite costly.

12 Suggested profile and training for users

The users of Clouz OneKnot Polyester are surgeons familiar with surgical procedures and techniques, with variable experience in tying suture knots. The users should study the Instructions for Use carefully before attempting to use Clouz OneKnot Polyester.

13 Relevant SSCP information for patients

- Clouz OneKnot Polyester is a non-absorbable suture that may be removed upon healing or left in the body indefinitely.
- Clouz OneKnot Polyester is contraindicated in patients with known sensitivities or allergies to polyester and/or silicone.
- Adverse reactions associated with the use of non-absorbable polyester sutures include minimal initial inflammatory tissue reaction and transient local irritation at the wound site.

14 Reference to applicable standards and CS

Standard Designation Number / Document type	**Title**	**Specialty Task Group Area**	**Used for showing compliance to (insert paragraph or clause)**	**Used for reference only (Y/N)**	**Harmonized? (Y/N)**
EN ISO 13485:2016/AC:2018	Medical devices - Quality management systems - Requirements for regulatory purposes	Quality	4, 5, 6, 7 (except 7.5.2, 7.5.3, 7.5.4), 8	N	Y
EN ISO 14971:2019	Medical devices - Application of risk management to medical devices	Risk	4, 5, 6, 7, 8, 9, 10	N	Y
EN ISO 15223-1:20162021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements	Labelling	4, 5.1. 5.2.1, 5.2.3, 5.2.6, 5.2.8, 5.3.2, 5.3.4, 5.3.7, 5.3.8, 5.4.2, 5.4.3, 5.4.4	N	Y

ISO IEC 62366 2015 +A1:2020	Medical devices – Part 1: Application of usability engineering to medical devices	Usability	4.1, 4.2, 4.3, 5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8	N	N
EN ISO 10993-1:20112020	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2009)	Biocompatibility	5,6	N	N
EN ISO 20417:2021EN 1041:2008+A1:2013	Medical devices — Information supplied by the manufacturer of medical devices	Labelling, IFUs	4, 5, 6	NN	N
EN ISO 11607-1:2009 2019	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems (ISO 11607-1:2006)	Packaging	4, 5, 6, 7	N	
EN ISO 11607-2:2020	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes (ISO 11607-2:2019)	Packaging		N	
EN 556-1:2002	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices	Sterilization		N	

EN ISO 11135:2014/A1:2019	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation, and routine control of a sterilization process for medical devices - Amendment 1: Revision of Annex E, Single batch release (ISO 11135:2014/Amd 1:2018)	Sterilization		N	