In accordance with 21 CFR 807.87(h) and 21 CFR 807.92, the 510(k) Summary for the 3C Patch System is provided below.

1. SUBMITTER

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2. DEVICE

Name of Device: 3C Patch System
Common Name: Peripheral blood processing device for wound management
Classification Regulation: 21 CFR 864.9245
Regulatory Class: II
Product Code: PMQ
Panel: Hematology

3. PREDICATE DEVICE

Predicate: Cytomedix, Inc. AutoloGel™ System, BK060007

4. DEVICE DESCRIPTION

The 3C Patch System is a single use medical device used to prepare an autologous platelet-rich plasma (PRP) gel from the patient's peripheral blood by centrifugation, without the addition of any reagents.

The 3C Patch System consists of:

- 3C Patch Kit
  - This kit includes the sterile 3C Patch Device and 3C Patch Needle Holder.
  - In addition, this kit includes accessory components to draw blood (venipuncture needle set, skin preparation alcohol swab, and post-sampling adhesive bandage) and to cover the 3C Patch wound gel patch. These accessories are existing legally marketed products for blood access and wound management.

- 3C Patch Centrifuge Insert Kit
  - This kit includes the 3C Patch Holder with Holder Inserts, Inner Spring and Inner Plate, and the 3C Patch Outer Spring.
- 3C Patch Counterbalance

The 3C Patch System is used with the Eppendorf 5702 centrifuge, a third-party commercially available centrifuge capable of driving the centrifuge insert at 3000g.

The 3C Patch System uses a 2-step mechanical centrifugation process, requiring no reagent additives, to produce an autologous PRP gel for direct application to cutaneous wounds as specified in the Indications for Use, below.

The key components of the 3C Patch System that are in the blood path include the legally marketed sterile venipuncture needle set, the 3C Patch Device, and the 3C Patch Needle Holder. The 3C Patch Device and 3C Patch Needle Holder are constructed of medical grade polyester (PET) and are sterilized by Reapplix ApS using gamma radiation. The other components/materials with blood contact are the brombutyl rubber plug and natural butyl rubber O-ring.

5. INDICATIONS FOR USE

The indications for use for the 3C Patch System are as follows:

> The 3C Patch System is intended to be used at point-of-care for the safe and rapid preparation of platelet-rich plasma (PRP) gel from a small sample of a patient's own peripheral blood. Under the supervision of a healthcare professional, the PRP gel produced by the 3C Patch System is topically applied for the management of exuding cutaneous wounds, such as leg ulcers, pressure ulcers, and diabetic ulcers and mechanically or surgically-debrided wounds.

6. COMPARISON OF TECHNOLOGICAL CHARACTERISTICS

The similarities and differences in technological characteristics between the subject 3C Patch System and the predicate AutoloGel™ System, as well as the system outputs, are summarized below.

6.1. Similarities

At a high level, the subject and predicate systems are based on the following same technological characteristics:

- Both systems include a single use medical device kit used to prepare, at point-of-care, an autologous PRP gel from the patient's own peripheral blood by centrifugation.
- Both systems use centrifugation to concentrate platelets from the patient's peripheral blood to create autologous PRP gels suitable for use in cutaneous wounds.
- Both systems use similar single-use, disposable blood drawing components.

  - 3C Patch System: sterile skin preparation alcohol swab (commercially available), sterile vacuum container/tube (3C Patch Device, for use in processing), sterile venipuncture needle set (commercially available); post-sampling adhesive bandage (commercially available); and sterile needle holder (connector/holder for venipuncture and 3C Patch Device).
  - AutoloGel™ System: tourniquet; alcohol skin prep pads; sterile blood collection tubes; sterile needle venipuncture needle set; gauze sponges; post-sampling adhesive bandage (band aid); foam tube holder; and a wound measuring guide (ruler).

- The physico-chemical attributes between the 3C Patch and AutoloGel™ PRP are substantially equivalent.

6.2. Differences

The following technological differences exist between the subject and predicate systems:

- The 3C Patch System uses only the patient's own peripheral blood (i.e., no reagents) to create the PRP gel. The predicate AutoloGel™ System uses exogenous thrombin to create the PRP gel.
- The 3C Patch System prepares the PRP gel in a 2-step centrifugation process while the predicate AutoloGel™ System prepares the PRP gel in a single centrifugation process. The 2-step centrifugation process of the 3C Patch System is accomplished with its main component - the 3C Patch Device. The design of the 3C Patch Device resembles the shape and general construction of standard centrifuge tubes but differs by inclusion of a "lifter" to help with the second centrifugation (or compaction) step.
- The 3C Patch System is used with the Eppendorf 5702 centrifuge, a third-party commercially available centrifuge capable of driving the centrifuge insert at 3000g. The AutoloGel™ System supplies a centrifuge.

7. PERFORMANCE DATA

Bench, physico-chemical, biocompatibility, sterility, and shelf life testing were performed to support the safety and effectiveness of the subject 3C Patch System in creating a PRP gel for wound management (referred to as the 3C Patch).

7.1. Bench Testing of 3C Patch System

Bench testing was performed on the 3C Patch System to establish that it can manufacture a consistent 3C Patch. The key bench testing of the system established the time from blood collection to first centrifugation and established the centrifugation force and time period.

7.2. Physico-chemical Testing of the 3C Patch and Predicate

System outputs were generated as per the protocol. Two sets of three PRP gels were generated from each donor using the 3C Patch and a protocol similar to that of the AutoloGel™ System. Each set from a donor was generated on separate, non-consecutive dates. Testing was performed the same day that the set was generated.

The following physico-chemical parameters were tested:

- Moisture content (%)
- Cell Recoveries (%) - Platelets
- Cell Recoveries (%) – White Blood Cells
- Cell Recoveries (%) – Red Blood Cells
- Clot strength, measured by the maximal break force
- Shear strength, measured by the percent elongation before first tear
- Gel stiffness, determined by the force needed to stretch the PRP gel (N/mm)

The physico-chemical test parameters of moisture content, clot strength, shear strength, and gel stiffness met the predefined study acceptance criteria of a 20% difference (0.8, 1.25).

The reproducibility was assessed by the coefficient of variation. The acceptance criterion was ≤20% for all parameters except RBC recovery. Across these parameters, the reproducibility ranged 0.6-14.3% for the 3C Patch and 1.4-16.3% for the AutoloGel™ PRP. These parameters met the acceptance criteria.

With regard to RBC recovery results, RBCs are regarded as an impurity when it comes to PRP preparation. Therefore, the study acceptance criterion for RBC recovery was set at <5%. Both the 3C Patch and predicate AutoloGel™ System met the acceptance criterion.

In summary, this physico-chemical testing demonstrates the substantial equivalence of the outputs from the 3C Patch System and predicate AutoloGel™ System.

7.3. Biocompatibility Testing of 3C Patch System

The biocompatibility assessment on the 3C Patch System followed the methodology of ISO 10993-1 Biological evaluation of medical devices -- Part 1. The 3C Patch System contacts the patient's body indirectly via the 3C Patch for less than 30 minutes. More specifically, the following biocompatibility testing was performed and no biocompatibility issues were found:

- Cytotoxicity testing as per ISO 10993-5:2009
- Irritation and Skin Sensitization as per ISO 10993-10
- Intracutaneous (Intradermal) Reactivity Test in the Rabbit as per ISO 10993-10.

7.4. Sterility Testing of 3C Patch System

The 3C Patch System is comprised of both sterile and non-sterile components. Sterility testing was performed consistent with the FDA guidances entitled, "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile" and "Updated 510(k) Sterility Review Guidance K90-1." The 3C Patch Device and 3C Patch Needle Holder are sterilized by gamma radiation for a sterility assurance level of 10^{-6}.

The 3C Patch Device is non-pyrogenic as confirmed by Limulus Amebocyte Lysate (LAL) testing performed as per "ANSI/AAMI ST72: 2011 Bacterial endotoxins – Test methods, routine monitoring, and alternatives to batch testing."

7.5. Shelf Life Testing of 3C Patch System

The shelf life testing supports a shelf life of 24 months of the 3C Patch System.

7.6. Clinical Studies of the 3C Patch

Reapplix conducted two prospective clinical studies[1,2,3] to evaluate the safety and clinical performance of 3C Patch System for the management of various chronic wounds. The clinical evidence supports substantial equivalence to the predicate device with comparable clinical benefits and adverse event profiles.

7.6.1. Study 1

This prospective, multicenter, open-label, and uncontrolled study[2] evaluated the safety and clinical performance of 3C Patch in the treatment of recalcitrant chronic wounds. The 16 wounds include five diabetic foot ulcers, five venous ulcers, three surgical heel wounds, two malleolar wounds, and one amputation wound. The wounds were 2 to 108 months (median 24 months) in duration, from 0.4 to 15.7 cm^2 (median 2.3 cm^2) in size, and had not responded to previous treatments. Fifteen patients, with 16 lower extremity chronic wounds were treated weekly with 3C Patch for 6 weeks, or until healing was complete.

Efficacy: Of the 15 subjects included for treatment, four healed completely (27%) during six weeks of study period. Two more wounds achieved complete healing four and eight weeks after the study period. The sizes of all six healed wounds were within $1cm^2$ at the baseline. Of note, three patients withdrew from the early phase of the study due to adverse event of foot infection and not meeting eligibility criteria; their wound healing status was unknown. Mean wound area decreased by 65% (95% confidence interval 45.6% to 83.8%) resulting in a median wound size of 0.9 cm^2 (range 0-9.6 cm^2). Two wounds showed no reduction in wound area.

Safety: There were no serious adverse events. One patient experienced increased exudate, redness, pain, and wound enlargement after fourth treatment with 3C Patch as a result of an infection with hemolytic Streptococcus B. The patient was treated with systemic antibiotics and this patient withdrew from the study.

7.6.2. Study 2

A prospective, open-label, uncontrolled study[3] evaluated the clinical performance of 3C Patch in chronic diabetic foot ulcers at five Danish and two Swedish hospital-based wound-care clinics. The diabetic foot ulcers were more than six weeks in duration, less than $10cm^2$ in size, and were classified as Wagner grade 1 or 2. Forty-four subjects were treated weekly with 3C Patch for up to 19 weeks or until wounds were completely healed.

Efficacy: Of 44 subjects included in treatment, complete wound healing was achieved in 14 (32%) wounds within 12 weeks and 23 (52%) wounds within 20 weeks. Of note, five patients who withdrew in early phase of the treatment with unknown healing outcome are included for the healing rate estimation. Mean time to complete healing was 11 weeks despite the average wound duration of 56.5 weeks at inclusion. Wound areas were reduced by 80% during the 20-week study period. Further, a statistically significant (P=0.002) area change was observed when comparing the two screening weeks with the first two treatment weeks.

Safety: 44 patients with diabetic foot ulcers who received at least one treatment with 3C Patch were evaluated. A total of 33 AEs and 12 SAEs were record during the two weeks of run-in and 20 weeks of study period. Three new ulcers and seven foot ulcer infections (three in target ulcers) were identified. Of seven cases of wound infection, three cases of osteomyelitis were diagnosed in early phase of study and treated with systemic antibiotics and bone resection. The other AEs, one of increased wound size and one new ulceration (1.5 cm from the study wound), were resolved by further off-loading and continued 3C Patch treatment. Five scheduled 3C Patch applications (<1% of all scheduled treatments) were canceled due to difficulty in blood draw and device/handling failure.

8. CONCLUSIONS

Reapplix has compared the technological characteristics of the subject 3C Patch System to those of the predicate AutoloGel™ System. This 510(k) information has demonstrated that the technological characteristics of the 3C Patch System are substantially equivalent to those of the predicate AutoloGel™ System with regard to its ability to produce autologous PRP gel at the point of care from a small sample of the patient's own peripheral blood.

The 3C Patch System and the AutoloGel System have nearly identical indications for use statements, and the two systems have many similarities in terms of the technological characteristics of the product and the intent to produce an autologous PRP gel by centrifugation and polymerization of an autologous PRP extract. Most of the components of the two systems are also similar or comparable.

The difference between the two systems is the inclusion and use of reagents in the AutoloGel™ System. The 3C Patch System eliminates the need for these by immediate point-of-care processing and use of the natural coagulation process in the patient's own blood to form a platelet rich gel.

The outputs of both systems are autologous PRP gels that are easily handled and applied to cutaneous wounds. The physico-chemical properties of the outputs are substantially equivalent.

Through both non-clinical and clinical testing, the 3C Patch System has been shown to perform as specified and in a comparable way to the predicate device that is currently marketed for the same intended use.

Two prospective clinical studies demonstrate that 3C Patch System has safety profiles and clinical performance comparable to those of the predicate device when used for the management of chronic wounds in combination with standard wound care.

In summary, the indications are nearly identical, and the technological characteristics between the 3C Patch System and the AutoloGel™ System are equivalent. They are both comprised of a set of components, including a centrifuge, that are designed to prepare an autologous PRP gel to be used for wound management. Based on the comparable indications for use, technological characteristics, and output performance, and safety profile, the 3C Patch System is substantially equivalent to the AutoloGel™ System.

References

[1] Please note that the clinical studies refer to the 3C Patch System and its output as the LeucoPatch® System and the LeucoPatch®, respectively.

[2] Jørgensen, B., Karlsmark, T., Vogensen, H., Haase, L. & Lundquist, R. A pilot study to evaluate the safety and clinical performance of Leucopatch, an autologous, additive-free, platelet-rich fibrin for the treatment of recalcitrant chronic wounds. The International Journal of Lower Extremity Wounds 10, 218–23 (2011).

[3] Löndahl, M., Tarnow, L., Karlsmark, T., Lundquist, R., Nielsen, A. M., Michelsen, M., … Zakrzewski, M. (2015). Use of an autologous leucocyte and platelet-rich fibrin patch on hard-to-heal DFUs: a pilot study. *Journal of Wound Care*, *24*(4), 172–178.