SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Mechanical and enzymatic autologous skin processor for preparing cell suspension, for stable vitiligo, with applicator
Device Trade Name:	RECELL® Autologous Cell Harvesting Device (Model Number: AVRL0102)
Device Procode:	QWY
Applicant's Name and Address:	AVITA Medical Americas, LLC. 28159 Avenue Stanford, Suite 220 Valencia, CA 91355
Date(s) of Panel Recommendation:	None

Premarket Approval Application (PMA) Number: BP220799

Date of FDA Notice of Approval: June 16, 2023

Breakthrough Device Designation: Granted November 1, 2022

II. INDICATIONS FOR USE

The RECELL Autologous Cell Harvesting Device is indicated for repigmentation of stable depigmented vitiligo lesions in patients 18 years of age and older. The RECELL Device is intended for use by an appropriately licensed and trained healthcare professional at the patient's point-of-care for the safe and rapid preparation of Spray-On Skin Cells from a small sample of a patient's own skin. The suspension of Spray-On Skin Cells is suitable for application to skin resurfaced by an ablative laser. A portion of the suspension of Spray-On Skin Cells may also be applied to the donor site.

III. CONTRAINDICATIONS

- RECELL is contraindicated for the treatment of patients with a known hypersensitivity to trypsin or compound sodium lactate solution (Hartmann's Solution).
- The skin sample collection procedure specified for use of RECELL should not be used with patients having a known hypersensitivity to anesthetics, adrenaline/epinephrine, povidone-iodine, or chlorhexidine solutions.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the RECELL Autologous Cell Harvesting Device labeling.

V. DEVICE DESCRIPTION

The RECELL Autologous Cell Harvesting Device (Model Number: AVRL0102, referred to as the RECELL Device throughout this document) is a stand-alone, battery powered cell separation device operated by an appropriately-licensed healthcare professional at the patient's point of care. The device enables the processing of a small, thin split-thickness skin sample 0.006-0.008 inch (0.15-0.20 mm) in depth to prepare a cell population in suspension for immediate delivery onto a prepared wound surface. Nonclinical performance testing demonstrates processing of harvested autologous skin samples ranging in size from 1 cm^2 to 6 cm^2 using the RECELL Device generates a viable cell suspension. By processing multiple (up to 4) samples of 6 cm^2 autologous thin split-thickness skin, a single RECELL Device can generate a volume of Spray-On Skin™ Cells (also previously referred to as Regenerative Epidermal Suspension, or RES®) sufficient to cover a prepared area (treatment and donor site) 20 times the area of the donor skin sample up to and including 480 cm^2.

The device is a sterile, single use, stand-alone unit with a built-in heater, process indicators, and work surface (the RECELL Processing Unit, RPU). The user can enzymatically and mechanically process a small skin sample to produce a suspension of Spray-On Skin Cells. Processing tools provided with the device include off-the-shelf syringes, scalpels,and fill needles. The device also includes nozzles that attach to syringes and can be used to aerosolize the cell suspension onto the wound. The proprietary RECELL Enzyme is reconstituted with sterile water (included) and used to facilitate disaggregation of cells from the harvested donor skin. A buffer solutionis also provided to suspend the disaggregated cells for delivery to the prepared wound site. The device is designed for point of care use. No cell culturing processes are involved in the procedure. The resulting suspension of cells comprises a mixed population predominantly of keratinocytes and fibroblasts. The presence of viable melanocytes has also been demonstrated. Additionally, sub-populations of keratinocytes critical for re-epithelialization have been identified in the Spray-On Skin Cells including basal keratinocytes, suprabasal keratinocytes, and activated keratinocytes. For vitiligo, the delivery of melanocytes, keratinocytes and fibroblasts is important for restoring natural pigmentation to the appropriately prepared recipient area.

The product is packaged to facilitate the processing steps for the system components, which are assembled within three (3) boxes, denoted as "A", "B" and "C". The component boxes are placed in a shelf box tray with the RECELL RPU, and a Procedure Guide.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are currently no point-of-care products to prepare a cellular suspension for autologous skin cell transfer intended for treatment of stable vitiligo. Current device treatments include phototherapy with cleared devices (Product Codes GEX and FTC), including narrowband ultraviolet (UV) B, psoralen with UVA, and khellin with UVA or UVB. However, these cleared devices are indicated for dermatologic conditions which include vitiligo but not specifically for repigmentation. Examples include the PALLAS 308/311 Solid-State UV Laser System (cleared under K191501) and the Zerigo (formerly

Clarify Medical) Phototherapy System (cleared under K170489). Additionally, Opzelura (ruxolitinib) cream (1.5%) was approved for the topical treatment of nonsegmental vitiligo in adult and pediatric patients 12 years of age or older. Opzelura, however, is associated with the JAK inhibitor class Black Box warning which includes risk of serious infection, mortality, malignancy, major adverse cardiovascular events, and thrombosis.

VII. MARKETING HISTORY

The RECELL Autologous Cell Harvesting Device has been marketed in the United States since 2018 for a different clinical indication (BP170122). It has received a Conformité Européene ("European Conformity",CE) mark and was commercialized in the European Union (EU) in 2005. Japan approval and commercialization occurred in 2022. In addition, the RECELL Device also has been commercially marketed in Australia since 2006 and in China since 2008. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Most potential adverse effects associated with the RECELL Autologous Cell Harvesting Device for vitiligo are those related to the procedure. These include scarring, erythema, Koebner phenomenon, pruritus, and worsening vitiligo.

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A summary of non-clinical laboratory studies that were performed on the RECELL Autologous Cell Harvesting Device is provided below:

A. Laboratory Studies

Bench Testing – Design Verification: Testing was performed on discrete components and assemblies of the device to verify that individual elements function and perform as specified. The purpose and results of the design verification testing performed are summarized in Table 1 below:

Table 1 – Design Verification Testing

Test Description	Test Purpose	Results
RECELL Processing Unit (RPU) Functional Testing	Verify the integrated RPU assembly functionality met specified device requirements. The functionof all features of the integrated RPU assembly was tested to established criteria as defined in the RPU specification.	Results demonstrated that all RPU assemblies passed the acceptance criteria for the self-test, run sequence, and device lock-out functionality. Temperature logs obtained during monitoring of theheating cycle of the RPU, verified that all units met the criteria and performed as specified.
RPU Environmental Use Conditions Testing	Verify the integrated RPU assembly functionality met specified device requirements at environmental operating limits.	Results of the environmental conditions testing demonstrated that all RPU assemblies passed the acceptance criteria for all functional tests at the following environmental conditions: • Temperature: 15 - 35ºC • Humidity: 10 – 90% relative humidity (RH) • Pressure: 65 – 106 kPa
Spray Nozzle – Cell Distribution	Demonstrate the cell distribution obtained using the RECELL Device spray nozzle provides sufficient coverage during application.	Sprayed cell suspensions demonstrated adequate coverage.The results indicate that the sprayed cells are spread over the surface and provide coverage overnearly the entire surface.
Enzyme Activity Verification	Verify that the reconstituted Enzyme maintained sufficient activity to make viable cell suspensions when processing multiple skin samples.	Results show the enzyme activity remained above the acceptance criterion for all test groups throughout the processing cycle. Use of the same Enzyme solution for multiple samples did not significantly impact cell disaggregation or viability of the cells.

Bench Testing – Integrated Device Performance: Testing was performed using complete RECELL Devices to establish that the different steps of tissue processing with the device are capable of reproducibly processing tissue into viable cell suspensions. The conditions and methods were planned to simulate the intended skin sample processing procedure forthe RECELL Device. The objective was to characterize and demonstrate thetechnical capability of the integrated device under controlled simulated conditions. The purpose and results of the design verification testing performed is summarized in Table 2 below:

Table 2 – Integrated Device Performance Testing

Test Description	Test Purpose	Results
Cell Suspension Characterization	To establish cell processing yields, to verify the viability of cellspre- and post-spray application, and to determine the proportion of cell types. The study also evaluated the	The following results were observed: • Verified that no significant differencesin cell viability occurred between pre- and post-spray suspensions produced by the RECELL Device, nor between small and large skin graft sizes.
Cell Suspension Characterization (cont.)	cell suspension for the proportion of single cells to aggregates and to confirm that the tissue processing did not significantly increase apoptotic activity. The intent of this study was todemonstrate the ability of the device to produce viable cell suspensions.	• Results demonstrated that fibroblasts and keratinocytes represent the largest proportions of cells, followed by a small proportion of melanocytes. • Determined the absence of cell aggregates of any size in amounts of significance that could affect the application of cell suspensions to patient wounds. • Only approximately 2%, of cells in the suspension were apoptotic, and verified that pre- and post-spray suspensions did not have statistically different apoptotic activity.
Cell Suspension Reproducibility	Establish that when used by different operators the RECELL Device can generate viable cell yields similar to or greater than yields established in the cell characterization study.	In all cases, users were able to prepare suspensions with viable cell yields at the average or above cell yields established in the cell suspension characterization study. This confirmed that different users could consistently process tissue samples using the RECELL Device to produce cell suspension with viable cells.
Enzyme Carry-Over Testing	Confirm that there is a significant decrease in (b) (4) in the final cell suspension	It was observed that even without (b) (4) in the (b) (4), the enzyme carry-over based on (b) (4) was minimal. With immersion in (b) (4), the average carry-over dropped slightly further than without (b) (4).

Biocompatibility: Biocompatibility testing was performed on the sterile RPU assembly, spray nozzles and Enzyme. Testing was performed by an independent testing facility on finished and sterilized product in accordancewith International Organization for Standardization (ISO) 10993-1:2009 "*Biological Evaluation of Medical Devices Part-1: Evaluation and Testing*" as specified in the FDA guidance *'Use of International Standard ISO 10993-1, Biological Evaluation of Medical Devices – Part 1: Evaluation and testing within a risk management process'* dated June 16, 2016.
Biocompatibility tests were conducted in compliance with U.S. Food and Drug Administration Good Laboratory Practice (GLP) regulations set forthin 21 CFR Part 58. All biocompatibility tests passed their corresponding acceptance criteria. Table 3 and Table 4 summarize the results of biocompatibility tests that were performed.

Table 3 – Biocompatibility Testing for RPU Assembly and Spray Nozzles

Biocompatibility Test	Results	PASS/FAIL
Cytotoxicity	Non-Cytotoxic	PASS
Guinea Pig Maximization Sensitization Test	No evidence of sensitization	PASS
Intracutaneous Reactivity Test	Non-irritant	PASS
Acute Systemic Injection Test	Non-Toxic	PASS
Rabbit Pyrogen Test (Material Mediated)	Non-pyrogenic	PASS

Table 4 – Biocompatibility Testing for Enzyme

Biocompatibility Test	Results	PASS/FAIL
Genotoxicity: *Salmonella typhimurium* Reverse Mutation Assay – Ames Test	Non-mutagenic	PASS
Genotoxicity: In Vitro Mouse Lymphoma Assay	Non-mutagenic and non-clastogenic	PASS
Genotoxicity: In Vivo Mouse Micronucleus Assay	Non-mutagenic	PASS

Sterility Assurance: The applicable components and assemblies of theRECELL Device are sterilized by the following traditional methods:

- Enzyme: Gamma radiation sterilization cycle;
- Buffer: Moist heat sterilization;
- RPU: Ethylene oxide gas sterilization;
- Spray Nozzle Assembly: Gamma radiation sterilization cycle.

For the Enzyme and the spray nozzle assembly, sterilization validations were completed in accordance with the following standards:

- ISO (b) (4)
- ISO (b) (4)

A Verification Dose Maximum (VD_{max}) method was used for the substantiation of the gamma radiation sterilization dose. All required testing as established by the above standards for sterilization validation was successfully performed and passed all acceptance criteria. The gamma sterilization dose has been successfully demonstrated to be effective in providing the sterility assurance level (SAL) of (b) (4) for the Enzyme and spray nozzle assembly of the RECELL Device.

For the Buffer, a sterilization validation was completed in accordance with ISO (b) (4). An (b) (4) validation method was employed to assure an SAL of (b) (4). All required testing as established by the above standard for moist heat sterilization validation was successfully performed and passed all acceptance criteria.

For the RPU, a sterilization validation was completed in accordance with ISO (b) (4) An (b) (4) validation method was employed to assure an SAL of (b) (4). All required testing as established by the above standard for ethylene oxide sterilization validation was successfully performed and passed all acceptance criteria. Representative samples of the RPU were evaluated for ethylene oxide (b) (4) Based on the results, ethylene oxide (b) (4) for the RPU were within specified limits for limited exposure (b) (4).

Packaging Integrity / Shipping Testing: The RECELL Device is packaged in a single corrugated shelf box that has a sliding inner tray that contains a single sterile-packaged RPU and three component set boxes.The capability of the device packaging to protect the device and maintain a sterile barrier has been validated in accordance with the following standards:

- ISO (b) (4)
- ISO (b) (4)

Applicable RECELL components were subjected to the following worst-case sterilization conditions prior to conditioning:

- Enzyme and Nozzles- Gamma radiation: Maximum dose (b) (4)
- Buffer- Moist heat: (b) (4) steam cycle
- RPU- (b) (4) ethylene oxide cycle

Finished packaged RECELL Devices were subjected to the following conditioning prior to testing:

- Environmental conditioning ((b) (4)
- Simulated transportation conditioning (in accordance with ASTM (b) (4))

Results of the device and package integrity testing demonstrate that all components of the RECELL Device met all defined acceptance criteria after being subjected to the environmental and shipping conditions. The integrity of all sterile barrier packages was demonstrated to be intact with (b) (4) detected and the seal strength was maintained within specification for all packages. Container closure integrity for all vials of Enzyme, Buffer, and water-for-injection (WFI) were demonstrated to remain intact with (b) (4) within the specified limits. All remaining tests for product integrity and functionality demonstrated that all components were unaffected by the conditioning and met their design specifications. The packaging configuration of the RECELL Device was qualified to provide a sterile barrier and sufficient protection for the device under expected storage, handling, and distribution conditions.

Shelf Life of RECELL Device: Product stability and sterile package shelf life are being qualified under an on-going stability test program.
Finished packaged RECELL Devices were initially subjected to the following conditioning prior to testing:

- Sterilization:
  - Enzyme and Nozzles- Gamma radiation: Maximum dose (b) (4)
  - Buffer- Moist heat: (b) (4) steam cycle
  - RPU- (b) (4) ethylene oxide cycle
- Environmental conditioning ((b) (4)
- Simulated transportation conditioning (in accordance with ASTM (b) (4))

RECELL Devices were subjected to real-time aging at ambient conditions (25°C/60% RH). Real-time aging will be performed from 3 months to (b) (4) months. At each time point, the product integrity and functionality testing is performed.

Currently, product stability and packaging shelf life at 3, 6, 12, 18, (b) (4) months real-time for the RECELL Device components (without Enzyme) have been completed. Results of testing demonstrate that the components of the RECELL Device met all defined acceptance criteria for product stability and package integrity after being subjected to the aging conditions.

It is noted that the Enzyme stability is evaluated separately. The finished and packaged Enzyme component will be subjected to the following conditioning prior to testing:

- Sterilization - Gamma radiation: Maximum dose (b) (4)
- Environmental conditioning ((b) (4)
- Simulated transportation conditioning (in accordance with ASTM (b) (4))

Real time aging was performed from 3 months under ambient temperature 25°C and 60% RH. At each time point, the product stability and container integrity testing is performed. Determining stability of the RECELL Enzyme device component includes measurement of the Enzyme's activity using a (b) (4) -based assay that has undergone prior validation.

A prospective study assessing Enzyme stability was performed to support the shelf-life of (b) (4) months.

Electromagnetic Compatibility and Electrical Safety Testing: Electromagnetic Compatibility (EMC) testing was performed on a standalone RPU of the RECELL Device. Testing included compliance for both emission and immunity tests in accordance with (b) (4) . The RPU assembly

of the RECELL Device met all the applicable requirements of (b) (4).

Electrical safety testing of the RECELL Device was performed in accordance with (b) (4) In addition, safety testing performed in accordance with (b) (4) for usability of the RECELL Device. Overall testing results demonstrate the RECELL meets all applicable requirements set forth in (b) (4).

Software Testing: Testing was conducted to ensure the performance of the embedded RPU firmware (the only software containing component of the RECELL Device) met the software requirements specifications. Verification and validation activities were completed for the device firmware according to the FDA guidance '*General Principles of Software Validation*' dated January 11, 2002. Testing of the firmware implementation was accomplished through unit, integrated system, and regression testing. The results of all software testing passed all test criteria and based on these results the RECELL Device firmware was verified and validated to meet its functional requirements.

Human Factors and Usability: The Human Factors information provided in the PMA original submission relied on previous Human Factors validation testing conducted on the RECELL Device that was approved for a different clinical indication (BP170122). The previous Human Factors Report contained summative validation results which demonstrate the RECELL Device user interface (including the device and accessories, Instructions for Use (IFU), Procedure Guide (PG), and representative training) allows for safe and effective operation for the intended use by intended users within the intended use environment, without compromise to medical care or patient or user safety for the clinical indication approved in BP170122. The Report was in alignment with FDA/Center for Devices and Radiologic Health (CDRH) Human Factors guidance and FDA-recognized Human Factors standards:

- FDA CDRH's final guidance: Applying Human Factors and Usability Engineering to Medical Devices that was issued on February 3, 2016
- IEC 62366-1:2015, titled Medical Devices – Part 1: Application of Usability Engineering to Medical Devices
- AAMI/ANSI HE75: 2009 Human Factors Engineering – Design of Medical Devices

The previous summative validation study was performed with a total of (b) (4) healthcare professionals who specialized or were experienced in burn care and with intended prior experience with aseptic technique. Each participant completed a series of simulated use scenarios in a representative operating room as they were observed and asked questions by independent moderators. During the collection of objective and subjective data, it was found that all users were able to prepare and apply a simulated cell suspension successfully. No user errors were observed that would lead to or result in death or a severe or permanent injury to the patient or

user. There were no critical user errors that would be further mitigated via modifications of the device or user interface and therefore the device has been demonstrated to be suitably designed for its intended use. Additional Human Factors validation testing will be conducted with participants, use environments, and uses that are realistically representative of the actual intended users, use environments, and uses of the RECELL Device for vitiligo as a Post-Approval Study.

B. Animal Studies

Three animal studies were conducted during the initial development of the RECELL Device to establish feasibility of applying autologous cell suspensions to a wound bed. The first two studies were performed early in the development life cycle of the RECELL Device to focus on the feasibilityand potential of using an autologous cell suspension to improve wound healing with split thickness autografts. These studies occurred prior to completion of the finished device but used a similar process to the current RECELL Device to generate and apply a cell suspension. A third study was performed using Spray-On Skin Cells from the RECELL Device in combination with a skin substitute. Each of these three studies were designed to evaluate the ability of a cell suspension to facilitate wound re-epithelialization. All three studies were performed in a porcine model, as this has been identified as an acceptable wound healing model. These studies demonstrated that use of an autologous cell suspension combined with autograft for full-thickness wounds can reduce the time required for wound re-epithelialization when compared to autograft alone. FDA has reviewed the findings in these publications and found them supportive of this approach for human studies.

C. Additional Studies

Viral Clearance Studies: The RECELL Device uses an animal-derived enzyme as the active ingredient of the RECELL Enzyme in the cell suspension preparation process.

To establish that the RECELL Enzyme poses a minimal risk of introducing adventitious viruses to a patient, a study based on peer-reviewed literature and expert interpretation has been performed to evaluate the risk control measures used to ensure adequate viral inactivation. A risk-based approach that combines the recommendations from the FDA draft guidance 'Medical Devices Containing Materials Derived from Animal Sources' dated January 23, 2014 with another regulatory guidance concerning the use of animal-derived enzyme in the manufacture of human biological medicinal products (EMA/CHMP/BWP/814397, effective September 1, 2014) was employed to evaluate the manufacturing process and procedural steps that facilitate viral inactivation.

Worst-case estimates of potential viral contamination of the most difficult viruses showed higher than a (b) (4), consistent with expectations set forth in the FDA draft guidance.

The effectiveness of the current control measures has been verified for viral clearance in the manufacture of the Enzyme of the RECELL Device.

Bacterial Endotoxin Testing: Routine bacterial endotoxin testing (BET) is performed on every lot of the device. Testing was conducted in accordance with the recommendations described in Section V part A.4 of the FDA Guidance "*Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile*" issued on January 21, 2016 to support this labeling. Due to the number of separate sterile components provided as part of the RECELL Device, routine testing is performed on separate components and then the total sum of endotoxin levels from all applicable components is used to determine if the lot has met the BET release criteria. The total combined endotoxin exposure attributable to all device components was demonstrated to be (b) (4) after considering a worst-case enzyme carryover scenario involving the final disaggregated skin cell suspension device output. (b) (4) test methods per (b) (4) are used to detect and quantify bacterial endotoxin for all applicable components of the RECELL Device, with an exception made for the RECELL Enzyme, which requires using a modified validated method for sample preparation followed by testing in accordance with (b) (4) .

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The safety and efficacy evaluation were based on a pivotal study, CTP009. The study was a prospective, multicenter, intra-subject randomized, standard of care (SOC)-controlled, central evaluator-blinded efficacy and safety study to evaluate the RECELL Device for repigmentation of stable depigmented lesions in subjects ≥18 years of age.

A prospective randomized clinical study, CTP009, was conducted (under BB-IDE 19457) to evaluate the safety and effectiveness of the RECELL® Device for repigmentation of stable vitiligo lesions in a total of 25 subjects. The study evaluated repigmentation results of RECELL-treated areas compared to the Control areas after both received NB-UVB phototherapy. Repigmentation outcomes were evaluated through Week 24. In addition to central, expert review of repigmentation, subjects and clinicians rated global treatment success, and patients reported on vitiligo noticeability. Study design, study subject demographics, safety and effectiveness endpoints for the study are summarized below.

The clinical outcome supports the use of the RECELL® Device for vitiligo procedures and demonstrates that the RECELL Device can be used to achieve ≥ 80% pigmentation in stable vitiligo lesions.

A. Study Design

In Study CTP009, each subject served as their own control by contributing a matched pair of stable depigmented areas that were randomized 1:1 to the RECELL area [received ablative laser treatment, RECELL treatment, and ultraviolet B (UVB) phototherapy] or the control area [UVB phototherapy alone]. On the treatment day, the

RECELL area skin was resurfaced using an FDA cleared ablative laser device (i.e., Er:YAG or CO_2) that is indicated for skin resurfacing prior to application of Spray-On Skin Cells, prepared from the RECELL Device. The control area did not receive any treatment (neither ablative laser resurfacing treatment nor the RECELL treatment). Once the RECELL area healed and was ready, both the RECELL and control areas received UVB phototherapy.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment was limited to subjects who were ≥ 18 year of age with stable focal, segmental or generalized vitiligo with < 30% depigmented body surface area (BSA) and had previously had unsatisfactory response to front-line therapy (topicals, phototherapy).

2. Follow-up

   Schedule:
   All patients were scheduled to return for follow-up examinations at 1, 4, 12, and 24 weeks after treatment.

   Assessments:
   Treatment (RECELL and control) areas were documented using standardized digital photography. Pigmentation of the treatment areas was evaluated by centralized image review by a Central Review Committee (CRC). The CRC was blinded to the treatment assignment and the investigative site.

   Treatment emergent adverse events (TEAEs) were recorded at all visits.

3. Clinical Endpoints

   The primary effectiveness endpoint was the difference in the proportion of responders for RECELL versus Control at Week 24. The pre-specified superiority margin was 10%. Responders were defined as study areas achieving ≥ 80% pigmentation as determined by an expert central review committee (CRC).

   The secondary effectiveness endpoint was CRC categorization of repigmentation (0-25%, 26-50%, 51-79% and 80-100%) for RECELL versus Control at Week 24.

   Safety assessment included reporting treatment emergent adverse events (TEAEs).

B. Accountability of PMA Cohort

The intent-to-treat (ITT) population consists of 25 subjects enrolled from 10 clinical sites. The ITT population was the primary analysis population for efficacy and safety analyses.

C. Study Population Demographics and Baseline Parameters

Twenty-five subjects from ten clinical sites were enrolled in the study.

Approximately half of the subjects were female (13/25); 80% of subjects were Caucasian, 12% were Asian, and 8% were African American. The mean age was 41 years (range 22-71 years). The mean disease duration was 11 years (range 1-32 years). The mean duration of stabilized lesions was 6.2 years (range 1-25 years). Most subjects (76%) had non-segmental vitiligo, including 48% of generalized vitiligo and 28% of focal vitiligo. Twenty-four percent (24%) of subjects had segmental vitiligo. The median size of RECELL and the control areas were 22 cm^2 (ranged 2 to 360 cm^2) and 24 cm^2(ranged 2 to 375 cm^2), respectively, and the depigmented areas were located at head, neck, dorsal hand, dorsal foot, arm, leg, trunk and other. The mean affected area was 5.3% of total body surface area (TBSA) (range 0.3-28.8% TBSA).

D. Safety and Effectiveness Results

1. Safety Results

The safety population consists of all 25 subjects. There were no deaths or serious adverse events (SAEs) reported. Seven treatment-emergent adverse events (TEAEs) were reported in five (20.0%) subjects, including scar, erythema and pruritus on RECELL areas, hypertrophic scar at a donor site, and Koebner Phenomenon at a non-study area. One subject developed a scar in the RECELL area, and the scar was reported ongoing 166 days post-treatment.

Device Failures:
There were two reports of RECELL Device malfunction in the study, one for a pivotal cohort subject and one for a roll-in cohort subject. In both instances, the RECELL Device reported an error condition because no Enzyme was present when the user initiated the device's heating cycle. This is not a malfunction, but a warning to the user to introduce the Enzyme prior to initiating the device's heating cycle. No AE or non-treatment was associated with either instance of the event.

2. Effectiveness Results

Efficacy was demonstrated based on the primary endpoint of the difference in the proportion of responders between the RECELL areas and the control areas at Week 24 in ITT population. Nine of the 25 (36%) RECELL areas had ≥ 80% repigmentation and none of the 25 control areas had ≥ 80% repigmentation. The treatment difference was 36% [95% confidence interval (CI): 13.0%, 55.0%; p=0.012], where the lower bound exceeded the superiority margin of 10%.

The efficacy was supported by the secondary efficacy endpoint of the differences in categorization of repigmentation (0% to 25%, 26% to 50%, 51% to 79%, and 80% to 100%) repigmentation assessment at Week 24, which indicated that 56% of RECELL areas achieved >50% repigmentation versus 12% of control areas. However, None of the RECELL or control areas achieved 100% repigmentation.

The efficacy was further supported by the overall better study subjects' satisfaction of the RECELL areas based on patient-reported outcome (PRO) analyses acknowledging the limitations of the exploratory nature of these analyses (i.e., not prespecified to control multiplicity and the open-label design).

3. Subgroup Analyses

The subgroup analysis was performed for the primary efficacy endpoint on visible areas on head and neck. The subgroup analysis was not prespecified and was considered post hoc analysis. Among the 12 randomized treatment areas on head and neck, 5 (5/12, 41.7%) RECELL areas had ≥80% repigmentation. None of the 12 control areas had ≥80% repigmentation. This Subgroup analyses showed consistent trends toward benefit for repigmentation in the RECELL areas.

4. Pediatric Extrapolation

The safety and efficacy of the use of RECELL in pediatric patients has not been studied.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. As certified in the FORM FDA 3454 submitted by the applicant, none of the 29 clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

No supplemental clinical information was included in this application.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this original PMA was not referred to an FDA advisory committee for review and recommendation because it was judged that the expertise of the FDA PMA review staff was sufficient to determine there is a reasonable assurance the device is safe and effective based on the information provided in the supplemental PMA application, when used in accordance with the indications for use for: repigmentation of depigmented lesions in patients with stable vitiligo.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICALSTUDIES

A. Effectiveness Conclusions

Efficacy was demonstrated based on the primary endpoint of the difference in the proportion of responders between the RECELL areas and the control areas at Week 24 in ITT population. Subgroup analyses of the primary efficacy endpoint on visible areas on the head and neck showed consistent trends toward benefit for repigmentation in the RECELL areas.

The efficacy was supported by the secondary efficacy endpoint of the differences in categorization of repigmentation (0% to 25%, 26% to 50%, 51% to 79%, and 80% to 100%) repigmentation assessment at Week 24 and the overall better study subjects' satisfaction of the RECELL areas based on patient-reported outcome (PRO) analyses acknowledging the limitations of the exploratory nature of these analyses (i.e., not prespecified to control multiplicity and the open-label design).

B. Safety Conclusions

The risks of the RECELL Device for repigmentation of stable depigmented areas are characterized based on the 25 subjects in the ITT population. The safety database is considered adequate bearing in mind the overall safety profile from the premarketing and postmarketing experience of the RECELL Device in the acute thermal burn wound population, and overall benefit and risk profile of the RECELL Device in study CTP009. The systemic safety evaluation was confounded due to the intra-subject randomization design; however, the systemic effect is unlikely considering topical route of administration of the autologous Spray-On Skin cell suspension. The overall safety profile did not raise significant concerns; however, a possibility of scar formation was observed.

C. Benefit-Risk Determination

Study CTP009 was an adequate and well-controlled clinical study. Topical application of Spray-On Skin Cells prepared by the RECELL Device to depigmented skin lesions resurfaced by an ablative laser was effective in promoting repigmentation of stable depigmented vitiligo lesions. The RECELL Device demonstrated reasonable assurance of effectiveness for repigmentation of stable depigmented vitiligo lesions in patients 18 years of age and older.

The safety database of 25 subjects is considered adequate bearing in mind the overall safety profile from the premarketing and postmarketing experience of the RECELL Device and safety findings in Study CTP009. The overall safety profile was characterized and did not raise significant concerns; however, a small chance of scar formation was observed. The reviewed safety data do not warrant any postapproval or postmarket surveillance studies.

Thus, when RECELL is used in accordance with instructions for use and patient care is performed according to recommended methods, the benefits associated with

use of the RECELL Device outweigh the risks.

D. Overall Conclusions

The data in this application provide a reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XIV. CBER DECISION

CBER issued an approval order on June 16, 2023. The final nonclinical conditions of approval cited in the approval order are shown below.

Human Factors Validation

1. AVITA Medical will conduct additional Human Factors (HF) validation testing with participants, use environments, and uses that are realistically representative of the actual population of intended users (healthcare professionals who specialize in dermatology), use environments (e.g., procedure rooms), and uses of the new RECELL Device for vitiligo. This additional HF validation testing will be performed according to the protocol from the existing HF validation conducted under BP170122 with any necessary modifications related to the participants, use environments, and uses. AVITA Medical will include in the validation testing protocol a comprehensive analysis of the intended users, use environments, and uses for the RECELL Device for vitiligo. AVITA Medical will submit the human factors engineering (HFE) report, inclusive of new HF validation data to support use safety and effectiveness of the RECELL Device for vitiligo, as a Post-Approval Study (PAS) Report within 1-year of the approval order.

Manufacturing Facility Pre-Approval Inspection

During review of the PMA application, the determination was made to recommend waiver of the pre-approval inspection of the applicant's manufacturing facility. This decision was based on information provided in the PMA application in conjunction with a prior inspection report and related correspondence supporting the overall compliance of the applicant's registered manufacturing facility with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications,Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

None