Individuals using assistive technology may not be able to fully access the information contained in this file. For assistance, please call 800-835-4709 or 240-402-8010, extension 1. CBER Consumer Affairs Branch or send an e-mail to: ocod@fda.hhs.gov and include 508 Accommodation and the title of the document in the subject line of your e-mail.

INSTRUCTIONS FOR USE

RECELL® Autologous Cell Harvesting Device

The RECELL Autologous Cell Harvesting Device (RECELL Device) should be used only by licensed healthcare professionals trained in the use of the device.

Warning:

The RECELL Autologous Cell Harvesting Device is internally powered by four non-replaceable AA batteries (1.5V). The device should not be used in the presence of flammable anesthetic mixtures. Do not incinerate batteries on disposal. The performance of the device may be affected by sources of electromagnetic radiation and if any malfunctions are noted, all possible sources of electromagnetic radiation must be removed before further use.

Caution:

Federal law restricts this device to sale by or on the order of a physician.

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A BACKGROUND

A1 DEVICE DESCRIPTION

RECELL is a single-use, stand-alone, battery-operated, autologous cell harvesting device containing enzymatic and delivery solutions, sterile surgical instruments, and actuators. The RECELL Device enables a thin split-thickness skin sample to be processed to produce a suspension of Spray-On Skin™ Cells for immediate delivery onto a prepared wound bed.

The regenerative epidermal suspension contains a mixed population of cells, including keratinocytes, fibroblasts, and melanocytes, obtained from the disaggregation of the skin sample. The preservation of melanocytes is important for restoring natural pigmentation to the recipient area. Additionally, sub-populations of keratinocytes critical for re-epithelialization have been identified in the suspension including basal keratinocytes, suprabasal keratinocytes, and activated keratinocytes.

The Enzyme used to process the cells is a biological agent and as such may have slight variations in color and texture.

A2 INDICATIONS FOR USE

The RECELL Autologous Cell Harvesting Device is indicated for the treatment of thermal burn wounds and full-thickness skin defects. The RECELL Device is used by an appropriately licensed and trained healthcare professional at the patient's point of care to prepare autologous Spray-On Skin Cells for direct application to acute partial-thickness thermal burn wounds in patients 18 years of age and older, or application in combination with meshed autografting for acute full-thickness thermal burn wounds in pediatric and adult patients and full-thickness skin defects after traumatic avulsion (e.g., degloving) or surgical excision (e.g., necrotizing soft tissue infection) or resection (e.g., skin cancer) in patients 15 years of age and older.

A3 CONTRAINDICATIONS

- RECELL is contraindicated for the treatment of wounds clinically diagnosed as infected or with necrotic tissue present in the wound bed.
- 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.

A4 WARNINGS

- Autologous use only.
- Control infections on wounds prior to application of the cell suspension.
- Excise the necrotic tissues on wound bed prior to application of the cell suspension.
- Wound beds treated with a cytotoxic agent (e.g., silver sulfadiazine) should be rinsed prior to application of the cell suspension.
- RECELL is provided to the healthcare professional sterile and is intended for single use.
- Do not reuse, freeze, or re-sterilize device components.
- Handle using aseptic technique.
- Do not use RECELL or device components if packaging is damaged or there are signs of tampering.
- Do not use RECELL or device components beyond the stated expiration date indicated on the adhesive Lot # and Expiration Date labels on the outer box packaging.
- Choose a skin sample donor site that shows no evidence of surrounding cellulitis or infection.
- For optimum cell viability, the skin sample should be processed immediately after harvesting.
- If a skin sample is harvested and processed according to these instructions, it should require between 15 and 30 minutes of contact with the Enzyme. Contact in excess of 60 minutes is not recommended.
- The Enzyme is derived from animal tissue and, although strict

controls have been implemented in the manufacturing process to minimize the risk of pathogen contamination, a small risk of contamination exists and absolute freedom from infectious agents cannot be guaranteed.

- Contaminated materials and waste must be disposed of using appropriate biohazard waste receptacles.

A5 PRECAUTIONS

- RECELL is not intended to be used alone (i.e., without meshed autograft) for treatment of full-thickness acute wounds or full-thickness skin defects after traumatic avulsion (e.g., degloving) or surgical excision (e.g., necrotizing soft tissue infection) or resection (e.g., skin cancer).
- The safety and effectiveness of RECELL used alone (i.e., without meshed autograft) have not been established for treatment of partial-thickness burn wounds:
  - On the hands and articulating joints
  - >320 cm^2
  - In patients with wounds totaling >20% Total Body Surface Area (TBSA)
- The safety and effectiveness of RECELL plus autografting have not been established for treatment of full-thickness burn wounds:
  - In patients younger than 28 days of age (neonates)
- The safety and effectiveness of RECELL plus autografting have not been established for application in combination with meshed autografting on full-thickness skin defects after traumatic avulsion (e.g., degloving) or surgical excision (e.g., necrotizing soft tissue infection) or resection (e.g., skin cancer):
  - On the hands and genitalia

A6 SPECIAL PATIENT POPULATIONS

- The safety and effectiveness of RECELL have not been established for treatment of acute thermal partial-thickness burn wounds in pediatric patients younger than 18 years of age.

A7 ADVERSE REACTIONS

Any adverse reaction or suspected adverse reaction related to RECELL should immediately be reported to AVITA Medical® [+1 833 GO AVITA].

A8 MEANING OF SYMBOLS

The packaging system is labeled with various symbols. These symbols are internationally harmonized and define certain characteristics of the product and the manufacturing process:

User must read instructions for use

User should refer to the accompanying instructions for use

Product is for single use only

Do not use if package is damaged

Caution

Expiration date

Manufacturer

Date of manufacture

Specifies the storage temperature range

Specifies the upper limit of storage temperature

Catalogue number

Lot number

Sterile components in package

STERILE EO

Product or components within have been sterilized using ethylene oxide

STERILE R

Product or components within have been sterilized using gamma irradiation

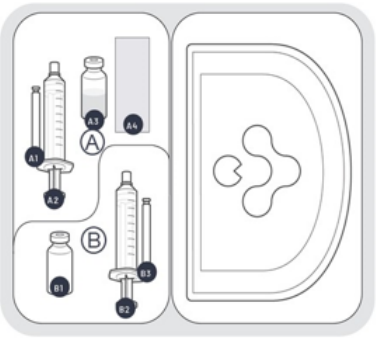
STERILE

Product or components within have been sterilized using steam

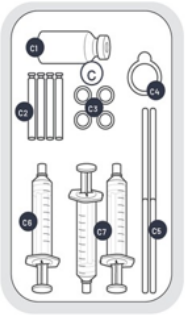
A9 DOSAGE

RECELL is supplied as a single-use device. The contents of each package are sufficient to prepare up to 24 ml of cell suspension which can be used to cover a wound area of up to and including 1,920 cm^2.

A10 HOW SUPPLIED



A/B Processing unit Tray



C Tray

The RECELL Device consists of:
Sealed vial of Enzyme (can be placed into A Tray at A4)
Processing Unit

- 1 x Processing Unit with built-in heating mechanism
- 1 x removable processing tray
- 1x removable

cell strainer A Tray

- 1 x 10 ml vial of water (A3)
- 1 x 10ml syringe (A2)
- 1 x 18G blunt fill needle (A1)

B Tray

- 1 x 10 ml vial of Buffer (B1)
- 1 x 10ml syringe (B2)
- 1x 18G blunt fill needle (B3)

C Tray

- 1 x 30 ml vial of Buffer (C1)
- 5 x 10 ml syringes (C6 and C7)
- 4 x 18G blunt fill needles (C2)
- 2 x disposable surgical scalpels (C5)
- 4 x spray nozzles (C3)
- 1 x cell

strainer(C4)
In addition

- Sterile syringe labels
- TELFA™ Clear Dressings
- Procedure Guide (non-sterile)

A11 STORAGE

Upon receiving RECELL, examine the packaging for external signs of damage. If the external packaging or the packaging for any of the individual trays or components appears damaged, contact your AVITA representative immediately. Do not use any components of the device if the packaging appears damaged. If returning RECELL, ensure all original packaging and components are returned with the device.

RECELL, including the Enzyme, may be stored at controlled room temperature, 20-25 °C. See **Section E1** for storage conditions of RECELL.

Do not open or use RECELL beyond the expiration date listed on the packaging.

A12 DISPOSAL

- RECELL and all individual components are intended for single use. RECELL components are not reusable and should be discarded after single use. Reuse may lead to infection or disease transmission.
- Follow local regulations for proper disposal.
- Contaminated materials and waste must be disposed of using appropriate biohazard receptacles.

⚠ CAUTION: RECELL contains batteries and electrical components. Do not incinerate until removal of batteries and electrical components**.**

- If required, a procedure for removal of Processing Unit Battery/electronics is as follows:
  - Take proper Biohazard precautions when handling the used Processing Unit.
  - Remove the Processing Unit top cover. Set top cover aside.
  - Remove Processing Unit inner tray and set aside.
  - Open inner main tray by pressing both sides of the outer housing simultaneously.
  - Verify that the parts are separated (inner main tray and outer housing). If the parts of the inner tray and outer housing are not separated, a small, flat-blade screwdriver may be used to assist in releasing the inner and outer parts.
  - Lift the battery inner tray to expose battery compartment.
  - Remove the batteries and the electronics and dispose of them in the appropriate waste streams.
  - Dispose of the remaining components in accordance with the appropriate methods.

B CLINICAL DATA SUMMARY

Two prospective randomized clinical studies were conducted to evaluate the safety and effectiveness of the RECELL Device in the treatment of acute thermal burn wounds in a total of 131 subjects. One prospective randomized clinical study was conducted to evaluate the safety and effectiveness of the RECELL Device in the treatment of acute non-thermal full-thickness skin defects in a total of 65 subjects. Further, retrospective analyses were conducted on data from 39 pediatric patients with acute full-thickness thermal burn wounds, who received the RECELL Device in Expanded Access and in Continued Access Protocols, 49 patients with >50% TBSA acute full-thickness thermal burn wounds, who received the RECELL Device in Expanded Access Protocols, and 61 patients with acute full-thickness wounds over a joint (including hands) in Expanded Access.

B1 RECELL Combined with Meshed Skin Graft for Treatment of Acute Burn Injuries (Full-thickness and Mixed-Depth Burns)

Demonstration of the Safety and Effectiveness of RECELL Combined with Meshed Skin Graft for Reduction of Donor Area in the Treatment of Acute Burn Injuries (Mixed-Depth Burns)

Study Design

In this randomized, multi-center, standard of care-controlled study, RECELL was used in combination with widely meshed autografts, allowing for the treatment of deep, extensive burn wounds. The study population included 30 subjects from 6 clinical sites. Subjects were eligible for enrollment if they were ≥ 5 years of age with 5-50% TBSA burn wounds requiring autografts for closure. Each subject served as their own control, using two comparable contiguous or non-contiguous areas of at least 300 cm^2 in size. The recipient sites were randomly assigned to receive autografting consistent with the investigator's pre-specified graft plan (Control) or application of Spray-On Skin Cells over an autograft meshed more widely (i.e., one ratio higher) than identified in the pre-specified graft plan. Acute healing and pain outcomes were evaluated through 12 weeks. Pain, healing, durability, and scar outcomes were evaluated in the longer-term follow-up visits conducted at 24, 36, and 52 weeks.

Endpoints. The co-primary endpoints were: 1) Non-inferiority of the incidence of complete wound closure for RECELL-treated burn wounds (treated with the combination of Spray-On Skin Cells and widely meshed autografts) compared to that observed in

Control-treated burn wounds (conventional autograft) by 8 weeks after treatment, as assessed by a blinded evaluator. The pre-specified non-inferiority margin (Control minus RECELL) was 10%. Complete wound closure was defined as complete skin re-epithelialization without drainage, confirmed at 2 consecutive study visits at least 2 weeks apart; and 2) Superiority in relative reduction in donor area requirements for RECELL versus Control treatment, as assessed by the Geometric Mean Ratio (GMR) of the RECELL: Control autograft expansion ratios. Safety assessment included evaluation of healing time based on the investigator's assessment, infection, allergic response to trypsin, wound durability, scarring outcomes, and device-related adverse events and serious adverse events.

Results

Demographics. Thirty subjects were enrolled in the study, and their wound sites were randomized to the control or treatment group. The majority of subjects were male (25/30, 83.3%); 66.7% were Caucasian (20/30). The mean age was 39.1 years (range 9-68 years). Nine subjects had risk factors (including smoking, drug and alcohol abuse, and inadequate nutrition) for impaired wound healing. All of the wounds were from acute thermal burn wounds, and the majority of the burn wounds were the result of fire or flames (22/30, 73.3%). The mean percent TBSA affected by burn wounds was 21.2% (±12.8%).

Effectiveness. Non-inferiority of RECELL relative to Control for recipient site healing was established using the pre-specified non-inferiority margin of 10%. Confirmed treatment area closure by Week 8 was 92.3% for RECELL vs. 84.6% for the Control treatment areas. The treatment difference (Control minus RECELL) was -7.7% (1-sided 97.5% CI upper bound of 6.40%). The progression of healing was similar between treatments, with both RECELL and Control treatments achieving 100% re-epithelialization for approximately 50% and 80% of treatment areas at Week 4 and Week 6, respectively.

Superiority of RECELL was established with respect to relative reduction in donor site harvesting ($p<0.001$). Treatment with RECELL required, on average, use of 32% less donor skin, compared to that required for autografting. Secondary effectiveness outcomes (patient satisfaction, Week 24 observer overall opinion on the Patient and Observer Scar Assessment Scale (POSAS), and Week 24 patient overall opinion on POSAS) were comparable between treatments. These outcomes were also comparable between treatments at Week 52.

Safety – Adverse Events. No unanticipated adverse device effects or device-related events

were reported. The number of subjects with any treatment-emergent adverse event (TEAE) at the RECELL treatment site was the same as the number of subjects with any TEAE at the Control treatment area (17/30, 56.7%). Similar numbers of TEAEs were reported in areas that were not involved in the study treatments (63.3%). Most subjects experienced TEAEs that were mild (26.7%) or moderate (36.7%). The incidence of TEAEs s (impaired healing, pain, graft loss, skin abrasion, and skin graft failure) was comparable between RECELL and Control treatment sites. The most common TEAE at both the RECELL and Control treatment areas was pruritus, experienced by 7 (23.3%) subjects. One or more severe TEAEs were experienced by 7 (23.3%) subjects; however, no TEAE was related to the RECELL Device. Twelve subjects had serious adverse events (SAEs). There was no difference in the incidence and types of SAEs at the RECELL and Control treatment areas.

Table 1. Summary of Recipient and Donor Site TEAEs by System Organ Class and Preferred Term

Primary System Organ Class/Preferred Term N=30	RECELL n (%)	Control n (%)	Donor Site n (%)	Non-Study Area n (%)
Any Primary System Organ Class	17 (57%)	17 (57%)	5 (17%)	19 (63%)
General disorders and administration site conditions				
Disease Susceptibility	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Impaired Healing	1 (3%)	3 (10%)	0 (0%)	1 (3%)
Pain	2 (7%)	1 (3%)	0 (0%)	1 (3%)
Secretion Discharge	0 (0%)	1 (3%)	0 (0%)	0 (0%)
Infections and Infestations				
Cellulitis	0 (0%)	0 (0%)	0 (0%)	3 (10%)
Purulent Discharge	0 (0%)	0 (0%)	1 (3%)	0 (0%)
Skin Graft Infection	0 (0%)	2 (7%)	0 (0%)	0 (0%)
Injury, poisoning, and procedural complications				
Graft delamination	1 (3%)	0 (0%)	0 (0%)	0 (0%)
Graft loss	3 (10%)	3 (10%)	0 (0%)	4 (13%)
Scratch	1 (3%)	0 (0%)	0 (0%)	1 (3%)
Skin abrasion	1 (3%)	1 (3%)	0 (0%)	1 (3%)
Skin graft failure	1 (3%)	2 (7%)	0 (0%)	1 (3%)
Wound	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Musculoskeletal and connective tissue disorders				
Arthralgia	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Extra skeletal ossification	0 (0%)	1 (3%)	0 (0%)	1 (3%)
Extremity contracture	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Joint range of motion decreased	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Muscle contracture	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Pain in extremity	1 (3%)	0 (0%)	0 (0%)	2 (6%)
Nervous system disorders				
Burning sensation	1 (3%)	1 (3%)	0 (0%)	1 (3%)
Neuralgia	1 (3%)	1 (3%)	0 (0%)	1 (3%)
Skin and subcutaneous tissue disorders				
Blister	0 (0%)	0 (0%)	1 (3%)	1 (3%)
Dermatitis	1 (3%)	1 (3%)	0 (0%)	1 (3%)
Dermatitis, contact	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Diabetic dermopathy	1 (3%)	1 (3%)	0 (0%)	0 (0%)
Pruritus	7 (23%)	7 (23%)	3 (10%)	5 (16%)
Rash	1 (3%)	1 (3%)	0 (0%)	1 (3%)
Surgical and medical procedure				
Scar excision	1 (3%)	1 (3%)	0 (0%)	1 (3%)

Safety – Additional Endpoints. Pre-specified safety events – including delayed healing, scar necessitating surgical intervention, allergic response to trypsin, wound durability issue, infection, and pain – were evaluated during the study. There was no difference in the incidence of delayed healing and scar revision surgery at RECELL compared to Control treatment areas. No patient had either an allergic response to trypsin or an issue related to durability of wound healing. Infection was not observed at the RECELL treatment areas but was observed at two Control treatment sites; however, the numbers were too small to draw conclusions regarding incidence of infection at wound-treatment sites. There was no clinically meaningful difference in the degree of pain associated with the two treatments.

Retrospective Reviews of Data from Expanded Access & Continued Access Protocols for RECELL Combined with Meshed Skin Graft for the Treatment of Full-thickness Burns

(1) In Patients ≥18 Years of Age with>50% TBSA Acute Thermal Injury and
(2) In Patients <18 Years of Age

Study Design

Two retrospective reviews were conducted to evaluate the safety and effectiveness of RECELL with meshed autograft for the treatment of full-thickness burns, utilizing data collected in patients who received RECELL combined with meshed autograft in Expanded Access and Continued Access protocols (RECELL Cohort). The RECELL Cohort data were compared with data from patients in the American Burn Association's National Burn Repository (NBR Control), who received standard of care (conventional autograft). Week 8 wound healing data (not available in the NBR) were reported for the RECELL Cohort. RECELL Cohort adverse events were compared with the adverse events in the randomized controlled trial (RCT Control). Propensity score (PS) stratification was used to reduce bias attributable to potential differences in key covariates such as age, gender, %TBSA and Baux Score, between RECELL and NBR Control datasets.

Endpoints. The primary endpoint was the number of autograft treatments required to achieve definitive closure per patient, comparing the RECELL Cohort to the NBR Control. Difference in length of hospital stay (LOS) between the RECELL Cohort and NBR Control was a secondary endpoint. LOS was measured as:

$$\textit{Days per \%TBSA} = \frac{\textit{Number of inpatients hospital days}}{\textit{Burn injury size (\%total body surface area)}}$$

Safety assessments included mortality in RECELL Cohort compared with NBR Control, specified adverse events (infections, skin graft failure, graft loss and/or impaired healing, compared to the RCT Control), and wound durability (no comparison).

Results

(1) In Patients ≥18 Years of Age with >50% TBSA Acute Full-thickness Thermal Injury:

Demographics and baseline characteristics. Data from 49 patients with 342 mixed-depth acute thermal burn wounds treated with RECELL combined with meshed autograft were included within the RECELL Cohort. Data from 277 patients were included in the NBR Control, and 28 patients were included in the RCT Control. The RECELL Cohort and NBR Control had comparable baseline characteristics regarding age, gender, %TBSA and Baux scores. Percent TBSA and Baux scores were greater for the RECELL Cohort compared with the RCT Control. (Table 2)

Table 2. Demographic and Baseline Characteristics

	RECELL Cohort N=49	RCT Control N=28	NBR Control N=277
Age			
Mean ± SD	37.9 ± 11.9	41.1 ± 14.3	39.6 ± 13.0
Range (Min, Max)	(20.9, 64.1)	(18.0, 68.0)	(18.0, 74.9)
Sex			
Female	26.5% (13/49)	17.9% (5/28)	24.2% (67/277)
Male	73.5% (36/49)	82.1% (23/28)	75.8% (210/277)
Race/Ethnicity [1]			
White	77.6% (38/49)	67.9% (19/28)	N/A
Black or African American	8.2% (4/49)	21.4% (6/28)	N/A
Asian	0% (0/49)	3.6% (1/28)	N/A
Hispanic	10.2% (5/49)	N/A	N/A
Not Hispanic or Latino	2.0% (1/49)	N/A	N/A
Other	2.0% (1/49)	7.1% (2/28)	N/A
Cause of Burn Injury			
Fire/flames	93.9% (46/49)	75.0% (21/28)	N/A
Hot water/steam	0% (0/49)	10.7% (3/28)	N/A
Other	6.1% (3/49)	14.3% (4/28)	N/A
Total Estimated Injury Size (% TBSA)			
Mean ± SD (N) [2]	65.6 ± 11.2 (49)	20.3 ± 12.5 (28)	61.9 ± 10.1 (277)
Range (Min, Max)	(51.0, 91.0)	(5.0, 46.0)	(50.0, 96.0)
Baux Score [2]			
Mean ± SD (N)	110.1 ± 19.8 (49)	62.0 ± 19.5 (28)	107.6 ± 17.4 (277)
Range (Min, Max)	(80.9, 161.8)	(24.0, 95.0)	(70.2, 170.0)

[1] Race/ethnicity were collected as a combined variable for CTP004. Data being presented as collected.
[2] Percent TBSA and Baux scores were significantly greater (p=<0.0001) for the RECELL Cohort compared with the RCT Control.

Effectiveness. Median number of autograft treatments required for definitive closure in the RECELL Cohort (2.0 treatments, range 1.0-6.0) was lower than in the NBR Control (5.0 treatments, range 1.0-32.0).

Mean number of autograft treatments required for definitive closure in the RECELL Cohort was 2.4 treatments (SD 1.3) and in the NBR Control was 5.9 treatments (SD 4.6).

Median Length of Hospital Stay was 1.2 days per %TBSA (range 0.6-3.0) in the RECELL Cohort and 1.2 (range 0.5-6.3) within the NBR Control Cohort (p= 0.60). By Week 8 after treatment, 90.6% of the wounds treated in the RECELL Cohort achieved ≥95% re-epithelialization.

Safety. There were no unanticipated adverse device effects or adverse events attributed to RECELL use. Mortality rates were similar between the RECELL Cohort (18.4%) and the NBR Control (20.2%). The incidence of infection and graft failures was greater in the RECELL Cohort compared to the RCT Control, which was anticipated due to greater burn size in the RECELL Cohort. Beyond Week 8, there was no occurrence of spontaneous breakdown of the

treated areas in either the RECELL Cohort or RCT Control. Table 3 summarizes the key safety events in patients ≥18 years of age with>50% TBSA acute thermal burn wounds in the RECELL Cohort and RCT Control.

Table 3. Key Safety Events in RECELL Cohort and RCT Control in Patients ≥18 Years of Age with>50% TBSA Acute Thermal Injury

Key safety Event	RECELL Cohort N= 49 Number of (%) Subjects with Event	RCT Control N=28 Number of (%) Subjects with Event
Graft Infection	7 (14.3%)	1 (3.6%)
Graft Failure	4 (8.2%)	1 (3.6%)
Graft Loss/Impaired Healing	9 (18.4%)	5 (17.9%)

(2) In Patients <18 Years of Age with Acute Full-thickness Thermal Injury:

Demographics and baseline characteristics. In the RECELL Cohort, 39 pediatric patients (mean age of 7.1 years) with 175 acute thermal burn wounds were treated with RECELL in combination with meshed autografts. In the NBR Control, 245 pediatric patients (mean age of 8.7 years) were treated with conventional autografts. Mean total estimated injury size(%TBSA) was greater in the pediatric RECELL Cohort (40.1%) compared with the NBR Control (28.1%). Other demographics including age, sex, and Baux scores were comparable between the two groups.

Table 4. Demographic and Baseline Characteristics

	RECELL Cohort N=39	NBR Control N=245
Age (years)		
Mean ± SD	7.1 ± 4.9	8.7 ± 5.0
Range (Min, Max)	(0.8, 17.0)	(0.2, 16.0)
Sex		
Female	53.8% (21/39)	26.9% (66/245)
Male	46.2% (18/39)	73.1% (179/245)
Race/Ethnicity [1]		
White	59.0% (23/39)	N/A
Black or African American	30.8% (12/39)	N/A
Asian	2.6% (1/39)	N/A
Hispanic	2.6% (1/39)	N/A
Not Hispanic or Latino	2.6% (1/39)	N/A
Other	59.0% (23/39)	N/A
Cause of Burn Injury		
Fire/flames	66.7% (26/39)	N/A
Hot water/steam	20.5% (8/39)	N/A
Other	12.8% (5/39)	N/A
Total Estimated Injury Size (% TBSA)		
Mean ± SD (N) [2]	40.1 ± 19.2 (39)	28.1 ± 15.5 (245)
Range (Min, Max)	(8.0, 90.0)	(8.5, 82.2)
Baux Score [2]		
Mean ± SD (N)	50.3 ± 24.4 (39)	39.3 ± 17.0 (245)
Range (Min, Max)	(16.0, 115.3)	(22.5, 95.2)

[1] Race/ethnicity were collected as a combined variable for CTP004. Data being presented as collected.
[2] Percent TBSA and Baux scores were significantly greater (p=<0.0001) for the RECELL Cohort compared with the NBR Control.

Effectiveness. Median number of autograft treatments required for definitive closure in the pediatric RECELL Cohort (1.0 treatment, range 1.0-5.0) was lower than in the NBR Control (2.0 treatments, range 1.0-20.0). Mean number of autograft treatments required for definitive closure was 1.6 treatments (SD 1.1) in the RECELL Cohort and was 3.6 treatments (SD 3.7) in the NBR Control.

Median Length of Hospital Stay was 1.7 days per %TBSA (range 0.6-3.3) in the RECELL Cohort and 1.2 (range 0.5-3.9) in the NBR Control. By Week 8 after treatment, 91.8% of wounds treated in the RECELL Cohort achieved ≥95% re-epithelialization.

Safety. No unanticipated adverse device effects or adverse events attributed to the use of RECELL were reported. Mortality rates were comparable between the RECELL Cohort (0%) and the NBR Control (0.4%). The incidence of treatment-related adverse events (graft infection, graft failure and graft loss/impaired healing) was greater in the pediatric RECELL Cohort compared with the adult RCT Control. This was anticipated due to greater burn size and increased number of treatment areas in the pediatric RECELL Cohort, providing a greater opportunity for treatment-area complications. The proportion of patients

experiencing at least one key safety event was similar between two groups; i.e., 17.9% in the pediatric RECELL Cohort and 20.0% for the RCT Control. Table 5 summarizes the key safety events in subjects age <18 years in the RECELL Cohort and RCT Control.

Table 5. Key Safety Events in Pediatric RECELL Cohort <18 Years of Age and RCT Control with Acute Full-thickness Thermal Injury

Key safety Event	RECELL Cohort (N= 39) Number of (%) Subjects with Event	RCT Control (N=30) Number of (%) Subjects with Event
Graft Infection	5 (12.8%)	2 (6.7%)
Graft Failure	3 (7.6%)	2 (6.7%)
Graft Loss/ Impaired Healing	6 (15.4%)	3 (10%)
Experienced at least 1 key safety event	7 (17.9%)	6 (20.0%)

Retrospective Review of Data from Expanded Access Protocol for RECELL Combined with Meshed Skin Graft for the Treatment of Full-thickness Burns on Joints (Including Hands)

A retrospective review and analysis of the available data from an expanded access protocol (CTP004) was conducted to evaluate the application of RECELL with meshed autograft for the treatment of full-thickness burns over joints and hands. The analysis included 61 patients who had 443 RECELL-treated areas (237 contained a joint including hands and 206 did not involve a joint or hand) with Week 8 wound closure. There were no appreciable differences with respect to safety or wound closure with the use of RECELL combined with meshed autograft for the treatment of wounds between areas involving joints (including hands) and the areas not involving joints (including hands).

B2 RECELL for Treatment of Acute Burn Injuries (Deep Partial-Thickness Burns)

A Comparative Study of RECELL Device and Autologous Split-thickness Meshed Skin Graft in the Treatment of Acute Burn Injuries (Deep Partial-Thickness Burns)

Study Design

The RECELL Device was studied as a primary intervention in the treatment of acute burn wounds in a randomized, multi-center, standard of care controlled (meshed split-thickness skin graft) study. The study population included consenting patients who were between the ages of 18 and 65 with 1-20% TBSA thermal burn wounds. Each subject served as their own control, using two comparable contiguous or non-contiguous areas of deep partial-

thickness thermal burns. One site was treated with RECELL (with Spray-On Skin Cells applied directly to the wound), and the other was treated with 2:1 meshed autograft.Subjects were evaluated at 1, 2, 3, 4, 8, 16, 24, and 52 weeks.

Endpoints. The co-primary effectiveness endpoints were: 1) Non-inferiority of the incidence of RECELL-treated recipient site (burn injury) wound closure (≥95% re-epithelialization) at 4 weeks compared to that observed in Control-treated recipient sites. The pre-specified non- inferiority margin (RECELL minus Control) was -10%; and 2) Superiority of donor site healing (100% re-epithelialization) at 1 week for RECELL versus Control. For both endpoints, healing was confirmed at two consecutive visits. Safety assessments included evaluation of delayed healing, infection, allergic response to trypsin, wound durability, scarring outcomes, device-related adverse events, and serious adverse events.

Results

Demographics and baseline characteristics. 101 subjects were enrolled in the study at 12 US Burn Centers. The mean age of the subjects was 39.5 (range: 18.2-63.5) with the majority being male (85/101, 84.2%) and Caucasian (59/101, 58.4%). Most of the burn wounds were the result of fire or flames (78/101, 77.2%). Mean percent TBSA affected by burn wounds was 10% (± 4.53%) with similarly sized recipient site areas for RECELL and Control (168.2 ± 68.0 cm^2 vs. 165.0 cm^2 ± 66.5 cm^2, respectively). On average, surgical intervention for definitive closure occurred 7 days following the burn injury, demonstrating that these partial-thickness burns failed to heal with conservative measures and confirming that autografting was indicated.

Effectiveness. At Week 4, using a Modified Per Protocol (MPP) population designed to exclude four subjects managed post-operatively with silver sulfadiazine, the incidence of complete wound healing was 97.6% in the RECELL-treated sites and 100% in the Control autografting sites. The difference in the incidence of complete wound healing (RECELL minus Control) was -2.4% (95% CI: -8.4 to 2.3%), establishing non-inferiority (by excluding the pre-specified NI margin of -10%) for RECELL compared to Control sites treated with meshed autograft.

Donor site healing was superior at Week 1 (the co-primary endpoint) for the RECELL donor sites versus the Control donor sites (21.8% vs. 10.0%, respectively p=0.0042).

At Week 4, mean percent re-epithelialization of the recipient site was 97.7 ± 12.0% and 100.0 ± 0.07%, for the RECELL and Control recipient sites, respectively. Subjects reported less pain at the RECELL donor site compared to the Control donor site within the 8 weeks following treatment.

Similarly, subjects expressed greater satisfaction with the visual appearance of the RECELL donor site compared with the Control donor site at all longer-term follow-up visits. The mean size of donor sites for burn wounds randomized to RECELL treatment was substantially less than that of the Control: 4.7 ± 3.19 cm^2 vs 194.1 ± 158.5 cm^2, representing a 97.5% reduction in donor skin requirements.

Safety – Adverse Events. Of the 101 subjects, 58.4% experienced an adverse event, with 35.6% having an adverse event at the RECELL sites and 22.8% at the Control sites. Overall, adverse experiences reported for RECELL-treated sites were typical for the type of injury sustained by subjects with burn wounds requiring skin grafting procedures. A numerically greater number of subjects had adverse events at the RECELL sites when compared with the Control sites; however, most of these events were mild in nature, were not considered device-related, and were not serious. Additionally, the greater incidence of adverse events noted at RECELL recipient sites is primarily attributed to events contributing to primary endpoint failures, re-injury at the recipient site, and other primarily self-limited skin and subcutaneous tissue disorders such as blisters and excessive granulation tissue. There were no meaningful differences in the incidence of adverse events at the RECELL vs Control donor sites (4.0% vs. 6.9%, respectively). The observed systemic AEs are consistent with a study population undergoing grafting. In ancillary burn injury areas not included in the randomized treatment areas, 27.7% of subjects experienced AEs that were similar to those that occurred at the treatment sites; these AEs included hypertrophy, hypertrophic scarring, and additional injury (i.e., laceration, skin wound, and skin injury).

Safety – Additional Endpoints. There was no difference in the incidence of graft loss, and graft and donor site infections between the RECELL and Control treatments. Recipient site scarring was measured by mean total Vancouver Scar Scale (VSS) scores with comparable scores for RECELL and Control. The RECELL donor sites had improved appearance at all time points based on the VSS total score outcomes when compared with the Control. Long-term durable wound healing was achieved for both the RECELL-treated and control wounds, as no events of late wound breakdown were reported.

Table 6. Summary of Recipient and Donor Site AEs by System Organ Class and Preferred Term

Primary System Organ Class/Preferred Term N=101	**Recipient Site RECELL n (%)**	**Recipient Site Control n (%)**	**Donor Site RECELL n (%)**	**Donor Site Control n (%)**	**Non-Study Area n (%)**
Any Primary System Organ Class	**36** (36%)	**22** (22%)	**4** (4%)	**7** (7%)	**28** (28%)
General disorders and administration site conditions					
Total	8 (8%)	5 (5%)	0 (0%)	0 (0%)	5 (5%)
Edema	1 (1%)	1 (1%)	0 (0%)	0 (0%)	1 (1%)
Hypertrophy	6 (6%)	3 (3%)	0 (0%)	0 (0%)	5 (5%)
Pain	2 (2%)	2(2%)	0 (0%)	0 (0%)	0 (0%)
Infections and Infestations					
Cellulitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2%)
Folliculitis	0 (0%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)
Infection	2 (2%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)
Rash, pustular	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Suspected wound infection	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Injury, poisoning, and procedural complications					
Laceration	2 (2%)	1 (1%)	0 (0%)	0 (0%)	3 (3%)
Scar	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Seroma	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Skin graft contracture	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Skin graft failure	4[a] (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Skin injury	1 (1%)	0 (0%)	0 (0%)	1 (1%)	1 (1%)
Skin scar contracture	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Skin wound	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Thermal burn	1 (1%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)
Wound decomposition	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Nervous system disorders					
Neuralgia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Neuropathy, peripheral	1 (1%)	1 (1%)	0 (0%)	0 (0%)	1 (1%)
Paresthesia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Skin and subcutaneous tissue disorders					
Blister	5 (5%)	0 (0%)	0 (0%)	1 (1%)	1 (1%)
Dermal cyst	0 (0%)	1 (1%)	0 (0%)	0 (0%)	3 (3%)
Dermatitis, contact	1 (1%)	1 (1%)	0 (0%)	1 (1%)	0 (0%)
Erythema	1 (1%)	1 (1%)	0 (0%)	0 (0%)	2 (2%)
Excessive granulation tissue	7 (7%)	1 (1%)	0 (0%)	0 (0%)	1 (1%)
Hypertrophic scar	10[b] (10%)	6 (6%)	0 (0%)	0 (0%)	8 (8%)
Pruritus	5 (5%)	5 (5%)	2 (2%)	2 (2%)	4 (4%)
Rash	3 (3%)	1 (1%)	1 (1%)	1 (1%)	0 (0%)

[a]2 events of graft loss were classified as device-related

[b]3 events of hypertrophic scar were classified as device-related although for 2 of the 3 events, hypertrophic scarring was also noted at the Control Sites.

B3 RECELL for Treatment of Acute Non-thermal Full Thickness Skin Defects

A Prospective Multicenter Randomized Controlled Clinical Study to Investigate the Safety and Effectiveness of the RECELL System Combined with Meshed Autograft for Wound Closure and Reduction of Donor Skin Requirements

Study Design

The efficacy and safety of the Spray-On Skin Cells prepared using the RECELL Device were evaluated in a prospective, multicenter, intra-subject randomized and controlled, evaluator blinded study. Two comparable wounds in each subject were selected and randomized at 1:1 ratio to receive either the prespecified meshed autografting (i.e., 2:1 meshed ratio) alone in control-treated area or more widely meshed autografting (i.e., 3:1 meshed ratio) plus RECELL in RECELL-treated area.

Endpoints. The co-primary effectiveness endpoints were: 1) Non-inferiority of the proportion of complete wound closure for RECELL-treated wounds (treated with the combination of Spray-on Cells and more widely meshed autografts) compared to that observed in Control-treated wounds (prespecified conventional autograft) by Week 8 after treatment, as assessed by a blinded evaluator in per protocol (PP) population. The pre-specified non-inferiority margin (Control minus RECELL) was 10%. Complete wound closure was defined as complete skin re-epithelialization without drainage, confirmed at 2 consecutive study visits at least 2 weeks apart; and 2) Superiority in relative reduction in donor area requirements for RECELL versus Control treatment, as assessed by the ratio of actual expansion ratios(RECELL to Control) of the treatment area (size) to the required donor skin area (e.g., RECELL treatment area/corresponding donor area to Control treatment area/corresponding donor area) in the intent-to-treat (ITT) population. Safety assessment included reporting treatment emergent adverse events (TEAEs).

Results

Demographics and baseline characteristics. Sixty-five patients with a mean age of 45.7 years (range 15-85 years) from 18 clinical sites were enrolled in the study. Majority of subjects were male (44/65, 67.7%). Seventy one percent of subjects were White, 22% were African American and the remainder were American Indian or Alaska Native or other. The types of wound included acute and chronic wounds of necrotizing (35.4%) and other (9.2%) infections, open (16.9%) and closed (6.2%) degloving injuries, fasciotomy/compartment

Syndrome (7.7%), surgical (7.7%), crush injury (4.6%), traumatic hematoma (3.1%), flap donor (3.1%), road rash (3.1%), gunshot wound (1.5%) and laceration wound (1.5%). The median size of RECELL-treated and the control-treated areas are 160 cm2 (ranged 80 to 1155 cm2) and 156 cm2(ranged 80 to 1155 cm2), respectively, and the wounds are located at arms, legs, back, buttocks, and anterior-torso. The mean affected area was 5.0% (±3.9%) of total body surface area (TBSA).

Effectiveness. Non-inferiority of RECELL-treated areas compared to Control-treated areas in promoting wound closure was established based on the pre-specified non-inferiority margin of 10%. Among the 52 subjects in PP population, 34 (65%) subjects in RECELL group achieved complete wound closure by Week 8. Thirty (58%) subjects in control group achieved complete wound closure by Week 8. The treatment difference (Control minus RECELL) was -7%, with a one-sided 97.5% CI upper bound of 6.2%.

Superiority of RECELL compared to control was established on reduction in donor area requirement for harvesting ($p<0.001$), in ITT population. Treatment with RECELL required, on average, 27% less donor skin, compared to that required for autografting.

Safety – Adverse Events. The safety population includes the ITT population that consists of all 65 subjects who were randomized and received treatment. Each subject received one time treatment of the prespecified meshed autografting (i.e., 2:1 meshed ratio) in control-treated area and a more widely meshed autografting (i.e., 3:1 meshed ratio) plus RECELL in RECELL-treated area. The adverse reactions observed on RECELL, control, RECELL-treated donor site and non-RECELL treated donor site are summarized in Table 7.

Table 7. Summary of Adverse Reactions

Primary System Organ Class/Preferred Term	RECELL n (%) N=65	Control n (%) N=65	RECELL-treated Donor Site n (%) N=43	Non RECELL-treated Donor Site n (%) N=29
Any Primary System Organ Class	36 (55%)	37 (57%)	9 (21%)	9 (31%)
General disorders and administration site conditions				
Impaired Healing	14 (22%)	16 (25%)	1 (2%)	4 (14%)
Oedema	0 (0%)	0 (0%)	0 (0%)	1 (3%)
Pain	0 (0%)	0 (0%)	2 (5%)	0 (0%)
Infections and Infestations				
Local Soft Tissue Infection	6 (9%)	5 (8%)	1 (2%)	2 (7%)
Other Infection	2 (3%)	2 (3%)	0 (0%)	0 (0%)
Injury, poisoning, and procedural complications				
Fall	1 (2%)	1 (2%)	0 (0%)	0 (0%)
Graft Loss	7 (11%)	9 (14%)	0 (0%)	0 (0%)
Skin Graft Failure	1 (2%)	2 (3%)	0 (0%)	0 (0%)
Skin Graft Scar Contracture	0 (0%)	1 (2%)	0 (0%)	0 (0%)
Skin Laceration	0 (0%)	0 (0%)	0 (0%)	2 (7%)
Soft Tissue Foreign Body	1 (2%)	1 (2%)	0 (0%)	0 (0%)
Suture Related Complication	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Wound Decomposition	4 (6%)	6 (9%)	2 (5%)	0 (0%)
Wound Necrosis	0 (0%)	1 (2%)	0 (0%)	0 (0%)
Wound Secretion	1 (2%)	1 (2%)	0 (0%)	0 (0%)
Product Issues[a]				
Device Malfunction	1 (2%)	1 (2%)	0 (0%)	0 (0%)
Skin and subcutaneous tissue disorders				
Blister	1 (2%)	1 (2%)	0 (0%)	0 (0%)
Blister Rupture	0 (0%)	0 (0%)	1 (2%)	0 (0%)
Excessive Granulation Tissue	12 (19%)	8 (12%)	0 (0%)	2 (7%)
Pruritus	3 (5%)	3 (5%)	3 (7%)	0 (0%)
Rash	2 (3%)	1 (2%)	1 (2%)	1 (3%)
Skin Exfoliation	5 (8%)	4 (6%)	2 (5%)	4 (14%)

a. Site-reported term is “wound vac malfunction.”

C TREATMENT

C1 REQUIREMENTS

The following materials and instruments will be needed during the procedure:

- Sterile field
- Personal protective equipment
- Skin preparation solution
- Local anesthetic with adrenaline where not contraindicated
- Sterile ruler and marker pen
- Appropriate wound dressings - see “Aftercare” section for details
- 1 or 2 x fine-point (long nosed) forceps of choice
- Skin harvesting instrument of choice
- Wound bed preparation tool of choice
- Clock or timer to monitor incubation time

C2 RECELL DEVICE SET-UP

⚠ CAUTION: Do not use RECELL or device components beyond the stated expiration date indicated on the adhesive Lot # and Expiration Date labels on the outer box packaging.

Perform the following set-up steps in the order shown to avoid setup errors. A procedure guide describing the set-up process is included with the device for reference during a procedure.

The RECELL Device contains both sterile and non-sterile components. Select and prepare sterile work areas.

Open the outer box.

Remove the TELFA Clear Dressings and Procedure Guide and place in non-sterile preparation area.

Remove RECELL Tray and place in non-sterile preparation area.

Pull tab to access RECELL Enzyme (located on left hand side).

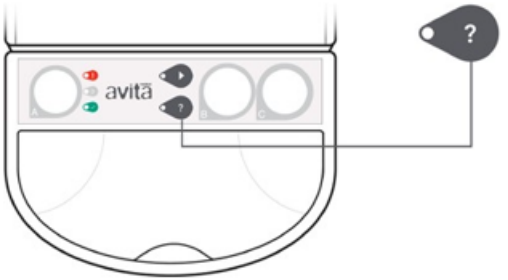
Remove the pouch containing the sterile RECELL Enzyme and place in non-sterile preparation area.

NON-STERILE PREPARATION AREA	*STERILE AREA*
Remove the peel off lid from the outer non-sterile RECELL Tray.	Starting with C Tray, transfer both inner sterile trays to the sterile field. Once in the sterile field, remove tear off lid from A/B/Processing Unit Tray. Remove clear retainer from the tray, starting from the upper left corner. 
Using aseptic technique, open Enzyme pouch 	Transfer RECELL Enzyme to sterile field. Place Enzyme Vial within housing in A Section of the A/B/Processing Unit Tray.

PERFORM SELF-TEST

(STERILE AREA)

- Remove Processing Unit from the A/B/Processing Unit tray.
- Open the Processing Unit.
- Remove labels and place in the sterile field.
- Perform the self-test to verify the device is functioning correctly.



Test the device to ensure functionality by opening the lid and pressing the button marked ( ). All lights by Well A should illuminate during the self-test.

When the unit has completed the self-test (this takes approximately 30 seconds), it will beep once and the green ready light ( ) will illuminate to indicate that the Processing Unit is functioning correctly.

DO NOT press the flashing run button ( ) at this time.

If lights do not illuminate, or the red light ( ) illuminates, this indicates device failure. Do not use the device. Use another device.

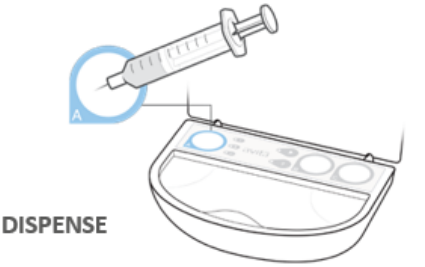
- The unit will automatically turn off after 1 minute if Enzyme heating is not initiated.
- If the device turns off after self-test, additional self-tests may be run.

PREPARE WELL A

- Remove the cover from the vial marked Enzyme to expose the injection diaphragm.
- Use syringe and needle from A Tray to add 10 ml of water to the Enzyme. **DO NOT USE** Buffer at this stage as this may inhibit the Enzyme action.

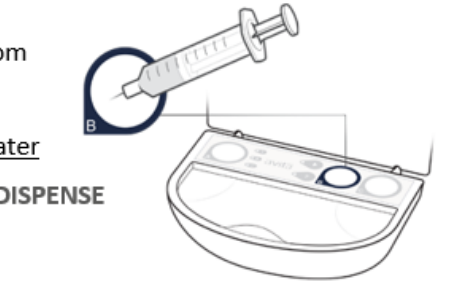
- Mix gently until dissolved. Do not shake; use care to avoid foaming. Draw the Enzyme back into the syringe.

- Using aseptic technique, dispense the entire volume of Enzyme into the left-hand well of the Processing Unit (Well A).
- Discard syringe and needle.



PREPARE WELL B

- Dispense 10 ml of Buffer into Well B. The "BUFFER" syringe will be used several times to draw Buffer from the vial.
- Set aside syringe and needle in the sterile field for later use.
- Discard A/B/Processing Unit Tray



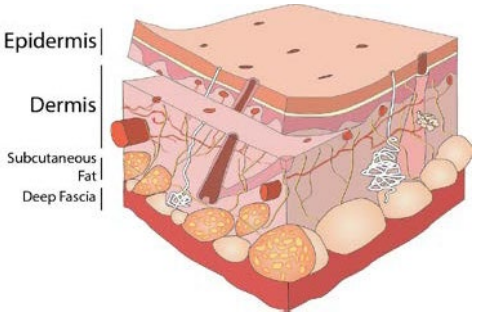
PREPARE WELL B

- Label syringe in B Tray with BUFFER label.
- Set aside remaining labels in the sterile field for later use.
- Use syringe and needle in B Tray to draw up 10 ml Buffer.

C3 BURN WOUND BED PREPARATION

- Clean, vascularized wound bed – To optimize the treatment, the cell suspension should only be applied to a clean, vascularized wound bed with no remaining necrotic tissue. This can be achieved with either dermabrasion using a rotating diamond-head burr, laser ablation, sharp dissection or other alternative techniques, depending on the nature of the wound.
- Infection free – The cell suspension must not be used in the presence of any contamination or infection, as initial re-epithelialization and long-term viability are highly dependent on the absence of infection. Prophylactic antibiotics may be prescribed if the patient is at risk of contamination or infection. Wound swabs for up-to-date microbiology are recommended 48 hours prior to the planned surgery.
- Pinpoint bleeding – The wound bed should be prepared so that pinpoint bleeding is observed. Accurate debridement to the level of viable tissue is essential; all necrotic tissue must be removed.
- When RECELL is used for treatment of acute thermal burn wounds, Spray-On Skin Cells can be directly applied to partial-thickness wounds or applied in combination with meshed autografts for full-thickness wounds.

C4 SKIN SAMPLE HARVESTING



Skin Sample Type

It is essential that the skin sample harvested is a thin, split-thickness skin sample that leaves pinpoint bleeding at the donor site. The thickness of the skin sample will vary with the body site and patient age and should be in the range of 0.006 – 0.008 in (0.15 – 0.20 mm). The use of a dermatome, or similar device is recommended.

Size of Skin Sample

Choose the appropriate skin sample size for the application. Each square centimeter of skin sample can create 1 ml of cell suspension for treatment of an area of up to 80 cm^2. Each 6 cm^2 (3 cm x 2 cm) skin sample can yield approximately 6 ml of cell suspension; each RECELL Device can process up to four 6 cm^2 skin samples for a maximum of 24 ml of cell suspension. This can be used to treat an area of approximately up to 1,920 cm^2.

The following table provides guidance for skin sample needed for several treatment area sizes.

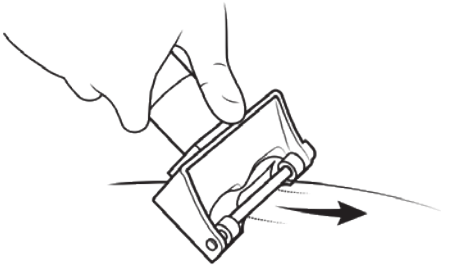
Treatment Area	up to 80 cm^2	up to 160 cm^2	up to 320 cm^2	up to 480 cm^2	up to 960 cm^2	up to 1440 cm^2	up to 1920 cm^2
Skin Sample Size	1 cm x 1 cm (1 cm^2)	2 cm x 1 cm (2 cm^2)	2 cm x 2 cm (4 cm^2)	3 cm x 2 cm (6 cm^2)	2 ea. 3 cm x 2 cm (12 cm^2)	3 ea. 3 cm x 2 cm (18 cm^2)	4 ea. 3 cm x 2 cm (24 cm^2)

Choice of Donor Site

It is essential the donor site is clean, of appropriate depth, and shows no evidence of surrounding inflammation or infection. Choose a donor site of glabrous tissue when creating suspension for glabrous tissue regeneration.

Using the preferred instrument such as a dermatome, take a split-thickness skin sample from the donor site of thickness 0.006 – 0.008 in (or 0.15 – 0.20 mm).

The skin sample may be trimmed from skin harvested for split-thickness skin grafting. Use the table above to estimate the skin sample size needed or calculate by taking 1/80 of the total treatment area.



Clean the donor site with antiseptic solution such as povidone-iodine or chlorhexidine. Allow the antiseptic to dry before removing with sterile saline (antiseptic solutions may be cytotoxic and as such, may affect cell viability if left on the skin sample site).

If desired, infiltrate the subcutaneous tissue with a tumescent solution of choice, to provide a firmer surface and anesthesia for taking the skin sample. Ensure that anesthetic is not injected intradermally.

The donor site area may be lubricated (e.g., with sterile mineral oil) to ease travel of the dermatome.

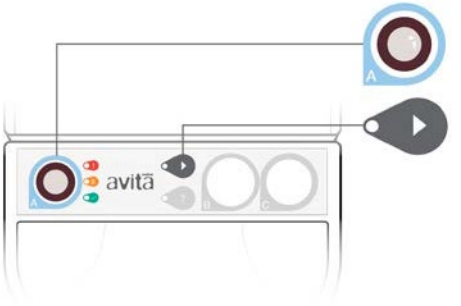
Due to the thick keratin layer found on glabrous skin, it is necessary to take two shaves over the same site in these areas. Discard the first sample and process the second skin sample to create the cell suspension.

Large pieces of harvested skin should be cut into skin samples appropriately sized for use in the device. Keep the skin samples moist in sterile gauze moistened with sterile saline prior to use.

C5 PREPARING CELL SUSPENSION USING THE RECELL DEVICE

Confirm Enzyme is in Well A

The Processing Unit will quickly overheat if the run button (⏵) is pressed before the Enzyme has been placed in the well. Any malfunctioning of the unit, including overheating, will be indicated by the red light (!) illuminating. Should this occur, use another RECELL Device and contact your local representative to arrange the return or replacement of the unit.



Ensure skin sample is available and press the run button to heat the Enzyme in Well A

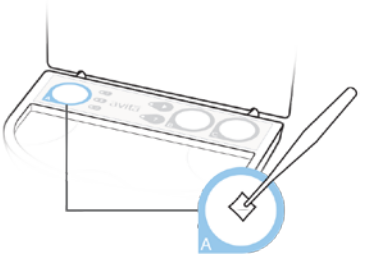
If more than one minute has passed since the last self-test, a self-test will automatically run, followed immediately by heating of the Well A. The orange warming light will illuminate when warming begins and the Enzyme will be heated and maintained at approximately 37°C.

When the target temperature is reached, the green ready light (✓) will illuminate and you can proceed to Enzymatic Processing.

ENZYMATIC PROCESSING

Incubate the Skin Samples

When the orange warming light turns off and the ready read light (✓) illuminates the Enzyme has reached its target temperature. This will take approximately 3 minutes. The orange warming light will flash from time to time, indicating that the heating element has been activated to maintain temperature.



Place 1 or 2 skin samples into the heated Enzyme for 15 to 20 minutes to allow the breakdown of protein-protein interactions. DO NOT incubate more than two 6 cm^2 skin samples at a time. Up to 4 samples may be processed using a single device, 2 initially, then 2 following those. If the skin samples are thick, they may require longer incubation. Each sample may be incubated for up to 60 minutes.

After approximately 60 minutes, an alarm will sound and will sound each minute for 15 minutes. At 75 minutes, the Processing Unit will turn off and stop heating the enzyme. Incubation of a skin sample for more than 60 minutes is not recommended.

May complete Prepare Buffer Step while skin is incubating.

Prepare C Tray

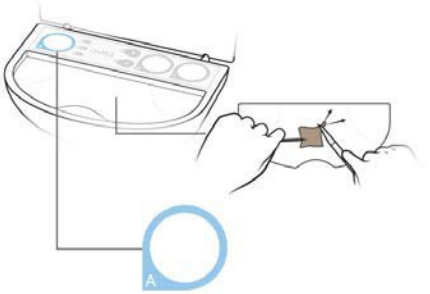
Peel off lid and remove clear retainer. Apply UNFILTERED SUSPENSION label to the single placed 10 ml syringe.

Apply SPRAY-ON SKIN CELLS labels to the 4 remaining 10 ml syringes.

Test Scrape for Cell Disaggregation

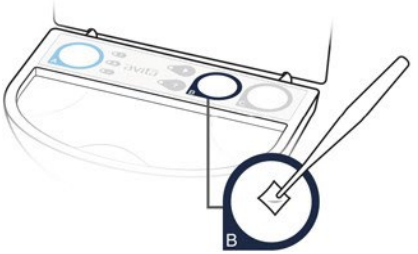
After 15 to 20 minutes, remove the skin sample from the heated Enzyme in Well A with sterile forceps and place the skin sample dermal side down on the sterile tray. Scrape the epidermis edge with the scalpel from C Tray to test if cells disaggregate, i.e., epidermal cells easily come off.

Once the test is complete STOP scraping. If the cells do not come off freely, return the skin sample to the heated Enzyme for a further 5 to 10 minutes and then repeat the test scrape. When the cells scrape off freely, proceed to Rinse Skin Sample(s) step.



Rinse Skin Sample

Upon a successful test scrape, rinse the skin sample in the middle well (Well B) containing the Buffer to rinse off the residual Enzyme. When applicable, place the 2nd incubated sample in Well B. Proceed to *Mechanical Processing.*



Multiple Skin Samples?

For 3 or 4 skin sample(s) initiate *Stage A - Enzymatic Processing* by placing them into Well A prior to proceeding with *Stage B - Mechanical Processing* for the 1st and 2nd skin samples.

MECHANICAL PROCESSING

Prepare Buffer

This step may be performed while the skin sample is incubating in Step 1.

Use the syringe labeled BUFFER, located in the sterile field, to draw up the required volume from the 30 ml Buffer vial in C Tray.

Draw up 1 ml of Buffer per square centimeter and add 0.5 ml Buffer to allow for loss during processing. The following table provides example surface areas to be treated, skin sample sizes needed, volumes of Buffer to use, and approximate resultant suspension volumes.

Surface Area to be Treated per Syringe	Up to 80 cm^2	Up to 160 cm^2	Up to 320 cm^2	Up to 480 cm^2
Skin Sample Size	1 cm^2 (1 cm x 1 cm)	2 cm^2 (2 cm x 1 cm)	4 cm^2 (2 cm x 2 cm	6 cm^2 (3 cm x 2 cm)
Starting Volume of Buffer, per Sample	1.5 ml	2.5 ml	4.5 ml	6.5 ml
Approximate Resultant Suspension Volume	1.0 ml	2.0 ml	4.0 ml	6.0 ml

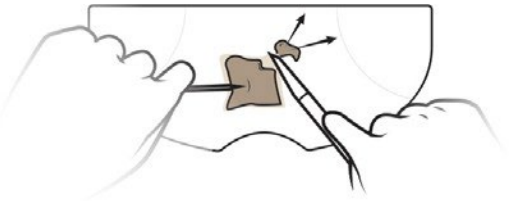
Each 1 ml of suspension may be used to treat up to 80 cm^2; however, a suspension volume of greater than or equal to 2 ml is required to spray the suspension on the wound. Volumes less than 2 ml may be applied using the drip method.

Place the Buffer filled syringe in the sterile field for later use.

Scrape Cells from the Skin Sample

Place the skin sample on the sterile processing tray with dermal side down. Apply a few drops of Buffer from the previously filled “BUFFER” syringe onto the skin sample. Using the forceps to anchor the skin sample, scrape the epidermal surface with the blade of the scalpel towards the tray slope of your dominant hand. Once the epidermis has been

scraped away into suspension, scrape the remaining dermis more vigorously. Continue scraping until the dermis is nearly disintegrated.

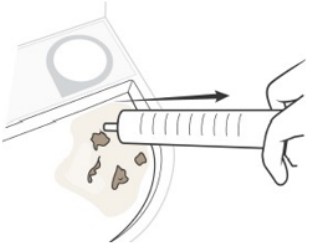


Rinse Tray and Draw up Cell Suspension

Use the remaining Buffer in the "BUFFER" syringe to rinse the scalpel and tray, collecting the cells into one corner of the ramped tray.

BUFFER syringe

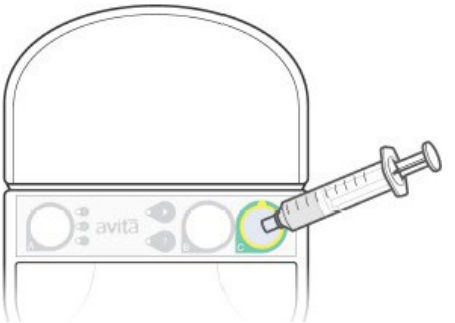
Set the "BUFFER" syringe aside for later use. Using the "UNFILTERED SUSPENSION" syringe (an attached needle is not required), collect and draw up the cell suspension. Using the drawn-up suspension, rinse the tray and repeat as required to maximize cell collection. Once the tray is rinsed several times, draw up all the cell suspension into the syringe.



UNFILTERED SUSPENSION syringe

Filter Suspension

Dispense the cell suspension into the cell strainer in Well C. The strainer removes particulates >100 µm and is critical in preventing nozzle blockage when spraying the cellular suspension. Set the “UNFILTERED SUSPENSION” syringe aside, within the sterile field, for use with subsequent suspensions from the remaining skin samples.

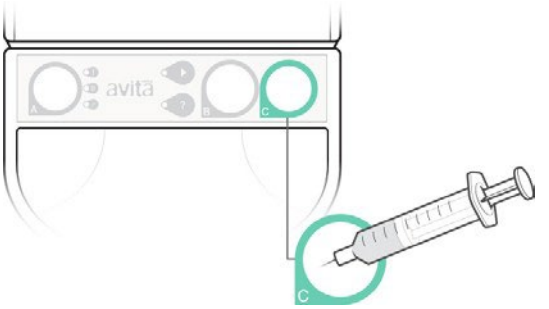


After the cell suspension has passed through the cell strainer, carefully remove the cell strainer and tap it over the well to release any drops of cell suspension into Well C.

If processing 3 or 4 skin samples, replace existing cell strainer with cell strainer located in C Tray.

Draw Up Cell Suspension

Attach a needle from C Tray to “SPRAY-ON SKIN CELLS” syringe. Draw up the filtered cell suspension using the “SPRAY-ON SKIN CELLS” syringe (Do not use “UNFILTERED SUSPENSION” syringe) from Well C. There is a conical point in the center of the bottom of Well C to aid in drawing up all of the cell suspension. Set the prepared “SPRAY-ON SKIN CELLS” syringe aside for later application.



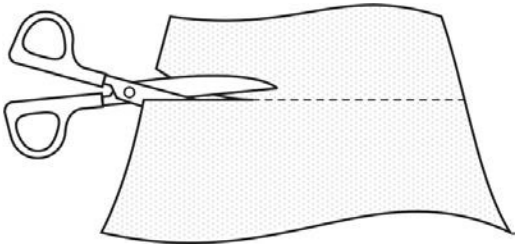
Return the cell strainer to Well C. “SPRAY-ON SKIN CELLS” syringe is ready for *Deliver Spray-On Skin Cells*.

Complete *Mechanical Processing* to create a syringe of “SPRAY-ON SKIN CELLS” for each skin sample; then proceed to *Deliver Spray.*

DELIVER SPRAY-ON SKIN CELLS

Prepare Dressings

Prior to applying the cell suspension, ensure the dressings are cut and prepared for immediate application. The primary dressing may be fixed using surgical glue, sutures, or staples, or held at the lower aspect of the wound prior to applying the cell suspension to reduce runoff. Section D – Aftercare, provides information on dressing selection and use.

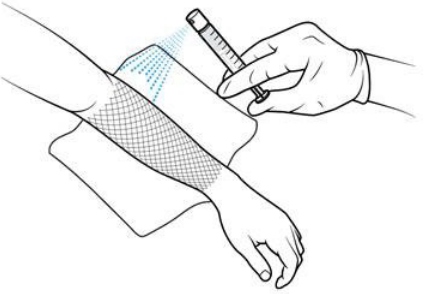


Prior to application, invert the syringe several times to ensure an even suspension.

Apply Cell Suspension to Wound

The cell suspension can be applied directly to partial-thickness wounds or in combination with meshed autografts for full-thickness wounds.

The cell suspension can be sprayed or dripped onto the wound bed, with the technique (i.e., spraying vs. dripping) dependent on the volume of cell suspension to be applied and size of wound bed.



Spray Application – Application of greater than or equal to 2 ml of cell suspension

The spray application technique should only be used when there is greater than or equal to 2 ml of cell suspension in the syringe.

Remove the needle from the syringe containing the cell suspension. Attach a supplied spray nozzle, located in the C Tray, to the syringe. Leaving the nozzle in the Tray, attach the syringe using firm downwards pressure. Be careful not to press the plunger.

Check that the aperture of the attached spray nozzle faces the wound. Hold the spray applicator approximately 10 cm from the most elevated point of the wound and in a position, such that the first drop of suspension falls onto the wound surface. Apply moderate pressure to the plunger of the syringe. Start spraying at the most elevated part of the wound so that any run-off helps to cover the more dependent areas of the wound. A fine mist of cell suspension should be delivered to the wound surface. To cover a larger area, carefully move the spray applicator in one continuous motion from one side of the wound to the other as you spray.

Drip Application – Application of less than 2 ml of cell suspension

The drip application should be used any time that the remaining volume of cell suspension in the syringe is less than 2 ml. Please note that if the remaining volume of cell suspension is less than 2 ml, there is an insufficient amount of cell suspension to cover a wound that is ≥160 cm^2.

Do not remove the needle from the syringe containing the cell suspension.

Starting at the most elevated point of the wound, carefully drip the cells onto the wound surface so that any run-off helps to cover the more dependent areas of the wound.

Note: Following application, it is typical to observe run-off of the suspension from the treated wound; results from prospective randomized clinical studies indicate sufficient cellular attachment is obtained post-application of the cellular suspension as epidermal regeneration for definitive closure is achieved.

Place Initial Dressing

After applying the cell suspension, cover the wound with a non-adherent, non-absorbent, small pore dressing. Always follow the instructions as set by the dressing manufacturer. Dry

dressings may be applied moist at the direction of the healthcare professional by lightly soaking the dressing in sterile saline before dressing the wound. The dressing may be fixed to the wound with surgical glue, sutures, or staples, as necessary.

Secondary dressings that are moderately absorbent, minimally adherent, low shear, and readily removable should be placed over the primary dressing followed by absorbent gauze. Use of known cytotoxic medication (for instance, silver sulfadiazine) is contraindicated for areas treated using RECELL. Additional absorbent gauze for padding, as well as a crepe or compression bandages, may be used.

D AFTERCARE

The following information, precautions, and notes provide guidelines for care after RECELL treatment. Discuss appropriate aftercare with your AVITA representative and provide the patient with aftercare instructions.

D1 SUBSEQUENT DRESSINGS

The outer dressings and compression bandages may need to be changed if exudate levels are high; however, the primary dressing should remain in place for 6-8 days, or as clinically indicated. Protect the primary dressing during secondary dressing changes.

The primary dressing must not be forcibly removed from area(s) to which it is still adhered. Typically, it can be separated (gently peeled back) as new epidermis is formed.

To prevent trauma, any dressing not easily removed should be soaked with an aqueous or oil-based solution prior to removal.

Once the primary dressing has been removed, an appropriate protective dressing should be applied to protect the wound surface.

Do not use dry dressings as protection over blisters or areas of punctate bleeding, as dried exudate could cause newly regenerated epidermis to adhere to the dressing, leading to potential injury upon dressing removal. Instead, use a sterile greasy or paraffin gauze dressing until any blistering or open areas resolve.

Any signs or symptoms of infection or impaired healing at this stage should be recorded and addressed.

D2 AFTERCARE PRECAUTIONS

- Patients should take necessary precautions to prevent the treated area from getting wet while the wound is still open.
- The primary dressing should remain in place as clinically indicated but is typically no longer required after 6-8 days.
- Up to two additional weeks may be needed after initial closure of the treated area for the newly regenerated epidermis to mature and become robust. During this time protective dressings must be worn, particularly on extremities.

- Use of known cytotoxic medication (for instance, silver sulfadiazine) is contraindicated for areas treated using RECELL.
- Patients and caregivers should be provided with adequate information and materials for appropriate protection against re-injury during healing and maturation of the treated area.
- Patients should be advised to refrain from strenuous activity.
- Patients should avoid direct sun exposure. A minimum SPF30 and protective clothing should be worn.
- Patients should be counseled about increased risks of skin cancers after thermal burn wounds, and to notify their treating physician of their prior treatment with RECELL if they develop skin cancers.

D3 SCAR MANAGEMENT

When the wound has healed, the patient should be advised to continue to protect the area from any surface trauma and to avoid direct sun. Regular use of sunscreen (SPF30) and twice-daily massage with a non-oily skin moisturizer is recommended.

The patient should be advised that the wound area will change over the subsequent weeks and months. The pigmentation and skin texture will continue to mature and improve during this time and the final result may take up to 12 months to be achieved.

Follow-up procedures should follow standard protocols for the specific injury and treatment given.

E SYSTEM SPECIFICATIONS

This device meets the following standard

IEC 60601-1 edition 3.1 Medical electrical

E1 OPERATION AND STORAGE CONDITIONS

	Operation	Storage
Temperature	15-35°C	20-25°C
Relative humidity	10-90%	10-60%
Atmospheric pressure	65-106 kPa	65-106 kPa

E2 INTENDED USE ENVIRONMENT

RECELL is intended for use in a hospital setting. However, do not use RECELL near active high-frequency surgical equipment, and do not use RECELL near RF shielded room of a magnetic resonance imaging equipment where electromagnetic disturbances are high. RECELL is internally powered by four non-replaceable AA batteries. The device should not be used in the presence of flammable materials and must not be incinerated on disposal.

E3 ESSENTIAL PERFORMANCE

RECELL maintains target temperature (34-39°C) of Enzyme in Well A for 60 minutes in the specified environmental conditions.

E4 COMPONENT STERILIZATION AND TESTING

- The RECELL components in the trays have been sterilized by ethylene oxide.
- The RECELL Enzyme has undergone filtration and terminal sterilization by gamma irradiation.
- The Buffer and sterile water have been sterilized using steam.

F ELECTROMAGNETIC COMPATIBILITY

RECELL is intended for use in the electromagnetic environment specified below. The customer or the user of RECELL should assure that it is used in such an environment.

Emissions Guidance and manufacturer's declaration – electromagnetic emissions

Emission Test	**Compliance**	**Electromagnetic environment – guidance**
Radiofrequency (RF) emissions CISPR 11	Group 1	RECELL uses RF energy only for its internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class A	RECELL is suitable for use in all establishments, other than domestic establishments.

Immunity Test Standard	**Compliance Level**	**Electromagnetic environment – guidance**
Electrostatic discharge (ESD) IEC 61000-4-2	± 8 kV contact ± 8 kV air	Floors should be wood, concrete or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 10%.
Electromagnetic compatibility (EMC) 61000-4-3	3 V/m	Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the RECELL. Otherwise, degradation of the performance of this equipment could result.
61000-4-8	30 A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment.

Immunity

Use of RECELL adjacent to or stacked with other equipment Warning

Use of RECELL adjacent to or stacked with other equipment should be avoided because it could result in improper operation. If such use is necessary, this equipment and the other equipment should be observed to verify that they are operating normally.

Use of accessories, transducers, or cables not specified Warning

Although RECELL is designed for electromagnetic immunity, use of accessories, transducers and cables other than those specified or provided by the manufacturer of this equipment could result in increased electromagnetic emissions or decreased electromagnetic immunity of this equipment and result in improper operation.

Electrostatic Discharge Warning

Although RECELL is designed to be unaffected by typical electrostatic discharge (ESD), very high levels of ESD can result in a temporary suspension of normal operation requiring the operator to press the run button (▶) to resume normal operations.

G TROUBLESHOOTING

Clogging of cell strainer
If the cell suspension does not easily pass through the cell strainer, the cell strainer may be clogged. Replace with the cell strainer found in C Tray. If clogging occurs, with the extra cell strainer, leave the cell strainer in Well C and carefully draw up all the cell suspension from the cell strainer back into the "UNFILTERED SUSPENSION" syringe and utilize a new cell strainer from a new RECELL Device.

Enzyme powder does not dissolve completely
Make sure that the Enzyme is mixed well with the sterile water by gently inverting the vial several times. Often a small amount of particulate matter remains undissolved in the reconstituted solution. This does not reduce the activity of the Enzyme.

Do not use Buffer to dissolve the Enzyme as it may interfere with the Enzyme action.

Skin sample is too large, too thick, or too thin
Take particular care when harvesting the skin sample. It should be a thin (0.006 – 0.008 in, 0.15 – 0.20 mm) split-thickness graft with just a very thin section of dermis. The skin sample of the appropriate thickness will ensure successful disaggregation of cells. The maximum size of skin sample recommended for use with the RECELL Device is 3 cm by 2 cm.

If the skin sample is too large (greater than the maximum recommended), cut it into a smaller size and discard the excess.

If the skin sample is too thick, cut the skin sample into 1 cm by 1 cm pieces before placing in the heated Enzyme. If the cells cannot be disaggregated, repeatedly return the skin sample to the heated Enzyme for a further 5 to 10 minutes, up to a maximum of 60 minutes of total time. If the cells still do not scrape off freely it may be necessary to take another thin, split-thickness skin sample (0.006 – 0.008 in, 0.15 – 0.20 mm) from a DIFFERENT donor site and repeat the process using a new RECELL Device.

If the skin sample is too thin, you should take another skin sample from a DIFFERENT donor site and repeat the process.

Buffer added to Enzyme vial

If Buffer, instead of sterile water, is mistakenly added to the Enzyme vial, the Enzyme activity may be inhibited. If Buffer is mixed with the Enzyme powder, the Enzyme should be discarded and a new RECELL Device used.

Difficult Cell Disaggregation

Ensure that the heating element is switched on. The green ready light (✓) will illuminate when the RECELL Device is switched on and ready for use. The orange warming light will illuminate when the device is warming. Disaggregation of the cells will take longer if the skin sample is too large or thick. See above for advice.

Nozzle blocked

If the cell suspension is not easily sprayed, the cell suspension may be dripped onto the wound bed. If the cell suspension does not come out at all, the nozzle attached to the syringe may be blocked by unfiltered particles. Filter the suspension and place in a new 10 ml syringe prior to attaching a new spray nozzle.

Insufficient treatment area coverage

If cell suspension is lost in the application process and sufficient coverage of the treatment area was not achieved, take another skin sample and repeat the process with a new RECELL Device to create additional cell suspension and complete the treatment.

For further information regarding the RECELL Autologous Cell Harvesting Device, contact:

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