FROST & SULLIVAN

# REAPPLIX A/S RECEIVES THE 2023 TECHNOLOGY INNOVATION LEADERSHIP AWARD

*Identified as best in class in the North American chronic wound treatment for patients with diabetes industry*

## Best Practices Criteria for World-Class Performance

Frost & Sullivan applies a rigorous analytical process to evaluate multiple nominees for each award category before determining the final award recipient. The process involves a detailed evaluation of best practices criteria across two dimensions for each nominated company. Reapplix A/S excels in many of the criteria in the chronic wound treatment for patients with diabetes space.


### *Ushering in a Paradigm Shift in Diabetic Foot Ulcer Treatment through a Revolutionary Autologous Point-of-care Regenerative Therapy*

A Diabetic foot ulcer (DFU) is one of the most challenging complications of poorly managed diabetes mellitus, with about 19 to 34% of patients worldwide developing the condition in their lifetime.[1] Optimal management of DFU is essential to prevent wound site infections, which can increase the risk of lower-extremity amputations, in turn affecting quality of life.

> *"The 3C Patch's ability to offer a high concentration of leukocytes, platelets, and fibrin to the DFU is akin to enabling a blood transfusion to the wound to help kill bacteria and improve microvascular flow, neovascularization, and collagen synthesis in the process, thus promoting faster wound healing and closure."*
>
> ***- Neeraj Nitin Jadhav, Industry Analyst***

Wound dressings, such as hydrogel, and autologous regenerative therapies containing growth factors, platelet-rich plasma, and tissues have been used for DFU management; however, these methods are unable to heal the DFU completely, with 40% of

[1] American Diabetes Association; Diabetes Care; Katherine McDermott, et al.; December 22, 2022; "Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers"

ulcers recurring after one year.[2] Moreover, hydrogel dressings may cause secondary damage to wounds, which can prolong the healing process. On the other hand, autologous regenerative therapies promote angiogenesis and granular tissue formation; however, ulcers complicated with infection from bacterial biofilms can hinder the wound healing process, thus limiting the ability of these therapies to manage DFUs effectively. Moreover, centrally processed autologous regenerative therapies use living cells and thus require storage at certain temperatures for preservation and need to be shipped to central laboratories for additional processing, which may take days or even weeks to produce the final product, thus delaying treatment for patients and, in turn, adversely impacting health outcomes.

To address the limitations of wound dressings and centrally processed autologous regenerative therapies for DFU management, Denmark-based Reapplix A/S, with offices in the United States and Europe, has developed its breakthrough 3C Patch® (formerly known as LeucoPatch), a US FDA 510(k)-cleared and CE marked autologous platelet-rich plasma gel prepared using the 3C Patch System® for treating DFUs.

**Remarkably Simple to Produce**

Using just 18 milliliters (ml) of the patient's blood collected into the 3C Patch System's 3C Patch device and then placed into the 3CP Centrifuge, the system can automatically perform the following three steps: proprietary high-speed centrifugation, which is used to separate cells in the patient's blood; coagulation, where fibrin is polymerized; and compaction, where the 3C Patch is produced at the point of care. The 3C Patch System can perform all three steps in only 20 minutes through an automated process, allowing healthcare professionals, irrespective of their skill levels, to produce the 3C Patch easily and then directly apply it to the DFU, without the need for preservation or additional processing steps.

**100% Autologous Wound Care Product**

The 3C Patch is derived entirely from the patient's blood, without using any additives or reagents, thus eliminating the risk of an immunogenic response and product rejection by the individual's body. The 3C Patch, therefore, is a 100% autologous wound care product that is rapidly produced at the point of care and immediately applied to the patient's DFU to provide timely treatment and improve the wound healing process, thereby limiting the long-term risk of amputation and associated disability. Using the 3C Patch improves the individual's quality of life and lowers the total medical cost associated with DFU management, which can range between $9 and $13 billion annually in the United States alone.[3]

**Three-layered Patch for Personalized Wound Healing**

The three distinct layers of fibrin, platelets, and leukocytes in the 3C Patch, generically described as the Autologous Multilayered Leukocyte, Platelet and Fibrin Patch (MLPF), are critical points of differentiation in the market. For example, unlike any other product in the market, the 3C Patch's three layers position the essential healing components from the patient's blood onto the wound site. The fibrin layer provides

[2] National Library of Medicine; National Center for Biotechnology Information; Andrew J.M. Boulton, MD, DSc, (Hon), FACP, FRCP, et al.; May 2022; "New Evidence-Based Therapies for Complex Diabetic Foot Wounds"
[3] National Library of Medicine; National Center for Biotechnology Information; Alok Raghav, et al.; January 2018; "Financial burden of diabetic foot ulcers to world: a progressive topic to discuss always"

polymerized fibrin, which is essential for moisture retention in the DFU and offers structural integrity to the 3C Patch. The platelet layer provides approximately 3 billion platelets, with 2.6 times and 9.8 times higher levels of platelet-derived growth factor-AB and vascular endothelial growth factor, respectively, compared to competing autologous regenerative therapies. The leukocyte layer provides an estimated 50 million leukocytes, including polymorphonuclear neutrophils, lymphocytes, and monocytes, known to assist in fighting infection in the wound bed caused from bacteria, such as *Pseudomonas aeruginosa*.

The 3C Patch's ability to offer a high concentration of leukocytes, platelets, and fibrin to the DFU is akin to enabling a blood transfusion to the wound to help kill bacteria and improve microvascular flow, neovascularization, and collagen synthesis in the process, thus promoting faster wound healing and closure. The 3C Patch, therefore, offers personalized wound treatment to accelerate wound healing for effective DFU management.

**Adaptive Nature**

Unlike commercially available products for DFU management, Reapplix's 3C Patch has a distinct property that responds to stimuli relevant for wound healing. For instance, multiplex analysis has detected more than 800 different types of cytokines and proteins in the 3C Patch, out of which 380, including interleukin-1β, interleukin 6, and interleukin 10, are produced in response to pro-inflammatory and anti-inflammatory events, thus highlighting the product's adaptive ability to generate an appropriate response based on detected stimuli in the wound environment. In addition to DFU management, including hard-to-heal DFUs, the 3C Patch can be used to treat other exuding cutaneous wounds, such as leg ulcers, pressure ulcers, and mechanically or surgically debrided wounds.

## *Extensive Research Highlighting Substantial Clinical Benefits to Ensure Scalable Commercial Success*

An independent multicenter, multinational clinical study, which was carried out between 2013 and 2017 in 32 specialist diabetic foot clinics across the United Kingdom, Denmark, and Sweden, demonstrated favorable outcomes in patients. For instance, out of the 269 subjects who participated in the study, 34% witnessed healing in hard-to-heal DFUs, compared to only 22% of participants receiving current standard of care.[4] Moreover, the time to heal in patients that received the 3C Patch was significantly shorter by 20 weeks, compared to the current standard of care, with the subjects experiencing no serious device-related adverse events when using the product.[5]

The promising results achieved in the clinical study have helped Reapplix receive backing from the International Working Group on the Diabetic Foot (IWGDF), which has recommended the use of the 3C Patch in its new intervention guideline to enhance the healing of DFUs. This inclusion in the well-respected IWGDF list of recommendations has helped drive the adoption of the 3C Patch among prominent wound

[4] The Lancet Diabetes & Endocrinology; Prof Frances Game, FRCP, et al.; November 2018; "LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked, randomised controlled trial"
[5] Annals of Translational Medicine (ATM); Francisco Javier Alvaro-Afonso, et al.; December 29, 2018; "Management of hard-to-heal diabetic foot ulcers: local use of autologous leucocytes, platelets and fibrin multi-layered patches (LeucoPatch)"

care centers and hospitals in the United States, and Denmark, including Casa Colina Hospital and Centers for Healthcare, Natchitoches Regional Medical Center, and Copenhagen Wound Healing Center, Bispebjerg Hospital. Furthermore, in 2021, the Centers for Medicare & Medicaid Services (CMS) issued the Healthcare Common Procedure Coding System (HCPCS) code of G0465 for the 3C Patch, allowing the national average reimbursement rate of $1,725.86 per treatment. This reimbursement offered by the CMS is expected to drive the adoption of Reapplix's product across all 50 states in the United States.

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A cornerstone of Reapplix's growth strategy is its comprehensive patent portfolio built from significant investments in research and development. The company has developed an extensive intellectual property portfolio that supports the unique triple layered structure of the 3C Patch and the methods used to produce the product. Reapplix has adopted a robust and multi-layered approach that provides an additional layer of patent protection for its invention related to product design and device methods of action. The robust patent portfolio, with patents filed in key markets, such as the United States, Canada, Europe, Japan, and China, offers a strong foundation for the company to achieve outstanding business growth in the near future.

## Conclusion

The management of DFUs in patients is severely affected by the limitation of the current standard of care. For example, wound dressings, such as hydrogel, can cause secondary damage to wounds, while the preparation of centrally processed autologous regenerative therapies is a time-consuming process that can delay treatment and thus negatively impact patient health.

To address these unmet needs, Reapplix developed the 3C Patch, a first-of-its-kind, 100% autologous wound care patch derived from a small volume of blood in only 20 minutes through an automated process, which can be easily produced by healthcare professionals, irrespective of their skill levels. The 3C Patch can be produced at the point of care and directly applied to the patient's wound, initiating timely treatment for the effective management of the DFU.

Frost & Sullivan commends Reapplix's ability to develop the 3C Patch with the three distinct layers of leukocytes, platelets, and fibrin, which provide the key components found in the blood to eliminate bacteria and facilitate collagen synthesis, microvascular flow, and neovascularization at the wound site, thus accelerating the healing process in the DFU. For its strong overall performance, Reapplix is recognized with Frost & Sullivan's 2023 North American Technology Innovation Leadership Award in the chronic wound treatment for patients with diabetes industry.

# What You Need to Know about the Technology Innovation Leadership Recognition

Frost & Sullivan's Technology Innovation Leadership Award recognizes the company that has introduced the best underlying technology for achieving remarkable product and customer success while driving future business value.

## Best Practices Award Analysis

For the Technology Innovation Leadership Award, Frost & Sullivan analysts independently evaluated the criteria listed below.

### *Technology Leverage*

**Commitment to Innovation**: Continuous emerging technology adoption and creation enables new product development and enhances product performance

**Commitment to Creativity**: Company leverages technology advancements to push the limits of form and function in the pursuit of white space innovation

**Stage Gate Efficiency**: Technology adoption enhances the stage gate process for launching new products and solutions

**Commercialization Success**: Company displays a proven track record of taking new technologies to market with a high success rate

**Application Diversity**: Company develops and/or integrates technology that serves multiple applications and multiple environments

### *Business Impact*

**Financial Performance**: Strong overall financial performance is achieved in terms of revenues, revenue growth, operating margin, and other key financial metrics

**Customer Acquisition**: Customer-facing processes support efficient and consistent new customer acquisition while enhancing customer retention

**Operational Efficiency**: Company staff performs assigned tasks productively, quickly, and to a high-quality standard

**Growth Potential**: Growth is fostered by a strong customer focus that strengthens the brand and reinforces customer loyalty

**Human Capital**: Commitment to quality and to customers characterize the company culture, which in turn enhances employee morale and retention

## About Frost & Sullivan

Frost & Sullivan is the Growth Pipeline Company™. We power our clients to a future shaped by growth. Our Growth Pipeline as a Service™ provides the CEO and the CEO's growth team with a continuous and rigorous platform of growth opportunities, ensuring long-term success. To achieve positive outcomes, our team leverages over 60 years of experience, coaching organizations of all types and sizes across 6 continents with our proven best practices. To power your Growth Pipeline future, visit Frost & Sullivan at http://www.frost.com.

### The Growth Pipeline Engine™

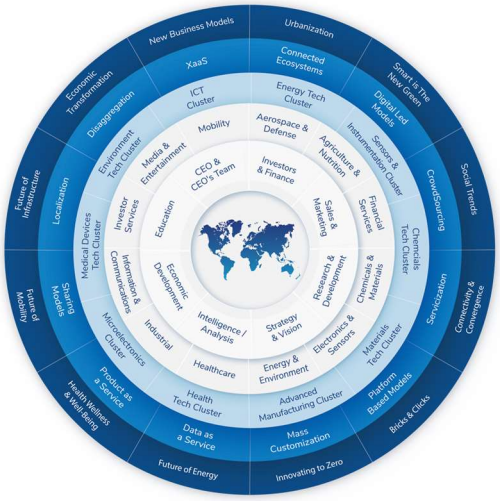
Frost & Sullivan's proprietary model to systematically create ongoing growth opportunities and strategies for our clients is fuelled by the Innovation Generator™.
Learn more.


***Key Impacts***:

- **Growth Pipeline:** *Continuous Flow of Growth Opportunities*
- **Growth Strategies:** *Proven Best Practices*
- **Innovation Culture:** *Optimized Customer Experience*
- **ROI & Margin:** *Implementation Excellence*
- **Transformational Growth:** *Industry Leadership*

### The Innovation Generator™

Our 6 analytical perspectives are crucial in capturing the broadest range of innovative growth opportunities, most of which occur at the points of these perspectives.




### *Analytical Perspectives:*

- Mega Trend (MT)
- Business Model (BM)
- Technology (TE)
- Industries (IN)
- Customer (CU)
- Geographies (GE)