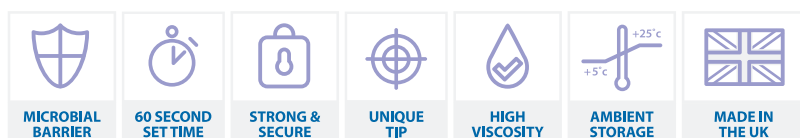




LiquiBand® Exceed™ XS

WE'VE DRAWN THE LINE FOR AN EVEN
CONSISTENT WOUND COVERAGE



✓ NO CLOG TECHNOLOGY

- ▶ Tip will not clog, allowing consistent flow of adhesive
- ▶ 0.4mL of adhesive per applicator delivers approximately 7cm of coverage

✓ PURE OCTYL FORMULATION

- ▶ Maximises durability and flexibility
- ▶ Provides high viscosity
- ▶ Creates intimate skin contact



✓ UNIQUE APPLICATOR TIP

- ▶ Elliptical shape allows for narrow or wide application
- ▶ Porous felt tip allows drip-free priming and even, consistent application

✓ EASY TO USE APPLICATOR

- ▶ Winged applicator allows for safe and easy activation
- ▶ Provides controlled delivery of adhesive

LiquiBand® Exceed™ Range

Offers the improved attributes of precision and controlled delivery with added advantages of our innovative tip design.

LiquiBand® Exceed™ XS

- ▶ 7cm Yield
- ▶ No clog tip
- ▶ Ideal for small incisions, laparoscopic port sites



LiquiBand® Exceed™

- ▶ 30cm Yield
- ▶ 90mins intraoperative reuse
- ▶ Ideal for medium to long surgical incisions



Key Benefits

- ✓ **High Viscosity**³
 - ▶ Provides optimal flexibility
- ✓ **Controlled Expression of Adhesive**⁴
 - ▶ Applicator offers control during expression of adhesive
- ✓ **Microbial Barrier**⁵
 - ▶ Acts as a barrier against gram-positive, gram-negative and fungal microbes. Proven effectiveness against S. aureus, Paeruginosa, E.coli, Candida albicans and MRSA
- ✓ **No Clog Formulation**⁶
 - ▶ Allows users to work at their own pace
 - ▶ The adhesive will remain in-tact throughout the wound healing process
- ✓ **Maintains wound closure throughout healing process**⁷
 - ▶ The adhesive will stay on the skin for 5-10 days and sloughs off naturally



Giving protection against:

Gram Positive Bacteria	Gram Negative Bacteria	Fungi
<ul style="list-style-type: none">▶ S. Epidermidis▶ S. Aureus & MRSA	<ul style="list-style-type: none">▶ Ps. Aeruginosa▶ E. Coli▶ E. Cloacae	<ul style="list-style-type: none">▶ Asp. Brasiliensis (niger)▶ C. Albicans

LiquiBand® Exceed™ XS

Size	Qty Per Box	Product Code
0.4g	6	72014020*

LiquiBand® Exceed™

Size	Qty Per Box	Product Code
0.8g	6	72014002*

*References available in our stock at REY Médical SA

References 1-77. Data on file at Advanced Medical Solutions (Plymouth) Ltd. 7: Dawson CC, A prospective, randomized controlled trial comparing n-butyl cyanoacrylate tissue adhesive (LiquiBand) with sutures for skin closure after laparoscopic general surgical procedures. Surg Laparosc Endosc Percutan Tech. 2006 Jun;16(3):146-50. 8: Gorozpe-Calvillo JJ, Closure of the skin with cyanoacrylate in cesarean section. Ginecol Obstet Mex. 1999 Oct;67:491-6. IRM 06 0296

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LiquiBand[®]Exceed[™]

**THE MICROBIAL BARRIER EFFECTIVENESS
OF LIQUIBAND[®]EXCEED[™]**

J Alarcon, BSc (Hons), CCRA
G Miller, BSc (Hons)



LiquiBand® Exceed™ Topical Skin Adhesive

Microbial Barrier Effectiveness

Background

Cyanoacrylate Topical Skin Adhesives (TSA) continue to gain acceptance as effective alternatives to conventional suture and staple closures in a wide variety of medical applications. LiquiBand® Exceed™, a new 2-octyl-cyanoacrylate adhesive device, has recently gained regulatory approval for topical wound closure. This device features a unique, winged applicator that along with a novel elliptical felt tip, provides broad and even application of adhesive to the wound site. The LiquiBand® Exceed™ Topical Skin Adhesive has been demonstrated to retain flexibility without cracking when subjected to standardized test methodology for determining adhesive film flexibility* on pig skin substrate *ex vivo*. Along with strength and flexibility of closure and cosmetic outcome, effectiveness of microbial barrier is also an important clinical requirement requiring review. Microbial contamination of wound sites often results in surgical site infection (SSI) that are reported following 10-20% of all surgical procedures. Approximately 157,500 cases of SSI were reported in US acute-care hospitals in 2011 resulting in an estimated cost of treatment for each case ranging between USD\$10,000 - \$25,000. Preventive strategies, such as providing an effective barrier to infection, may help alleviate this considerable strain to healthcare resources. In this study, the barrier properties of LiquiBand® Exceed™ Topical Skin Adhesive are evaluated *in vitro* against various pathogenic gram positive, gram negative, yeast, and mold organisms commonly implicated in surgical site infections (SSI), including antibiotic resistant MRSA (*S. aureus*).

Objective

To determine the effectiveness of an intact film of LiquiBand® Exceed™ Topical Skin Adhesive as a microbial barrier to *in vitro* challenge from a variety of pathogenic bacteria, yeast and mold species.

Methodology

Testing was performed using industry standard methodology for determining barrier properties of cyanoacrylate films against microorganisms. A single layer of LiquiBand® Exceed™ Topical Skin Adhesive was applied, in accordance with manufacturer's instructions for use, to nutrient-rich agar plates, impregnated with a color indicator that respond to microbial colonization. Eight different pathogenic bacteria, yeast and mold species ($1-2 \times 10^6$ CFU) were applied directly on top of the cyanoacrylate film, and then incubated for 7 days at 30-35°C. One hundred plates were tested per species for a total of 800 inoculations. Plates were visually inspected at day three and day seven, and the adhesive barrier was deemed to remain intact when the underlying agar media remained unchanged in color, as compared to a negative control.

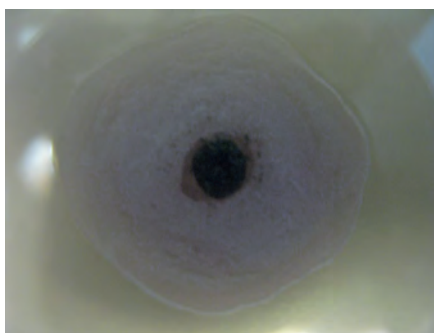


Figure 1: Image of a test plate following inoculation.

Results

LiquiBand® Exceed™ Topical Skin Adhesive was found to maintain an effective barrier for three days, preventing contamination of underlying agar in 99.5% total plates assessed (Figure 1). Specifically, 100% of plates inoculated with *E. coli*, *S. aureus* spp. and *Asp. brasiliensis* remained uncontaminated, as did 99% of plates inoculated with the other four species tested. At seven days post-inoculation, the LiquiBand® Exceed™ Topical Skin Adhesive film continued to provide an effective barrier in 100% of plates inoculated with both *S. aureus* species, including MRSA and was found to provide an effective barrier for seven days post bacterial challenge in 97.9% of all tests conducted (Table 1).

			% maintaining microbial barrier (n = 100 tests)	
Organism	ATCC#	Challenge CFU	Day 3	Day 7
<i>C. al cans</i>	10231	1.245 x 10 ⁶	99	99
<i>E. coli</i>	8739	1.275 x 10 ⁶	100	95
<i>S. reus (MRSA)</i>	43300	1.210 x 10 ⁶	100	100
<i>S. reus</i>	6538	1.095 x 10 ⁶	100	100
<i>S. epidermid</i>	12228	1.250 x 10 ⁶	99	95
<i>Ps. aeruginosa</i>	9027	1.975 x 10 ⁶	99	97
<i>E. clo cae</i>	13407	1.450 x 10 ⁶	99	98
<i>Asp. brasiliensis</i>	16404	1.250 x 10 ⁶	100	99
% maintaining microbial barrier (n = 800 tests)			99.5	97.9

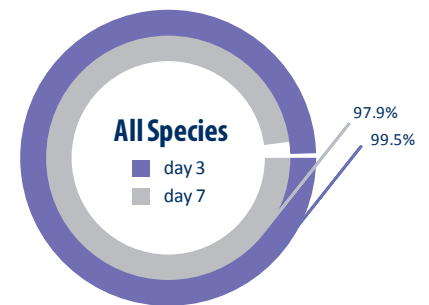


Table 1: Details of test methods and percentage of agar plates coated with cyanoacrylate ÿlm applied by LiquiBand® Exceed™ Topical Skin Adhesive maintaining barrier to various pathogenic microorganism species 3 to 7 days post challenge. The ÿgure on the right of the table represents percent of barrier maintained against all species.

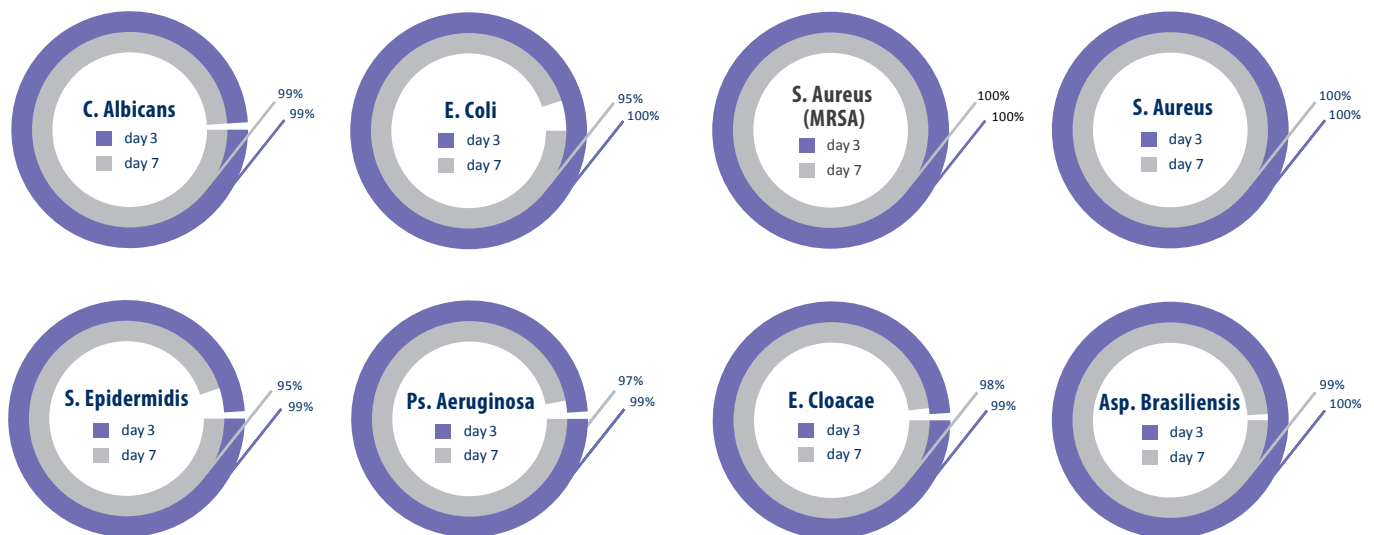


Figure 2: Percentage of agar plates coated with cyanoacrylate ÿlm applied by LiquiBand® Exceed™ Topical Skin Adhesive maintaining barrier to various pathogenic microorganism species 3 to 7 days post challenge.

Conclusions

In this in vitro evaluation, LiquiBand® Exceed™ Topical Skin Adhesive provided an e~ effective barrier to contamination, despite challenge from high concentrations of pathogenic bacteria, yeast and mold species. As previously mentioned, microbial contamination of the wound site can result in SSI.~ The adhesive barrier was found to be robust, with 99.5% of the test plates uncontaminated three days post inoculation and 97.9% uncontaminated seven days post inoculation by eight di~ erent pathogenic microorganism species. Previous clinical studies have demonstrated that within 48-72 hours of wound closure, the natural wound healing cycle results in an e~ effective microbial barrier.^{5,6} A wound closure device that provides an e~ effective barrier for up to 72 hours would provide sufficient time to allow for the natural wound healing process. Ideally, the wound closure device would resist cracking from wound site ÿe xion, as previously demonstrated following ASTM testing of LiquiBand® Exceed™ Topical Skin Adhesive.~ Overall, these results demonstrate the potential for LiquiBand® Exceed™ Topical Skin Adhesive to provide a ÿe xible and robust wound closure, and an e~ effective barrier to microorganism contamination.

References:

1. Data on File at Advanced Medical Solutions (Plymouth) Ltd.
2. Leaper D, Ousey K. Evidence update on prevention of surgical site infection. Curr Opin Infect Dis. 2015 Feb 17.
3. Magill SS, Edwards JR, Bamberg W, et al. Multistate Point-Prevalence Survey of Health Care–Associated Infections. N Engl J Med 2014;370:1198-208.
4. Scott RD II. The Direct Medical costs of Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention. Centers for Disease Control and Prevention. March 2009.
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*ASTM D4338-97: Flexibility Determination of Supported Adhesive Films by Mandrel Bend (2011)

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LiquiBand® Exceed™

WE'VE DRAWN THE LINE FOR AN EVEN CONSISTENT WOUND COVERAGE

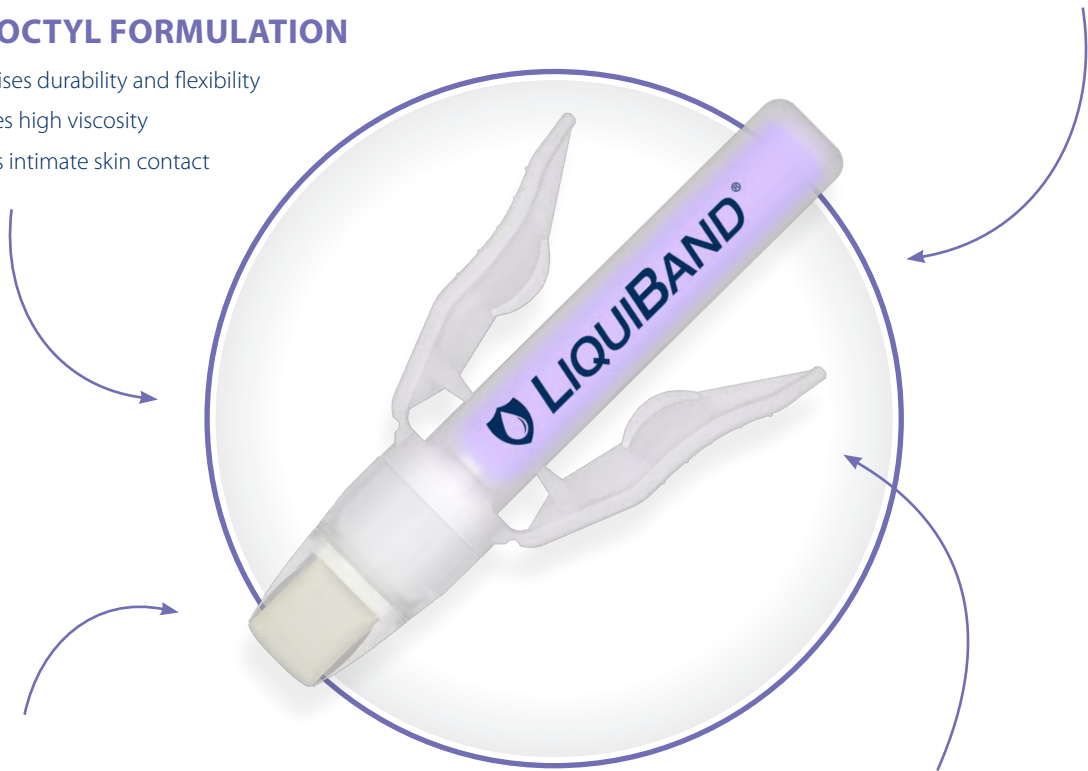


✓ MARKET LEADING YIELD

- ▶ 0.8ml per applicator allows for closure of wounds up to 30cm in length
- ▶ No clog technology allows intraoperative reuse for up to 90 minutes on a single patient

✓ PURE OCTYL FORMULATION

- ▶ Maximises durability and flexibility
- ▶ Provides high viscosity
- ▶ Creates intimate skin contact



✓ UNIQUE APPLICATOR TIP

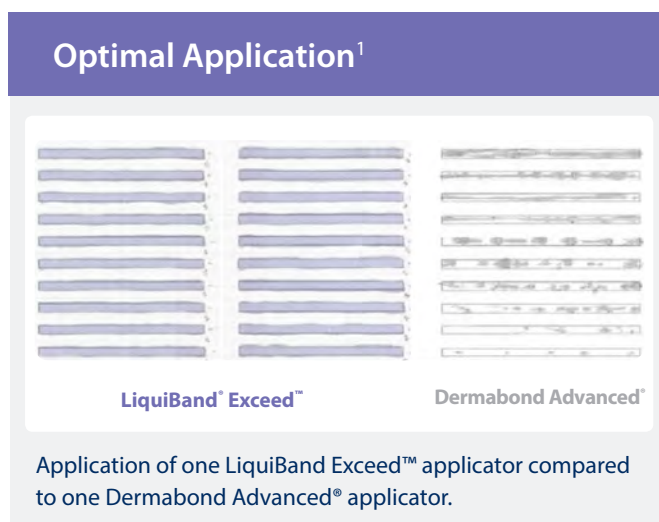
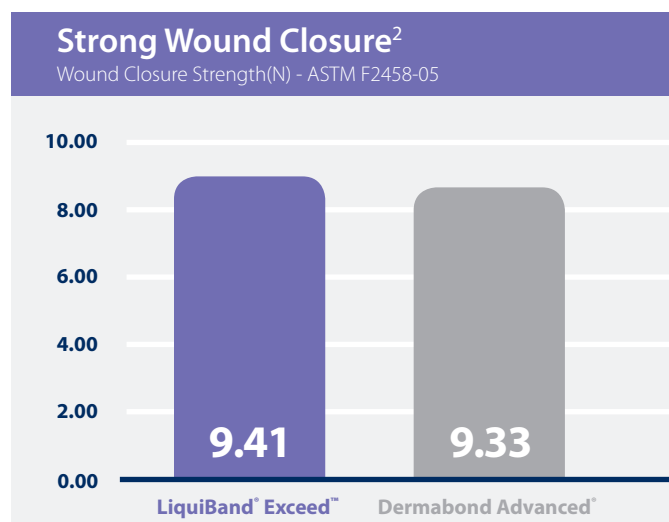
- ▶ Elliptical shape allows for narrow or wide application
- ▶ Porous felt tip allows drip-free priming and even, consistent application

✓ EASY TO USE APPLICATOR

- ▶ Winged applicator allows for safe and easy activation
- ▶ Provides controlled delivery of adhesive

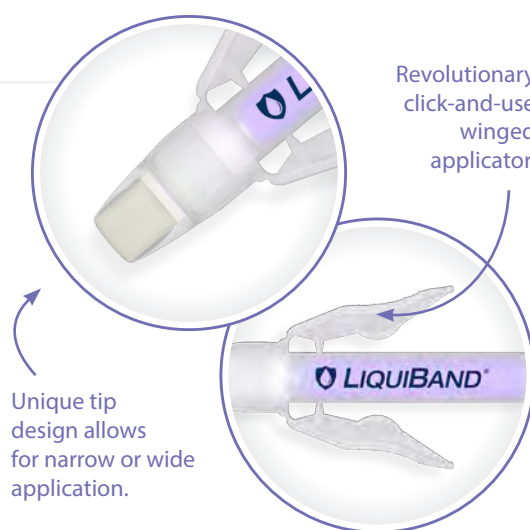
LiquiBand® Exceed™

Offers the improved attributes of precision and controlled delivery with added advantages of a new tip design.



Key Benefits

- ✓ **High Viscosity³**
 - ▶ Provides optimal flexibility
- ✓ **Controlled Expression of Adhesive⁴**
 - ▶ Applicator offers control during expression of adhesive
- ✓ **Microbial Barrier⁵**
 - ▶ Acts as a barrier against gram-positive, gram-negative and fungal microbes. Proven effectiveness against S. aureus, Paeruginosa, E.coli, Candida albicans and MRSA
- ✓ **Better Yield of Adhesive⁶**
 - ▶ 0.8 mL volume allows for greater wound coverage, up to 30cm, making it more cost effective
 - ▶ Intraoperative reuse for up to 90 minutes on a single patient
- ✓ **Maintains wound closure throughout healing process⁷**
 - ▶ The adhesive will stay on the skin for 5-10 days and sloughs off naturally



LiquiBand® Exceed™

Size	Qty Per Box	Product Code
0.8g	6	72014002

References 1-7. Data on file at Advanced Medical Solutions (Plymouth) Ltd.
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LiquiBand[®] Exceed[™]

TOPICAL SKIN ADHESIVE SUMMARY OF EFFECTIVENESS DATA

J Alarcon, BSc (Hons), CCRA
G Miller, BSc (Hons)



LiquiBand® Exceed™ Topical Skin Adhesive

Summary of Effectiveness Data

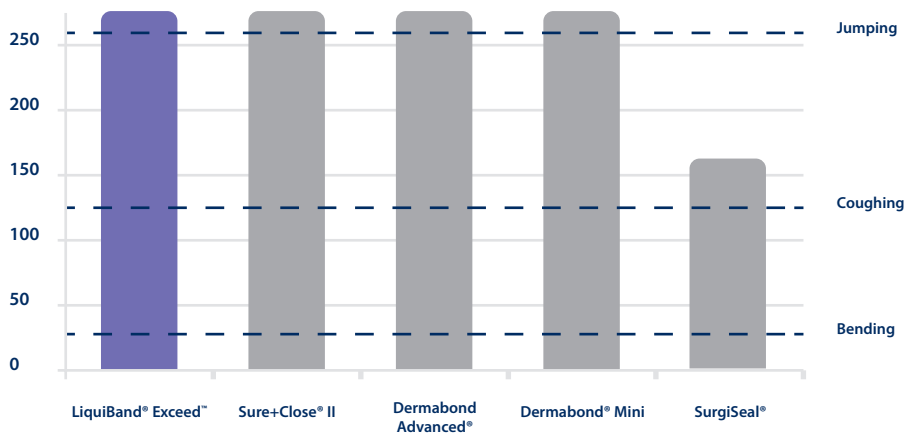
Introducing LiquiBand® Exceed™, A Next Generation 2-Octyl Cyanoacrylate Topical Skin Adhesive

Cyanoacrylate adhesives have been extensively evaluated as alternatives to conventional topical wound closure devices such as sutures and staples. Cyanoacrylates provide strong wound closure with good cosmetic outcomes and speed of use which is why they have become commonplace for medical applications. Recent studies have found the microbial barrier properties of cyanoacrylates protects wounds from microbial contamination.^{1,2}

LiquiBand®Exceed™, a next generation 2-octyl-cyanoacrylate adhesive device developed by Advanced Medical Solutions (Plymouth) Ltd. has recently gained regulatory approval for topical wound closure. Here we present results following extensive testing of LiquiBand® Exceed™ by *in vitro* laboratory assessments and *in vivo* skin model evaluations. These assessments include evaluating the strength and flexibility of topical wound closure, ease of use and barrier properties to microbial contamination.

- ▶ High Wound Burst Strength
- ▶ Low Weight of Adhesive per Centimeter of Wound Coverage
- ▶ Flexible and Water Resistant Wound Closure
- ▶ Controlled Application of Adhesive
- ▶ Safe and Effective Wound Closure
- ▶ Low Exothermic Reaction
- ▶ Effective Barrier to Microbial Contamination

Proven Strength Provides Confidence In Wound Closure...



In a porcine wound model study comparing topical wound closure by commercially available medical adhesives³, LiquiBand® Exceed™ withstood pressures experienced from common activities such as bending (30mmHg), coughing (127mmHg) and jumping (252mmHg) (chart 1).⁴

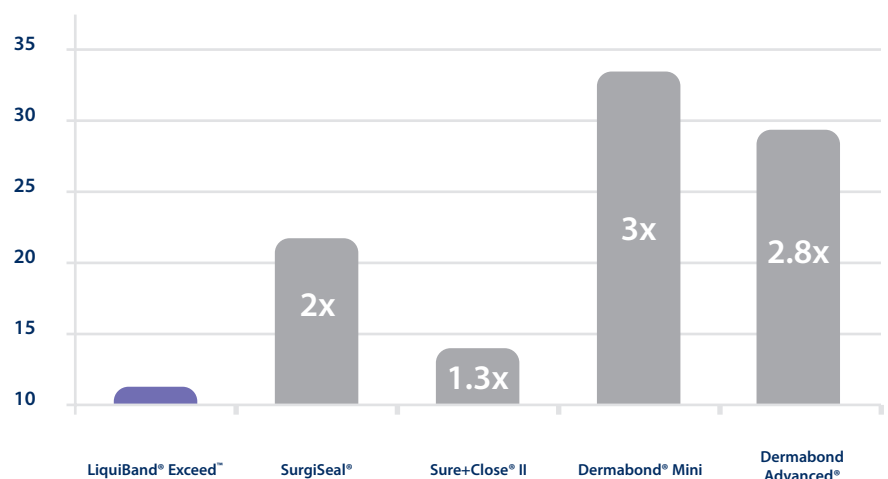
Chart 1: Two centimeter incisions closed by various commercially available adhesives were subjected to increasing pressure (mmHg) using a biomechanical test system (BTC- 2000™, Surgical Research Laboratory Inc.).

...While Using Less Adhesive

Only 10µg of LiquiBand® Exceed™ adhesive were required to confidently close each cm of wound, up to three times less than comparative devices.³ One device can be used for topical closure of wounds up to 30cm (chart 2).³

Additional standardized strength testing (ASTM F2255-05, F2458-05, F2256-05) demonstrated similar tensile, lap-shear and t-peel strength as Dermabond Advanced®.³

Chart 2: Devices were weighed before and after application as per manufacturer's instructions to determine amount of adhesive used (µg) per cm of wound length.



A Safety Profile That Offers Peace Of Mind

Extensive standardized biocompatibility testing (ISO 10993: biological evaluation of medical devices) demonstrates that LiquiBand® Exceed™ is non skin-sensitizing and non toxic.³ *In vivo* wound model (porcine) testing and *ex vivo* histological analysis demonstrates that topical wound closure with LiquiBand® Exceed™ does not interfere with the natural wound healing process or adversely affect intact skin.³

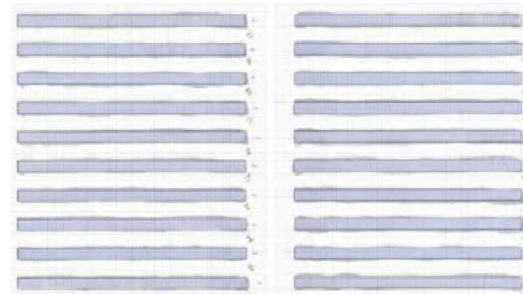
A Device Designed For Controlled Application Of Adhesive

Laboratory testing³ demonstrated that the novel broad felt tip design and winged applicator body of LiquiBand® Exceed™:

- ▶ Optimizes coverage & yield of adhesive,
- ▶ Helps to avoid stuttering and
- ▶ Provides consistent coat weight compared to Dermabond Advanced®

LiquiBand® Exceed™ was able to be applied consistently in an even layer across more than two times the area compared to Dermabond Advanced® (Figure 1).

LiquiBand® Exceed™



Dermabond® Advanced



Figure 1: An example of application of one LiquiBand® Exceed™ applicator compared to one Dermabond Advanced® applicator.

Additionally, LiquiBand® Exceed™ has been designed to be easy to activate and apply adhesive, without dripping or squirting.³

Formulated For Low Heat On Application

With only a 0.34°C measured increase in temperature during the polymerization reaction, LiquiBand® Exceed™ adhesive avoids the burning sensation commonly experienced following application of other topical skin adhesive wound closure devices.³

Effective Barrier To Microbial Contamination

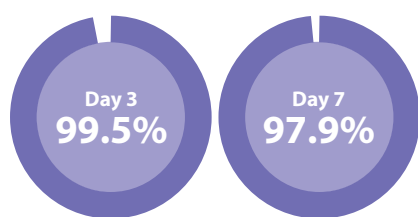


Figure 2: Percentage of agar plates layered with LiquiBand® Exceed™ that remained uncontaminated following 3 and 7 days incubation with 8 different pathogenic micro-organism species.¹

Standardized testing of microbial barrier properties found LiquiBand® Exceed™ to provide:

- ▶ Protection against 8 different species of pathogenic fungi (*C. albicans*, *Asp. brasiliensis*), and bacteria species (*E. coli*, *S. aureus*, *S. epidermidis*, *Ps aeruginosa*, *E. cloacae*), including MRSA, commonly implicated in SSI (Surgical Site Infections) as long as the adhesive film remains intact³
- ▶ Once polymerized, LiquiBand® Exceed™ provides an instant barrier to contamination, allowing for the innate process of wound healing previously shown to generate a natural microbial barrier at 48- 72hrs post wound closure^{5,6}

Flexible And Water Resistant Wound Closure

When subjected to standardized testing for flexibility (ASTM D4338-97), LiquiBand® Exceed™ was found to be as flexible as Dermabond Advanced® without cracking or blushing following flexion.³

Light showering does not affect wound closure strength of LiquiBand® Exceed™ as evaluated following standardized strength testing (ASTM F2458-05).³

Conclusion

LiquiBand® Exceed™, a regulatory approved 2-octyl cyanoacrylate adhesive, was subjected to multiple testing methodologies for the topical closure of wounds. LiquiBand® Exceed™ adhesive was found to have high tensile strength in standardized ASTM testing and also in a wound simulation model where wounds closed with LiquiBand® Exceed™ adhesive withstood pressures experienced from everyday activities including jumping, coughing and bending. While this strength of wound closure was found to be similar to other wound closure devices, LiquiBand® Exceed™ required up to three times less volume of adhesive to close the same length of wound as Dermabond Advanced®. Only one LiquiBand® Exceed™ device was required to close wounds up to 30cm in length.

Additionally, the broad tip applicator and winged design of LiquiBand® Exceed™ was found to provide users with controlled and consistent application of adhesive.

Standardized safety testing found that LiquiBand® Exceed™ adhesive is non-toxic or skin-sensitizing, which was also demonstrated following *ex vivo* histological analysis of wounds closed with the adhesive.

While strong and durable closure and ease of use are primary requirements for topical adhesives, protecting wounds from microbial contamination may prevent potential SSI. LiquiBand® Exceed™ was demonstrated to be an effective barrier to high titre challenge from 8 different pathogenic microbial species including MRSA, commonly implicated in SSI.

These results demonstrate that LiquiBand® Exceed™ is a proven choice for strong and durable topical wound closure that protects against microbial contamination and provides users with control and precision of application.



References:

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Application Guide **LiquiBand® Exceed™**

LiquiBand® Exceed™ Topical Skin Adhesive has a unique, felt applicator tip to facilitate even, consistent application in three simple steps.

✓ STEP ONE

- ▶ While holding upright, squeeze the applicator wings until a cracking sound is heard.



✓ STEP TWO

- ▶ Invert the tip and gently squeeze wings to prime the device. When the tip turns violet, LiquiBand® Exceed™ XS is ready to use.
- ▶ Ensure that wound is thoroughly clean and dry prior to closure.



✓ STEP THREE

- ▶ While holding the wound edges together, apply an even coat of LiquiBand® Exceed™ XS over the length of the wound.
- ▶ Continue to hold the wound edges together for 60 seconds.



i If using on the eye area, adjust the patient's position. Use petroleum jelly to create a barrier close to the wound, and use surgical gauze to protect the patient's eyes.

References 1-7. Data on file at Advanced Medical Solutions (Plymouth) Ltd. IRM 06 0251

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