Summary of Effectiveness Results Comparing Low Viscosity DERMABOND® Adhesive to Sutures (U.S.P. size 5-0 and Ethicon Prolene) Staples, and Mechanical Closure

Clinical Study Outcomes	***NSS*** DERMABOND® Adhesive N (%)	Control N (%)	***WSS*** DERMABOND® Adhesive N (%)	Control N (%)
Accounting				
N, patients enrolled	240	243	167	168
N, patients treated	239	242	167	166
Patients completed	228 (95%)	215 (88%)	164 (98%)	162 (96%)
N, control: sutures/strips/staples/ missing		194/46/1/1		116/45/5/0
Wound Closure Assessment				
Immediate: Additional Devices	18 (7.5%)	13 (5.4%)	2 (1.2%)	11 (6.6%)
@ 5-10 days: 100% epidermal apposition	169 (75.1%)	199 (88.8%)	140 (84.3%)	160 (96.4%)
>50% epidermal apposition	205 (91.1%)	214 (95.5%)	163 (98.2%)	165 (99.4%)
@ 3 months: Cosmesis Score*= 0 (optimal)	188 (82.5%)	180 (83.7%)	128 (78.0%)	128 (79.0%)
Median Time for Treatment (Minutes)	1.5	6.0	1.3	2.9

*** Cosmesis: Modified Hollander Cosmesis Scale**

The study population included patients at least one year of age, in good general health, who signed informed consent and agreed to follow-up visits. Patients were excluded if presenting with: significant multiple trauma, peripheral vascular disease, insulin dependent diabetes mellitus, blood clotting disorder, keloid formation or hypertrophy history (patient or family), cyanoacrylate or formaldehyde allergy, burst or stellate lacerations due to crush or hard blow, animal or human bite, and decubitus ulcer.

Follow-up was at 5-10 days and at 3 months. All wounds were assessed by visual inspection at 5-10 days after wound closure. The total kinds of wounds treated in the study were 46.1% lacerations and 53.9% incisions. The incisions were comprised of 47.8% excisions of skin lesions, 27.4% minimally invasive surgery punctures, and 24.8% general surgery incisions.

For wounds closed without subcuticular stitches, mean wound length was 1.5 cm, mean wound width was 2.5 mm, and mean wound depth was 5.8 mm. For wounds closed with subcuticular stitches, mean wound length was 3.2 cm, mean wound width was 5.3 mm, and mean wound depth was 3.8 mm.

If the primary method of closure was insufficient for closure, an additional securing device was placed. The time to perform treatment included the time required later to remove the closure device when applicable.

The Modified Hollander Cosmesis Scale (MHCS), a validated scale, was used to evaluate cosmesis at three months: step-off borders, edge inversion, contour irregularities, excess inflammation, wound margin separation, and overall appearance.

DIRECTIONS FOR USE

1. The application of high viscosity DERMABOND® Adhesive requires thorough wound cleansing. Follow standard surgical practice for wound preparation before application of high viscosity DERMABOND® Adhesive (i.e., anesthetize, irrigate, debride, obtain hemostasis, and close deep layers).
2. Pat the wound dry with dry, sterile gauze to ensure direct tissue contact for adherence of the high viscosity DERMABOND® Adhesive to the skin. Moisture accelerates high viscosity DERMABOND® Adhesive's polymerization and may affect wound closure results.
3. To prevent inadvertent flow of liquid high viscosity DERMABOND® Adhesive to unintended areas of the body, the wound should be held in a horizontal position and the high viscosity DERMABOND® Adhesive should be applied from above the wound.
4. High viscosity DERMABOND® Adhesive should be used immediately after crushing the glass ampule, since the liquid high viscosity DERMABOND® Adhesive will flow freely from the tip for only a few minutes. Remove the applicator from the blister pouch. If using the pen applicator, refer to the instructions on the pouch for crushing the glass ampule and expressing the liquid adhesive. If using the plastic vial, hold the applicator with the thumb and a finger and away from the patient to prevent any unintentional placement of the liquid high viscosity DERMABOND® Adhesive into the wound or on the patient. While holding the applicator, and with applicator tip pointed upward, apply pressure at the midpoint of the ampule to crush the inner glass ampule. Invert and gently squeeze the applicator just sufficiently to express the liquid high viscosity DERMABOND® Adhesive to moisten the applicator tip.
5. Approximate wound edges with gloved fingers or sterile forceps. Slowly apply the liquid high viscosity DERMABOND® Adhesive in multiple (at least two) thin layers to the surface of the approximated wound edges using a gentle brushing motion. Wait approximately 30 seconds between applications or layers. Maintain manual approximation of the wound edges for approximately 60 seconds after the final layer.

   NOTE: High viscosity DERMABOND® Adhesive polymerizes through an exothermic reaction. If the liquid high viscosity DERMABOND® Adhesive is applied so that large droplets are allowed to remain without being evenly spread, the patient may experience a sensation of heat or discomfort. The sensation may be higher on sensitive tissues. This can be minimized by applying high viscosity DERMABOND® Adhesive in multiple thin layers (at least two).

   NOTE: Excessive pressure of the applicator tip against the wound edges or surrounding skin can result in forcing the wound edges apart and allowing high viscosity DERMABOND® Adhesive into the wound. High viscosity DERMABOND® Adhesive within the wound could delay wound healing and/or result in adverse cosmetic outcome.

   NOTE: Full apposition strength is expected to be achieved about 2.5 minutes after the final layer is applied, although the top adhesive layer may remain tacky for up to approximately 5 minutes. Full polymerization is expected when the top high viscosity DERMABOND® Adhesive layer is no longer sticky.

6. Do not apply liquid or ointment medications onto wounds closed with high viscosity DERMABOND® Adhesive because these substances can weaken the polymerized film, leading to dehiscence (skin edge separation).
7. Protective dry dressings such as gauze, may be applied only after high viscosity DERMABOND® Adhesive film is completely solid/polymerized: not tacky to the touch (approximately five minutes after application). Allow the top layer to fully polymerize before applying a bandage.

   If a dressing, bandage, adhesive backing or tape is applied before complete polymerization, the dressing can adhere to the film. The film can be disrupted from the skin when the dressing is removed, and dehiscence (skin edge separation) can occur.
8. Patients should be instructed to not pick at the polymerized film of high viscosity DERMABOND® Adhesive. Picking at the film can disrupt its adhesion to the skin and cause dehiscence (skin edge separation). Picking at the film can be discouraged by an overlying dressing.
9. Apply a dry protective dressing for children or other patients who may not be able to follow instructions for proper wound care.
10. Patients treated with high viscosity DERMABOND® Adhesive should be provided the printed instruction sheet entitled, "How to Care for Your Wound After It's Treated With High Viscosity DERMABOND® Adhesive". This instruction sheet should be reviewed with each patient or guardian to ensure understanding of the proper care for the treatment site.
11. Patients should be instructed that until the polymerized film of high viscosity DERMABOND® Adhesive has sloughed naturally (usually in 5-10 days), there should be only transient wetting of the treatment site. Patients may shower and bathe the site gently. The site should not be scrubbed, soaked, or exposed to prolonged wetness until after the film has sloughed naturally and the wound has healed closed. Patients should be instructed not to go swimming during this period.
12. If removal of high viscosity DERMABOND® Adhesive is necessary for any reason, carefully apply petroleum jelly or acetone to the high viscosity DERMABOND® Adhesive film to help loosen the bond. Peel off the film, do not pull the skin apart.

HOW SUPPLIED

High viscosity DERMABOND® Adhesive is supplied sterile, in a pre-filled, single-use applicator. The applicator is composed of a crushable glass ampule contained within a plastic vial with attached applicator tip. The applicator contains the liquid adhesive. The applicator is packaged in a blister pouch to maintain the device sterile until opened or damaged.

High viscosity DERMABOND® Mini is available in boxes of 12 applicators.

STORAGE

Recommended storage conditions: below 30°C, 86°F, away from moisture, direct heat, and direct light. Do not use after expiry date.

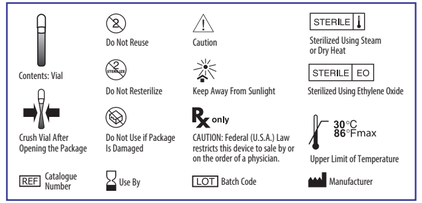
STERILITY

High viscosity DERMABOND® Adhesive is originally sterilized by dry heat and ethylene oxide gas. Do not resterilize. Do not use if package is opened or damaged. Discard any unused material following completion of medical procedure.

STERILE SINGLE USE ONLY

CAUTION

Federal (U.S.A.) Law restricts this device to sale by or on the order of a physician.



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DERMABOND® Mini

TOPICAL SKIN ADHESIVE

2-Octyl Cyanoacrylate

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DERMABOND® Mini

TOPICAL SKIN ADHESIVE

DESCRIPTION

High viscosity DERMABOND® Topical Skin Adhesive is a sterile, liquid topical skin adhesive containing a monomeric (2-octyl cyanoacrylate) formulation and the colorant D & C Violet #2. It is provided in a single-use applicator packaged in a blister pouch. The applicator is composed of a crushable glass ampule contained within a plastic vial with attached applicator tip. As applied to skin, the liquid is syrup-like in viscosity and polymerizes within minutes. *In vitro* studies have shown that high viscosity DERMABOND® Adhesive acts as a barrier to microbial penetration as long as the adhesive film remains intact. Clinical studies were not conducted to demonstrate microbial barrier properties.

High viscosity DERMABOND® Adhesive is different from the regular, or low viscosity DERMABOND® Adhesive due to the increased viscosity of the liquid adhesive formulation. Low viscosity DERMABOND® Adhesive has a viscosity slightly greater than water, while high viscosity DERMABOND® Adhesive has a syrup-like viscosity. The increased viscosity of high viscosity DERMABOND® Adhesive is intended to reduce the risk of unintended placement of the adhesive during application due to migration of the liquid adhesive from the wound site.

INDICATIONS

High viscosity DERMABOND® Adhesive is intended for topical application only to hold closed easily approximated skin edges of wounds from surgical incisions, including punctures from minimally invasive surgery, and simple, thoroughly cleansed, trauma-induced lacerations. High viscosity DERMABOND® Adhesive may be used in conjunction with, but not in place of, deep dermal stitches.

CONTRAINDICATIONS

- Do not use on any wound with evidence of active infection, gangrene, or wounds of decubitus etiology.
- Do not use on mucosal surfaces or across mucocutaneous junctions (e.g., oral cavity, lips), or on skin which may be regularly exposed to body fluids or with dense natural hair (e.g., scalp).
- Do not use on patients with a known hypersensitivity to cyanoacrylate, formaldehyde, or benzalkonium chloride.

WARNINGS

- High viscosity DERMABOND® Adhesive is a fast setting adhesive capable of adhering to most body tissue and many other materials, such as latex gloves and stainless steel. Inadvertent contact with any body tissue, and any surfaces or equipment that are not disposable or that cannot be readily cleaned with a solvent such as acetone should be avoided.
- Polymerization of high viscosity DERMABOND® Adhesive may be accelerated by water or fluids containing alcohol. High viscosity DERMABOND® Adhesive should not be applied to wet wounds.
- High viscosity DERMABOND® Adhesive should not be applied to the eye. If contact with the eye occurs, flush the eye copiously with saline or water. If residual adhesive remains, apply topical ophthalmic ointment to help loosen the bond and contact an ophthalmologist.
- When closing facial wounds near the eye with high viscosity DERMABOND® Adhesive, position the patient so that any run-off of adhesive is away from the eye. The eye should be closed and protected with gauze. Prophylactic placement of petroleum jelly around the eye, to act as a mechanical barrier or dam, can be effective in preventing inadvertent flow of adhesive into the eye. High viscosity DERMABOND® Adhesive will not adhere to skin pre-coated with petroleum jelly. Therefore, avoid using petroleum jelly on any skin area where high viscosity DERMABOND® Adhesive is intended to adhere. Use of DERMABOND® Adhesive near the eye has inadvertently caused some patients' eyelids to be sealed shut. In some of these cases, general anesthesia and surgical removal has been required to open the eyelid.
- High viscosity DERMABOND® Adhesive should not be used below the skin because the polymerized material is not absorbed by tissue and can elicit a foreign body reaction.
- High viscosity DERMABOND® Adhesive should not be used in high skin tension areas or across areas of increased skin tension, such as knuckles, elbows, or knees, unless the joint will be immobilized during the skin healing period or unless skin tension has been removed by application of another wound closure device (e.g., sutures or skin staples) prior to application of high viscosity DERMABOND® Adhesive.
- High viscosity DERMABOND® Adhesive treated wounds should be monitored for signs of infection. Wounds with signs of infection, such as erythema, edema, warmth, pain and pus, should be evaluated and treated according to standard practice for infection.
- High viscosity DERMABOND® Adhesive should not be used on wound sites that will be subjected to repeated or prolonged moisture or friction.
- High viscosity DERMABOND® Adhesive should only be used after wounds have been cleaned, debrided and are otherwise closed in accordance with standard surgical practice. Local anesthetic should be used when necessary to ensure adequate cleansing and debridement.
- Excessive pressure of the applicator tip against wound edges or surrounding skin can force the wound edges apart and allow adhesive into the wound. Adhesive within the wound could delay wound healing and/or result in adverse cosmetic outcome. Therefore, high viscosity DERMABOND® Adhesive should be applied with a very light brushing motion of the applicator tip over easily approximated wound edges.
- High viscosity DERMABOND® Adhesive polymerizes through an exothermic reaction in which a small amount of heat is released. With the proper technique of applying high viscosity DERMABOND® Adhesive in multiple thin layers (at least two) onto a dry wound and allowing time for polymerization between applications, heat is released slowly and the sensation of heat or pain experienced by the patient is minimized. However, if high viscosity DERMABOND® Adhesive is applied so that large droplets of liquid are allowed to remain unspread, the patient may experience a sensation of heat or discomfort.
- High viscosity DERMABOND® Adhesive is packaged for single patient use. Discard remaining opened material after each wound closure procedure.
- Do not resterilize high viscosity DERMABOND® Adhesive.
- Do not place high viscosity DERMABOND® Adhesive in a procedure pack/tray that is to be sterilized prior to use. Exposure of high viscosity DERMABOND® Adhesive, after its final manufacture, to excessive heat (as in autoclaves or ethylene oxide sterilization) or radiation (such as gamma or electron beam), is known to increase its viscosity and may render the product unusable.

PRECAUTIONS

- Do not apply liquid or ointment medications or other substances to the wound after closure with high viscosity DERMABOND® Adhesive, as these substances can weaken the polymerized film and allow for dehiscence (skin edge separation). High viscosity DERMABOND® Adhesive permeability by topical medications has not been studied. Prior to application, cleanse the application site thoroughly to remove any remaining blood, fluids or topical medications/ anesthetics.
- High viscosity DERMABOND® Adhesive permeability by fluids is not known and has not been studied.
- High viscosity DERMABOND® Adhesive, as a liquid, is syrup-like in viscosity. To prevent inadvertent flow of liquid high viscosity DERMABOND® Adhesive to unintended areas: (1) the wound should be held in a horizontal position, with high viscosity DERMABOND® Adhesive applied from above, and (2) high viscosity DERMABOND® Adhesive should be applied in multiple (at least two), thin layers rather than in a few large droplets.
- Hold applicator away from yourself and the patient and break ampule close to its center one time only. Do not crush the contents of the applicator tube repeatedly as further manipulation of the applicator may cause glass shard penetration of the outer tube. Glass shard penetration can result in inadvertent skin punctures, which may result in the transmission of bloodborne pathogens.
- High viscosity DERMABOND® Adhesive should be used immediately after crushing the glass ampule as the liquid adhesive will not flow freely from the applicator tip after a few minutes.
- If unintended bonding of intact skin occurs, peel, but do not pull the skin apart. Petroleum jelly or acetone may help loosen the bond. Other agents such as water, saline, Betadine® Antibiotics, Hibiclens® (chlorhexidine gluconate), or soap, are not expected to immediately loosen the bond.
- Safety and effectiveness of high viscosity DERMABOND® Adhesive on wounds of patients with peripheral vascular disease, insulin-dependent diabetes mellitus, blood clotting disorders, personal or family history of keloid formation or hypertrophy, or burst stellate lacerations, have not been studied.
- Safety and effectiveness of high viscosity DERMABOND® Adhesive on the following wounds have not been studied: animal or human bites, puncture or stab wounds.
- Safety and effectiveness on wounds that have been treated with high viscosity DERMABOND® Adhesive and then exposed for prolonged periods to direct sunlight or tanning lamps have not been studied.
- Safety and effectiveness of high viscosity DERMABOND® Adhesive on wounds in vermilion surfaces has not been studied.

ADVERSE REACTIONS

Adverse reactions related to either the wound closure procedure or the use of DERMABOND® Adhesive are possible. The following events have been identified as potentially associated with the wounds closed with DERMABOND® Adhesive.

- Infection (redness more than 3-5 mm from the wound margin, swelling, purulent discharge, pain, increased skin temperature, fever)
- Acute inflammation (erythema, edema, pain, warmth)
- Dehiscence (skin edge separation)
- Excessive itching
- Skin blistering

Events potentially associated with the wound closure procedure include bleeding, skin edge necrosis, seroma, and hematoma.

Adverse reactions encountered during the clinical study for closure of trauma-induced lacerations using high viscosity DERMABOND® Adhesive and the clinical study comparing low viscosity DERMABOND® Adhesive to sutures, staples, and adhesive strips are listed below:

The safety of both high viscosity DERMABOND® Adhesive and the low viscosity DERMABOND® Adhesive control was measured in a randomized clinical study of 84 patients, 42 patients receiving high viscosity product and 42 receiving low viscosity product, by 1) the presence or the extent of an inflammatory reaction, 2) the presence of signs of clinical infection, 3) cosmetic outcome at Day 30, 4) assessment of thermal discomfort, and 5) the reported adverse events associated with use of the device. No significant differences between the two treatment groups were observed for any of these safety outcome measures, although 17 patients (44%) randomized to the high viscosity DERMABOND® Adhesive treatment group experienced a sensation of heat during application of the skin adhesive compared to 10 patients (26%) randomized to the low viscosity DERMABOND® Adhesive treatment group. Of those 17 patients in the high viscosity group, 5 of the patients noted that sensation of heat was uncomfortable. None of the patients in the low viscosity group observed objectionable sensation of heat.

Adverse reactions encountered during clinical study comparing low viscosity DERMABOND® Adhesive to sutures, staples, and adhesive strips are listed in the table below:

Clinical Study Outcomes	***No Subcuticular Sutures***		***With Subcuticular Sutures***	
	DERMABOND® Adhesive	Control	DERMABOND® Adhesive	Control
	N (%)	N (%)	N (%)	N (%)
Accounting				
N, patients enrolled	240	243	167	168
N, patients treated	239	242	167	166
Patients completed	228 (95%)	215 (88%)	164 (98%)	162 (96%)
Adverse Reactions				
Suspected Infection*	8 (3.6%)	2 (0.9%)	6 (3.6%)	2 (1.2%)
Wound type # Lacerations	8	2	1	0
# Incisions	0	0	5	2
Dehiscence with Need for Retreatment	6 (2.5%)	5 (2.1%)	3 (1.8%)	0
Acute Inflammation				
Erythema	26 (11.5%)	74 (33.0%)	52 (31.3%)	75 (45.1%)
Edema	22 (9.7%)	28 (12.5%)	62 (37.3%)	71 (42.8%)
Pain	14 (6.1%)	13 (5.8%)	56 (33.7%)	57 (34.3%)
Warmth	3 (1.3%)	6 (2.6%)	3 (1.8%)	4 (2.4%)

*In the clinical study, presence of infection was to be identified by observation of redness more than 3–5 mm from the repaired wound, swelling, purulent discharge, pain, increased skin temperature, fever, or other systemic signs of infection. Confirmatory culture was not routinely obtained. Among cases of suspected infection for low viscosity DERMABOND® Adhesive, 7/14 (50%) were in patients less than 12 years old with traumatic lacerations; overall, 8 of the 14 (approximately 60%) low viscosity DERMABOND® Adhesive wounds with suspected infections were associated with sub-optimal cosmetic outcome.

- Reactions may occur in patients who are hypersensitive to cyanoacrylate or formaldehyde. See CONTRAINDICATIONS.
- Adverse reactions may be experienced following high viscosity DERMABOND® Adhesive contact with the eye.

CLINICAL STUDIES

Clinical Study Comparing High Viscosity DERMABOND® Adhesive and Low Viscosity DERMABOND® Adhesive for Closure of Trauma-Induced Lacerations

Description: A prospective, randomized, controlled, unmasked study was conducted to evaluate the safety and effectiveness of closing the approximated skin edges of trauma-induced lacerations using high viscosity DERMABOND® Adhesive in comparison to the currently marketed low viscosity DERMABOND® Adhesive, with or without stitches placed below the skin surface according to investigator judgment.

The study population included patients at least one year of age, in good general health, who signed informed consent and agreed to follow-up visits. Patients were excluded if presenting with: significant multiple trauma, peripheral vascular disease, insulin dependent diabetes mellitus, blood clotting disorder, keloid formation or hypertrophy history (patient or family), cyanoacrylate or formaldehyde allergy, burst or stellate lacerations due to crush or hard blow, animal or human bite, and decubitus ulcer. One unit of either the high viscosity or low viscosity DERMABOND® Adhesive was used to close the wound. Wound length and width were measured in millimeters; wound depth was not measured. Most wounds in the study were clean, small, superficial lacerations which did not penetrate the dermis completely nor sufficiently to require dermal suture placement (average wound length=18.7 mm).

Follow-up was at 14 days (± 2 days) and at 30 days (± 2 days). The Modified Hollander Cosmesis Scale (MHCS), a validated scale, was used to evaluate cosmesis at the 30-day (± 2 days) follow-up visit. This scale evaluates step-off borders, edge inversion, contour irregularities, excess inflammation, wound margin separation, and overall wound appearance.

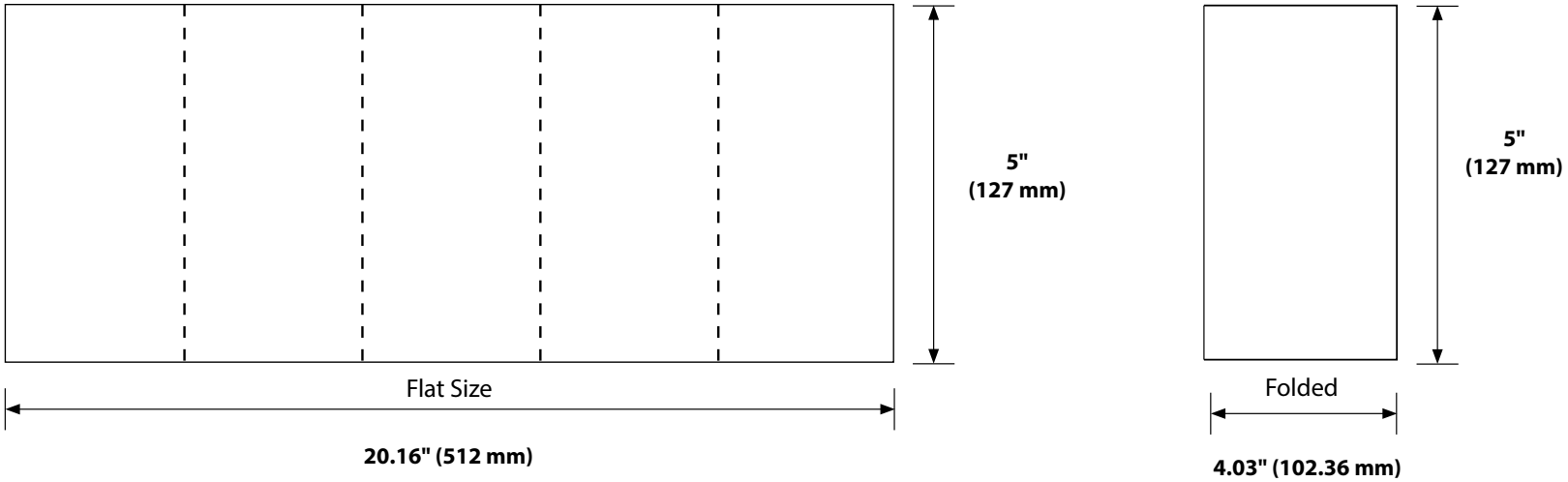
Results: The primary measure of device effectiveness in the study was wound closure at day 14, defined as continuous approximation of wound margins from the time of wound closure until the day of evaluation. Results indicate that high viscosity DERMABOND® Adhesive was equivalent to the low viscosity DERMABOND® Adhesive control for effectiveness of wound closure at day 14. Secondary effectiveness measures included an assessment of migration of the liquid adhesive from the wound site during application and an assessment of the presence of the polymer film on the wound at the time of the 14 day follow-up. Results show a significant reduction in the occurrence of migration of the liquid adhesive from the wound site during application for the high viscosity DERMABOND® Adhesive compared to the low viscosity DERMABOND® Adhesive control. No significant difference was observed between the two treatment groups for the presence of the polymer film at day 14.

Clinical Study Comparing Low Viscosity DERMABOND® Adhesive to Sutures, Staples, and Adhesive Strips

Description: A prospective, randomized, controlled, unmasked study was conducted to evaluate the safety and effectiveness of closing the approximated skin edges of surgical incisions, including punctures from minimally invasive surgery, and trauma-induced lacerations using low viscosity DERMABOND® Adhesive in comparison to U.S.P. size 5-0 or smaller sutures, adhesive strips or staples, with or without dermal closure (subcuticular stitch) as per investigator judgment.

IFU PRINTING SPECIFICATION SHEET

PAGE LAYOUT



TITLE	DESCRIPTION	LAB NUMBER	SPECIAL INSTRUCTIONS/COMMENTS	BINDING	COLORS
DERMABOND® Mini	**Domestic IFU**	**LAB0018680v5**	**n/a**	**n/a**	**Black, PMS266, PMS3115**

FLAT SIZE	FOLDED SIZE	RMC NUMBER	PAGE COUNT	LANGUAGES	SELF COVER	PLUS COVER	SEALING METHOD	WAFER SEAL
20.16" x 5" **512 mm x 127 mm**	**4.03" x 5"** **102.36 mm x 127 mm**	**389921R05**	**2**	**EN**	[X]	☐	**n/a**	☐

BLEED SIZE .5" (12.7 mm)	.125" (3.175 mm)	NONE	BLEED ALL SIDES	BLEED TOP	BLEED RIGHT	BLEED LEFT	BLEED BOTTOM
☐	☐	[X]	☐	☐	☐	☐	☐

DRAWING IS NOT TO SCALE: DRAWINGS REFLECT INFORMATION FOR PRODUCTION OF PRINTED PIECES AND DO NOT CONTAIN ACTUAL ARTWORK.

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