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from concept to market

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February 9, 2006

Food and Drug Administration
Center for Devices and Radiological Health
Regulations Staff (HFZ-215)
1350 Piccard Drive
Rockville, MD 20857

Re: 513(e) Petition For Reclassification
Tissue Adhesive For Soft Tissue Approximation

To Whom It May Concern,

This Petition For Reclassification is being submitted in accordance with Section 513(e) of the Food, Drug and Cosmetic Act (FDCA), 21 CFR 860.123, 21 CFR 860.130 and FDA's guidance document Changes in Device Classification in support of the reclassification of Tissue Adhesive devices (device classification code MPN) from Class III to Class II. In accordance with 21 CFR 860.123(b)(4), an original and two copies of this Petition are enclosed.

Tissue Adhesives for Soft Tissue Approximation (hereafter, referred to as Tissue Adhesive(s)) are post-Amendment devices and as such were automatically classified by Section 513(f)(1) of the FDCA into Class III.

This Petition presents evidence that Tissue Adhesives do not conform to the criteria for Class III described in Section 513(a)(1)(C) of the FDCA but conform to the criteria described in Section 513(a)(1)(B) for Class II medical devices. This Petition also describes how the application of General Controls, including Premarket Notification and Quality System Regulations, and Special Controls, such as the currently available guidance document (Cyanoacrylate Tissue Adhesive for the Topical Approximation of Skin – Premarket Approval Applications, February 13, 2004) and conformance to existing ASTM performance standards will provide a reasonable assurance of safety and effectiveness.

Please feel free to contact me at the numbers below should you have any comments or questions concerning this Petition for Reclassification.

Sincerely,

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1.0 BACKGROUND AND REGULATORY HISTORY

Tissue adhesive medical devices for soft tissue approximation (hereafter referred to as tissue adhesives) were first marketed in the United States after the Medical Device Amendments of 1976 (MDA) to the Food, Drug and Cosmetic Act (FDCA) as Class III, post-amendments devices requiring an approved Premarket Approval Application prior to marketing. The MDA as amended by the Safe Medical Device Act (SMDA) of 1990 and the FDA Modernization Act (FDAMA) of 1997 provide regulations for the classification and regulation of medical devices intended for human use. Further, a medical device may be reclassified into a lower regulatory class provided reasonable safety and effectiveness for their intended use can be ensured.

The FDCA established three categories (classes) of medical devices depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three classes are Class I (general controls), Class II (special controls), and Class III (pre-market approval). General controls are sufficient to provide reasonable assurance of safety and effectiveness of Class I devices. General controls include the following: prohibition against adulterated or misbranded devices, premarket notification (510(k)), banned devices, the quality system regulation that includes design controls and good manufacturing processes, registration of manufacturing facilities, listing of device types, record keeping, etc.

Class II devices are those that cannot be classified into Class I because general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness of such devices. These devices are regulated using special controls and general controls. Special controls include guidelines (guidance documents), performance standards, postmarket surveillance, clinical data, labeling, tracking requirements, and other appropriate actions the Secretary of the Department of Health and Human Services deems necessary to provide such assurance.

Class III devices are those for which insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness. These devices are life sustaining, life supporting, or substantially important in preventing impairment of human health, or they present unreasonable risk of illness or injury. Class III devices are regulated by using “valid scientific evidence” to establish the safety and effectiveness of the device. Valid scientific evidence includes well-controlled investigations, partially-controlled studies, uncontrolled studies, well-documented case histories, and reports of significant human experience.

FDA has regulated tissue adhesive medical devices as a Class III, Post-Amendments device. Presently, there is no a codified regulation number and device identification for this device. New devices require a premarket approval under section 515 of the FDCA to allow commercial distribution.

To date, CDRH has approved two tissue adhesive device PMAs which are presented in the Table below:

PRODUCT	APPLICATION HOLDER/ NUMBER/ APPROVAL DATE	PRODUCT CHARACTERISTICS	PRODUCT INDICATION
Dermabond	Closure Medical Corporation P960052 Aug 26, 1998	2-Octyl cyanoacrylate	"… for topical application to hold closed easily approximated skin edges from surgical incisions, including punctures from minimally invasive surgery and simple thoroughly cleansed trauma-induced laceration. Dermabond may be used in conjunction with but not in place of subcuticular sutures."
Indermil Tissue Adhesive	United States Surgical P010002 May 22, 2002	n-Butyl-2-cyanoacrylate	"… for the closure of topical skin incisions including laparoscopic incisions and trauma-induced laceration in areas of low skin tension that are simple, thoroughly cleansed, and have easily approximated skin edges. Indermil may be used in conjunction with but no in place of deep dermal stitches."

2.0 DEVICE DESCRIPTION

21CFR860.123(a)(1)

2.1 DEVICE DESCRIPTION

Tissue adhesives are sterile, liquid adhesives composed of a cyanoacrylate monomer (either n-Butyl-2 cyanoacrylate or 2-Octyl cyanoacrylate) along with trace quantities of free radical stabilizers and possibly a colorant (e.g., D&C violet #2).

Tissue adhesives are supplied in single patient use ampules and remain in a liquid state until anionic initiation of the polymerization process occurs.

This process can be initiated by moisture or other active groups such as proteins present on skin and continues until the liquid monomer becomes a solid polymer. Due to the method of polymerization the adhesive comes into very intimate contact with the skin providing optimal adhesion.

When applied topically to pre-apposed wound edges, the tissue adhesive sets rapidly to hold the wound closed. The adhesive film bonding the approximated skin edges is sufficiently water resistant to permit showering by the patient and typically sloughs off with keratinized epithelium 5-10 days after application.

Butyl and Octyl cyanoacrylate tissue adhesives differ in that butyl tissue adhesives, with their smaller molecular size provide higher tensile strength but are less flexible than the lower tensile strength but more flexible octyl materials. Butyl materials also polymerize faster than octyl cyanoacrylates.

2.2 INTENDED USE

Tissue adhesives are intended for the closure of topical surgical incisions and simple traumatic lacerations.

2.3 INDICATION FOR USE

Indications For Use for the two FDA approved tissue adhesive devices is provided below:

Dermabond (P960052):

Dermabond Topical Skin Adhesive is intended for topical application to hold closed easily approximated skin edges from surgical incisions, including punctures from minimally invasive surgery, and simple, thoroughly cleansed, trauma-induced laceration. DermaBond may be used in conjunction with, but not in place of, subcuticular sutures.

Indermil (P010002):

Indermil tissue adhesive is indicated for the closure of topical skin incisions including laparoscopic incisions, and trauma-induced laceration in areas of low skin tension that are simple, thoroughly-cleansed, and have easily approximated skin edges. Indermil may be used in conjunction with, but not in place of, deep dermal stitches.

Following the original PMA approvals for tissue adhesive, supplemental applications have been approved which include the approval of high viscosity formulations, modified applicator systems, and expanded labeling claims. Most noteworthy are claims relating to greater application control and recognition that the polymerized tissue adhesive provides a microbial barrier.

2.4 CONTRAINDICATIONS

Contraindications that have been labeled with the currently FDA approved tissue adhesives include the following:

- Use on any wounds with evidence of active infection, gangrene, or wounds of decubitus etiology.
- Use on mucosal surfaces or across mucocutaneous junction (e.g., oral cavity, lips) or on skin which may be regularly exposed to body fluids or with dense natural hair (e.g., scalp).
- Use on patients with a known hypersensitivity to cyanoacrylate or formaldehyde.
- Use on subdermal layers of tissue.
- Use on any internal organs, blood vessels, nerve tissue, or within the conjunctival sac of the eye.
- Use on the surface of the eye.
- Use on wounds subject to high skin tension or on areas of increased skin tension such as the elbows, knees or knuckles. Use in areas of skin excision.
- Use on patients with known preoperative systemic infections, uncontrolled diabetes, or disease or condition that are known to interfere with the wound healing process.

2.5 ADVERSE EVENTS

Potential adverse events for tissue adhesives include: infection, dehiscence with need for retreatment, acute inflammation, and allergic reaction.

2.6 ALTERNATIVE PRACTICES AND PROCEDURES

Surgical incisions and traumatic lacerations can be closed using various alternative medical devices. The most commonly used device is the nonabsorbable monofilament suture. The sutures are to remain in place approximately 7-10 days until there is sufficient epithelialization to prevent wound dehiscence. The sutures must then be removed and the wound continues to heal. In addition, removable metal skin staples and strip-type adhesive wound closures (narrow strips of fabric or polymeric material with adhesive backing)have also been used to hold skin edges together. Metal staples also require that the patient return to the clinic for removal.

2.7 MARKETING HISTORY

Tissue adhesives have been broadly accepted into the wound closure industry since the market introduction of DermaBond (1998) and Indermil (2002) due to the consistent results published comparing cyanoacrylate tissue adhesives with traditional skin closing devices(sutures, staples or adhesive devices) (refer to Section 7.0 and ATTACHMENT C). Numerous studies have repeatedly concluded that cyanoacrylate tissue adhesives are equally safe and effective for the repair of low-tension, easily approximated traumatic lacerations and surgical incisions. Unlike sutures, cyanoacrylate tissue adhesives do not require special instruments, routine use of anesthesia or a removal procedure. They can also be applied more rapidly and the decrease the amount of required wound care from patients by serving as their own dressings.

Due to this wide spread market acceptance, current estimates of the number of cyanoacrylate tissue adhesive devices sold/used per year in the US is expected to increase between 8.5-9.5% per year between 2006 and 2010[1]

2.8 SIMILARITY OF TISSUE ADHESIVE MEDICAL DEVICES

All currently-approved cyanoacrylate tissue adhesives have the same basic chemistry and the same basic mechanical properties. The similarity in the chemical and physical nature of the two FDA-approved devices is demonstrated by their similar clinical safe and effective performance published in the literature, their PMA Summary of Safety and Effectiveness' and is discussed further in Section 7.2.

Through the use of General Controls (21CFR807.81 Premarket Notification Procedures) which require the establishment of substantial equivalence to an already-cleared predicate and Special Controls, including recognized standard test methods and FDA guidance documents (see Section 9.0), new tissue adhesives would be developed and tested in accordance with these standards and guidance documents and would also be expected to perform substantially equivalently to the products already cleared by the FDA.

[1] Medtech Insight. Analysis #A120; U.S. Markets for current and emerging wound closure technologies, 2001-2011. August 2002.

3.0 PROPOSED CLASSIFICATION REGULATION

21CFR860.123(a)(2)

The petitioner seeks to reclassify Tissue Adhesives for Soft Tissue Approximation product code MPN, from Class III (Premarket Approval) to Class II (Special Controls) due to the ability of the General and Special Controls to provide a reasonable assurance of safety and effectiveness.

4.0 SUPPLEMENTAL DATA SHEET

21CFR860.123(a)(3)

A completed Supplemental Data Sheet applicable to tissue adhesives (product code MPN) has been completed and is provided in ATTACHMENT A.

5.0 CLASSIFICATION QUESTIONNAIRE

21CFR860.123(a)(4)

A completed Classification Questionnaire applicable to tissue adhesives (product code MPN) has been completed and is provided in ATTACHMENT B.

6.0 SUMMARY OF REASONS FOR DOWNCLASSIFICATION

21CFR860.123(a)(5)

In support of reclassifying tissues adhesives from class III to class II, the petitioner has summarized the benefits, risks and proposed general and special controls that will provide reasonable assurance of the safety and effectiveness of future cyanoacrylate tissue adhesives.

Due to the fact that a) the risk of significant clinical adverse events when using tissue adhesives is low; b) the benefits include effective wound closure, faster closure time, improved cosmesis, less-invasive/less-tissue trauma, no secondary dressing, and no suture/staple removal; and c) the risk of field issues is extremely low, the petitioner proposes that the application of General Controls, including Premarket Notification Procedures (21CFR807.81) which require the establishment of substantial equivalence to an already-cleared predicate and compliance with the Quality System Regulations (21CFR820), and Special Controls, including use of recognized performance standards and a guidance document, will be adequate to provide reasonable assurance of safety and effectiveness for tissue adhesives. The remaining sections of this petition will discuss how these known risks are controllable through general and special controls, therefore supporting the petition that cyanoacrylate tissue adhesives may, therefore, be regulated by the FDA as a Class II medical device.

7.0 SAFETY/EFFECTIVENESS OF TISSUE ADHESIVES

21CFR860.123(a)(6)

7.1 PUBLISHED SAFETY AND EFFECTIVENESS DATA

The petitioner conducted a literature search with the intent to summarize the published knowledge of the performance of cyanoacrylate tissue adhesives. The literature available on cyanoacrylate tissue adhesive products is comprehensive and describes the benefits of its use for tissue adhesion. This literature demonstrates that tissue adhesive products used for closure of surgical incisions, lacerations or other wounds are safe and effective.

Following is a discussion of how the literature review was conducted and the outcome of the process. This literature review is organized into the following six sections with respect to the various benefits of tissue adhesives: (1) effective surgical wound closure, (2) faster closure time, (3) cosmesis (4) Non-invasive – less tissue trauma, (5) No requirement for secondary dressing, (6) No requirement for suture/staple removal

In summary, a minimum of 3200 surgeries and 2600 lacerations were evaluated in the literature. The majority of these studies (57) are prospective in nature and demonstrate that cyanoacrylate is a safe and effective method of tissue closure for surgical procedures and laceration repair. These findings are also supported by retrospective studies. Evidence of the clinical studies presented here demonstrate: cyanoacrylate tissue adhesives are effective for wound closure, have shorter closure time than standard suturing methods, are a non-invasive method not requiring secondary dressings and suture/staple removal, and offer overall improved patient satisfaction.

7.1.1 Literature Search Procedures

The literature review conducted for this reclassification petition resulted in the identification of over 1500 articles. One-hundred and nineteen (119) of these articles are included in the discussion of effectiveness information in this section of the petitions. The following methodology was applied to obtain these articles.

A search of the PubMed database, a service of the National Library of Medicine which provides access to over 12 million MEDLINE citations and life science journals, was conducted using the following combination of key words:

- Cyanoacrylate
- Octylcyanoacrylate
- Butylcyanoacrylate
- Indermil
- Dermabond
- Tissue Adhesive
- Wound Closure
- Skin Closure
- Adverse Event(s)
- Safety and Effectiveness
- Absorbable Tissue Adhesive
- Medical Adhesives

Searches were conducted from the time period ranging from as far back as articles could be found through 2005. Limits only applied to this search were English and Human.

A summary of the number of articles found using PubMed is found in ATTACHMENT C, Table 1. The literature review can be found in ATTACHMENT C, Table 5.

The petitioner also used an outside research source engine Nerac, Inc. (located in Tolland, CT) to aid in the search of related literature. One hundred twenty-eight (128) articles were identified; 87 of which were not found in the PubMed search. Eleven articles were found to be relevant to this petition and two of these were used for analysis.

Abstracts were reviewed for relevance to include in the petition. One hundred fifty-two (152) of the original 204 articles were selected for in-depth analysis following this review. 121 of these were determined to be applicable to the effectiveness discussion within this petition.

In addition to the 121 articles, the petitioner conducted a separate search of the literature used in support of marketing applications for the Tissue Adhesives currently in commercial distribution in the United States. This search included review of available and appropriate PMA Summary of Safety and Effectiveness (SSEs), labeling provided for legally marketed devices at the time of their approval, and other sources.

During the in-depth review of these articles, certain information was extracted in order to summarize the data. Information pertaining to the type of study (prospective or retrospective), control group or treatment, surgery type and tissue adhesive type can be found in ATTACHMENT C, Table 5.

7.1.2 Benefits of Effective Surgical Wound Closure

Topical Cyanoacrylate Skin Adhesives (TCAs) are now used extensively in Emergency Rooms for closure of trauma wounds. Although the type of trauma wound treated by this technique varies considerably – their usage is mainly for clean, superficial dermal wounds that are not subjected to flexion or stress (i.e. over joints). Both n-butyl and octyl-cyanoacrylates have been successfully used in this application – although the preference seems to be for the n-butyl product due to its fast setting, less pain on application than the octyl material and ease of use[23].

A total of 57 prospective studies have reported on the use of TCAs for closure of surgical incisions or lacerations. Both n-butyl and octyl-TCAs have been used, the majority of studies looking at the use of these adhesives for closure of short surgical wounds not subjected to excess tension or flexion. There are studies on the use of TCAs for longer surgical wounds[12] as well as numerous case reports.

The recently published independent Cochrane review[25] concluded that: “Surgeons may consider the use of tissue adhesives for the closure of incisions in the operating room”. Effectiveness of closure was assessed by analyzing dehiscence rates reported in various studies (see ATTACHMENT C, Table 3). A total of 21 prospective studies were reviewed; no statistically significant difference was detected between the proportion of the wounds with dehiscence for each type of tissue adhesive individually or for butyl- and octyl-TCA’s together.

Two studies (Harold et al[49] and van den Ende et al[117]) concluded that butyl-TCA was inferior to sutures when reporting dehiscence. Harold et al[49] reported on closing 5mm trocar incisions using either octyl-TCA, sutures or tapes and demonstrated higher dehiscence rates as well as inferior scar formation and more patient pain when octyl-TCA’s were used. The authors speculate that this could be due to tension of the abdominal trocar wounds. Review of the study reveals that each wound took on average 34.7+/-24.5 seconds to close when using octyl-cyanoacrylate (Dermabond), and hence

poor results are thus probably due to the slow setting time allowing the wound edges to become poorly approximated. Van den Ende et al[117] published a prospective trial comparing n-butyl-TCA (Indermil) to Vicryl sutures for closure of pediatric groin incisions. They reported significantly higher dehiscence in the TCA group as well as poorer cosmesis.

Although the Cochrane review[25] and a study by Osmond (1999)[81] reported no difference in results between different types of TCAs, there is in theory, and some evidence to suggest which TCA may be optimal for surgical usage. It appears that although n-butyl TCAs provide the quickest and easiest skin closure for surgical wounds, the inherent flexibility of octyl-TCAs make them more suitable as a flexible dressing, post skin closure and useful in closure of longer wounds. Direct comparison between butyl-TCA's and octyl-TCAs is complicated by the fact that as butyl-TCA's set quickly, they tend to be applied as a single layer/spot, whereas butyl-TCA's tend to be applied as multiple layers as they set slowly. The implication is that a combination of, or sequential use of n-butyl for rapid and strong skin closure, followed by secondary application of an octyl-TCA as an occlusive, flexible reinforcement dressing may optimize wound closure for a wider range of surgical wounds.

The majority of papers report that the use of TCA's is faster than, and provide equivalent closure compared to conventional closure techniques (sutures, staples). Refer to ATTACHMENT C, Table 2, 3.

However, as stated previously – most clinical studies report that TCA's are equivalent/better to conventional closure techniques for closure of surgical incisions (in areas not subjected to significant tension or flexion)[25,109]. Switzer (Switzer et al[110]) did not feel that octyl-TCA was an acceptable alternative to subcuticular sutures specifically for hernia repair.

7.1.3 Benefits of Faster Closure Time

The majority of published clinical studies report that the use of TCAs for closure of surgical wounds is faster than conventional closure techniques[25,109,113] (i.e. sutures). Of the 119 articles reviewed, 36 specifically discussed closure time and 21 of the 36 were prospective studies. Refer to ATTACHMENT C, Table 2. Like any new technique, there is a learning curve with TCA application with most reports showing effective use after a very short learning period.

In general the finding is that TCAs affect faster wound closure than suturing (and slightly longer than using skin tapes). Obviously the type of surgery, size of wound and surgeons competence with closure type used, will all affect the results. It is generally considered that Octyl-TCAs are slower to polymerize than butyl-TCAs, but despite this, and with many studies being performed with Octyl-TCA's – cyanoacrylates have been shown to allow faster wound closure than conventional sutures.

However, in one of the studies above (Harold et al[49]) the use of TCAs was reported to have a longer closure time vs. conventional closure techniques. Ong et al[79] also reported that closure time in the TCA group as compared to suture was longer but, it was deemed nonsignificant.

7.1.4 Benefits of Improved Cosmetic Outcome

Cosmetic outcome is an important long-term outcome of wound repair for the patient. Although a surgical procedure may be 100% successful – an unsatisfactory skin scar may lead to dissatisfaction, both by the surgeon and for the patient. Hollander[52] and

Singer[107] noted that *"patients are most concerned with the cosmetic appearance of their healed lacerations".*

A total of 61 literature articles were reviewed that discussed cosmesis as a study end-point. The majority of these articles stated that there was no significant difference between TCAs and conventional wound closure methods; 35 of which were prospective studies. 8 literature articles stated that TCA was equivalent or superior to conventional closure methods[10,16,18,31,58,65,83]. Six of these eight were prospective studies.

However, in two literature articles (Harold et al[49] andVan den Ende et al[117]) the use of octyl- TCA was inferior to that of sutures or tape.

Topical Cyanoacrylate adhesives have been shown in both trauma and surgical settings to provide as good as (and sometimes better) wound cosmesis as subcuticular sutures. It is important to note that accurate skin approximation is critical for good cosmesis when TCA's are setting, as the polymerized TCA will rapidly set the skin in a fixed position. Hence a fast setting TCA's may allow more accurate approximation. Cosmesis may also be affected if the TCA is allowed to get into the wound. Hence a quick setting, precise topical application of TCA with good skin approximation may provide optimal results. As discussed previously, studies reporting inferior cosmetic results with TCA may be due to choice of optimal TCA in respect of incision to be closed[49, 117] or where application has been in high tension areas[10]. Refer to ATTACHMENT C, Table 4.

7.1.5 Benefits of Non-Invasive, Less-Tissue Trauma

As compared to sutures[(122-124)], tissue adhesives have

- No tissue puncturing, trauma caused by suture needle or pulling suture through the wound site.
- If there is tissue swelling or edema – there is no risk of tissue strangulation or damage.
- Do not introduce foreign materials (i.e. by the suture itself, or contaminates drawn into the wound-site by the suture).
- No wound disruption/trauma caused by removal of non-absorbable sutures.
- As TCAs require no additional dressings – there is no risk of wound trauma/scar disruption caused by dressing removal.

Once the sutures have been implanted, edema of the skin and subcutaneous tissues will ensue. This can cause significant patient discomfort during recovery, as well as scarring secondary to ischemic necrosis. These factors should be considered when placing tension upon the closure material.

Sutures are invasive and are foreign bodies; as such, they cause a local, immunologically mediated tissue response, clinically evident as erythema. Many factors may contribute to suture reactivity. The longer the sutures are in, the more reactivity occurs. The larger the caliber of the suture, the more reactivity; the increase of one suture size results in a 2- to 3-fold increase in tissue reactivity. Synthetic or wire sutures are much less reactive than natural sutures (eg, silk, cotton, catgut); a monofilament suture is less reactive than a braided suture and is also less likely to introduce debris/microbial contamination into the wound.

Percutaneous sutures create puncture tracks through the skin and the subcutaneous tissue; these tracks begin to re-epithelialize as wound healing progresses. In general, if sutures are removed within 7-10 days, these epithelial cells tend to regress; if left in for a

longer time, a foreign body reaction ensues, which may result in erythematous papules or stitch abscesses surrounding the sutures. Stitch abscesses are sterile pustules that result from tissue reaction to the keratinizing epithelial cells, which have migrated along the wound created by suture placement; this process may lead to permanent fibrosis and scarring.

Suture spitting results from subcutaneous sutures being placed too high in the dermis. Suture splitting can occur from several weeks to several months after surgery. It usually presents as a non-inflammatory papule and progresses with extrusion of the suture through the skin. The suture material may be trimmed or removed if loose, and it is not needed for maintaining wound strength.

Suture tracking results from the sutures being tied too tightly or being left in place too long. Puncture scars on either side of the wound connected by a linear scar in the area where sutures were placed give a railroad track appearance.

An allergic reaction to suture material is a rare complication. Hypersensitivity to chromic catgut suture is the most commonly reported reaction; however, allergies to silk and nylon sutures have also been reported. Patients suspected of suture allergy should be patch tested to guide future treatment.

7.1.6 Benefits of No Secondary Dressing

When tissue cyanoacrylate adhesives polymerize, they form a semi-occlusive wound dressing over the surgical wound, which remains in place for 5-7 days (until the skin and TCA slough off naturally). Thus, it is usual that when TCAs are used for surgical wound closure, a secondary dressing is not used (unless required as padding or further mechanical protection). The reduction in dressing costs will depend on; type and size of dressings used as well as how often these are replaced over the period of wound healing.

Dressing changes can cause some degree of wound trauma and patient pain and discomfort. Disruption of the wound scar may delay healing and can also potentially introduce microbial contamination into the wound (CDC recommendation on aseptic technique during wound dressing)[127].

Borley et al[13] states that TCA is an ideal dressing because it provides additional support, it creates a sealed, flexible, water resistant membrane over the incision, TCA does not interfere with stoma or drain site dressings, no risk of fluid accumulation in skin folds, maintains visibility of the wound and does not require maintenance. Bruns et al[19] also discuss the advantages of using TCA, specifically no need for needles, faster repair time, better acceptance by patients, water resistant and that removal of sutures is not required. Another article stated that patients found TCA to be superior to bandaids in terms of protection during daily activities; no dressing changes were required[32].

7.1.7 Benefits of No Suture/Staple Removal

With the use of TCAs, there is no requirement for non-absorbable suture /staple removal several days post-surgery. There are several benefits to patients and healthcare systems[13, 15, 19, 32,48, 59, 63, 66, 77, 95]:

- Patient does not have to return to clinic/outpatients etc to have sutures /staples removed
- Less wound trauma/disruption/infection risk

- No potential for discomfort and pain (psychologically easier for patient)
- Reduction in costs – no suture removal kit or staple removal kit required, no further dressings or Steri-strips.
- No clinician/nursing time to take out /remove sutures or staples.

7.2 APPROVED PMA SAFETY AND EFFECTIVENESS DATA

In addition to the published literature, the clinical evaluations of the two commercially available tissue adhesives were evaluated in support of the PMA approval of those devices. In the interest of brevity, the publicly-available Summaries of Safety and Effectiveness for these two PMA submissions have not been included within this petition. Since the PMA approval of one of these devices (DermaBond P9600052) occurred greater than six years ago, the PMA and associated documents are available to the FDA for review and consideration in support of this petition for reclassification in accordance with Section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and FDA's guidance document "*Guidance on Section 216 of the Food and Drug Modernization Act of 1997*", dated August 9, 2000.

Both Dermabond and Indermil were found to appose surgical incisions and lacerations (100% apposition ranging from 75.1-98.4%). Reported adverse events for both studies included: dehiscence (ranging from 1.6-3.5%), infection (ranging from 0.4% to 3.6%(suspected infection)), erythema (ranging from 7.5-31.3% (with subcuticular sutures)), edema (ranging from 2.4-37.3% (with subcuticular sutures)), pain (ranging from 6.1-33.7% (with subcuticular sutures)), hypersensitivity, warmth, drainage, and sinus tracts.

In summary, the risk and benefit profile of the first tissue adhesive brought before the FDA (DermaBond P9600052) was found to be beneficial enough such that the General and Plastic Surgery Device Panel recommended 8-0 in favor of approval of the premarket approval application. Regarding the second tissue adhesive brought before the FDA (Indermil P010002), "based on the preclinical and clinical data in the PMA, CDRH determined the data provide reasonable assurance that the device is safe and effective when used in accordance with the labeling" and a panel meeting/ recommendation was not deemed necessary.

8.0 RISKS TO HEALTH OF TISSUE ADHESIVES

21CFR860.123(a)(6)

Published risks to health associated with the use of cyanoacrylate tissue adhesive devices were presented in Section 7.1.

Likewise, risks identified during the clinical evaluations of the two commercially available tissue adhesive devices were referred to in Section 7.2. In accordance with Section 216 of FDAMA, FDA has access to the original PMA and associated documents in support of DermaBond (P060052) as the approval was more than six ago (P060052 PMA approval August 26, 1998).

Following are summaries of other publicly available databases (Medical Device Reports (MDR), Manufacturer and User Facility Device Experience (MAUDE) and FDA Enforcement Reports further characterizing the risk of using, manufacturing, and commercially distributing cyanoacrylate tissue adhesive devices.

8.1 MDR/MAUDE DATABASE SEARCH

Medical Device Reports Database Search and Results for Product Code MPN: Tissue Adhesive for Soft Tissue Approximation

The petitioner conducted a review of the FDA Medical Device Reports (MDR) and Manufacturer and User Facility Device Experience (MAUDE) databases to demonstrate that the risk associated with tissue adhesives products for soft tissue approximation do not pose an unreasonable risk of illness or injury.

A search for product code MPN in both the MDR and MAUDE databases generated a total of 296 events. A summary of these reports is provided for review (ATTACHMENT E, Table 9). The FDA databases cover from present back to December 13, 1984. An overview of the reported events is provided below in Table 6. The events are categorized according to the type of report that was filed by the manufacturer with the FDA, and further analysis was made by the petitioner to determine if the event pertained to the device or if the patient experienced an unrelated adverse event. After categorizing the event by report type, the petitioner summed the number of specific events that were reported and accounted for each of these events as a percent.

Of the 296 reported events, 133 (44.9%) were classified as product-related and 159 (53.7%) were reported as an adverse event (4 events were reported as not being related to the product but had no notation of adverse event). These results can be seen in Table 7. The most prevalent adverse event reported was eye bonding (59.4%) which the manufacturers reported as a result of user error, the functional performance of the device was not out of specification. 14.2% of the reported events were dehiscence and 39 of the 296 reported events were infection. Upon review of the adverse event reports, it was found that dehiscence and infection were post operative complications (or post-use of product) that can be attributed to a variety of factors such as type of laceration, wound cleansing procedure, or the patient's condition prior to device application and may not be a result of the device itself. Table 8 summarizes the events by product. Dermabond accounted for the majority of the reported adverse events (289 (97.6%)) with only 4 (1.3%) of the 296 adverse events pertaining to Indermil. Three (3) adverse events reported were from an unknown manufacturer and product.

Based on the review of the FDA safety database for tissue adhesives products, the risks of illness or injury reported were relatively minor and consistent with the events reported

in the published literature and the PMA approved device SSE's. Regulatory mitigation of these risks could include the use of General and Special Controls in addition to clinician training and labeling and are specifically outlined in Section 9.0.

8.2 SAFETY ALERT DATABASE SEARCH

The petitioner conducted a search of the weekly FDA Enforcement Reports to characterize the volume of recalls or field corrections associated with either of the two cyanoacrylate medical devices currently being commercially distributed in the U.S. The following key words were used for the search: tissue adhesive, cyanoacrylate, Indermil, DermaBond. No time period was used to limit the search. A total of two (2) enforcement reports were identified for tissue adhesive medical devices since 1998 (first introduction of DermaBond Tissue Adhesive). A summary of the two reports is provided below. Note a third enforcement report involving cyanoacrylate tissue adhesive for veterinary use was identified and is included in the table in the interest of completeness.

PRODUCT	RECALLING FIRM/ MANUFACTURER	RECALL CLASS	DATE	REASON	VOLUME IN COMMERCE
DermaBond Model BD12	Closure Medical Corp	Medical Device Class II recall	November 27, 2001	Inadequate seal in the blister packaging	130,116 units
MSI-EpiDermGlu (Iso-Butyl 2 Cyanoacrylate) tissue adhesive for soft tissue approximation	Recall firm: Elite Medical Group, Bloomington IL Manufacturer: Medisav Services, Inc., Ontario Canada	Medical Device Class II recall	July 2, 2003	The liquid tissue was marketed without FDA premarket clearance	129 cases.
Nexaband S/C topical adhesive	Closure Medical Corp	Veterinary Medicine Class III recall	April 14, 2003	Insert mix-up. Nexaband Liquid package inserts were discovered in Nexaband S/C product containers.	5,506 units

Of the two recalls involving cyanoacrylate tissue adhesive medical devices, one represented a possible sterilization breach and the other recall occurred when a product was being distributed in the US without FDA approval. The paucity of recalls involving cyanoacrylate tissue adhesive medical devices support the petitioner's proposal that adherence to the existing Quality System Regulations (21CFR820) will provide reasonable assurance of safety and effectiveness of tissue adhesive devices. The regulatory mitigation of these risks is specifically outlined in Section 9.0.

9.0 REGULATORY CONTROL OF RISKS

21CFR860.123(a)(6)

Due to the fact that a) the risk of significant clinical adverse events when using tissue adhesives is low; b) the benefits include effective wound closure, faster closure time, improved cosmesis, less-invasive/less-tissue trauma, no secondary dressing, and no suture/staple removal; and c) the risk of field issues is extremely low, the petitioner proposes that the application of General Controls, including Premarket Notification Procedures (21CFR807.81) which require the establishment of substantial equivalence to an already-cleared predicate and compliance with the Quality System Regulations (21CFR820) and Special Controls, including use of recognized standards and a guidance document, will be adequate to provide reasonable assurance of safety and effectiveness for tissue adhesives. Therefore, cyanoacrylate tissue adhesives should be classified as Class II medical devices

9.1 GENERAL CONTROLS

General controls include the following: a) prohibition against adulterated or misbranded devices, b) premarket notification (510(k)), c) banned devices, and d) the quality system regulation that includes design controls and good manufacturing processes, registration of manufacturing facilities, listing of device types, record keeping, etc..

9.2 SPECIAL CONTROLS

The petitioner proposes that in addition to General Controls, the Special Controls used to mitigate any risk associated with the use tissue adhesive medical devices will include the use of recognized performance standards and a guidance document which has already been drafted by the FDA.

Performance Standards

ASTM International (formerly known as American Society for Testing and Materials (ASTM)), has developed the following standards for testing cyanoacrylate tissue adhesive devices. The first three standard test methods are intended to provide a means for comparison of the adhesive strengths of tissue adhesives intended for use as surgical adhesives or sealants, or both, on soft tissue. The fourth standard test method is intended to provide a means for comparison of wound closure strength of tissue adhesives used to help secure the apposition of soft tissue. With the appropriate choice of substrate, these test methods could also be used for purposes of quality control in the manufacture of tissue adhesive based medical devices.

- F2255-05 Standard Test Method for Strength Properties of Tissue Adhesives in Lap-Shear by Tension Loading
- F2256-05 Standard Test Method for Strength Properties of Tissue Adhesives in T-Peel by Tension Loading
- F2258-05 Standard Test Method for Strength Properties of Tissue Adhesives in Tension
- F2458-05 Standard Test Method for Wound Closure Strength in Tissue Adhesives and Sealants

FDA Guidance Document:

A guidance document for cyanoacrylate tissue adhesive devices has already been drafted by the FDA and is titled "Cyanoacrylate Tissue Adhesive for the Topical Approximation of Skin – Premarket Approval Applications", dated February 13, 2004. The petitioner proposes that the title of the FDA guidance document be changed to read: "Class II Special Controls Guidance: Cyanoacrylate Tissue Adhesive for the Topical Approximation of Skin". This guidance document already addresses the following parameters when considering a marketing application:

- Device description
  - Viscosity and ease of expression
  - Setting time
  - Bond strength
  - Degradation rate
  - Chemical components
  - Packaging Components
- Chemistry
  - Chemical name
  - Chemical abstracts service number
  - Trade name
  - Structural formula
  - Molecular formula and molecular weight
  - Source and purity
  - Formulation additives
  - Monomer impurities
  - Degradation products
- Manufacturing
  - Manufacturing process flow
    - All non-reactants and reactants
    - The monomer production
    - Bulk formation
    - Cracking
    - Distillation
    - Sterilization of the product monomer
    - Cyanoacrylate formulation
    - Bottling
    - Ampule filling
    - Assembling
    - Final packaging
  - Final product release specification
    - Viscosity determination
    - Analysis of residual content of the components of bulk formation by gas chromatography, nuclear magnetic resonance, mass spectrometry, etc.
    - Purity of final product
    - Moisture determination
    - Setting time determination
    - Physical and mechanical testing
    - Stability/shelf life determination
    - sterility
- Mechanical properties
  - Tensile strength
  - Tensile or overlap shear strength

  - Peel adhesion strength
  - Impact strength
  - Adhesion expression force test
  - Water vapor transmission test
- Biocompatibility
  - For implanted devices contacting tissue for 24 hours to 30 days.
- Animal in vivo performance
  - Delay/prevention of healing
  - Performance
- Shelf life
- Sterility
- Clinical studies
  - To be conducted as significant risk devices (21CFR812.3(m) under IDE regulations (21CFR812), IRB regulations (21CFR56) and informed consent regulations (21CFR50)
  - The guidance document provides significant details regarding the clinical trial design, endpoints, data to be collected, and statistical methods.
- Labeling
  - Instructions for use
  - precautions

9.3 RISK MITIGATION

Following is a table presenting the risks of using, manufacturing and distributing cyanoacrylate tissue adhesive medical devices identified via a) scientific publication, b) PMA SSE (for approved devices), 3) MDR/MAUDE databases and 4) FDA weekly enforcement reports, along with the proposed mitigating regulatory controls.

The petitioner believes that all of the issues identified to date can be mitigated through compliance with General Controls (including 21CFR807.81 Premarket Notification Procedures and 21CFR820 Quality Systems Regulations) and Special Controls, including recognized standard test methods and FDA guidance documents. New tissue adhesives would be developed and tested in accordance with these regulations, standards and guidance documents and would also be expected to perform substantially equivalently to the products already cleared by the FDA. This comprehensive collection of regulatory controls would provide reasonable assurance of safety and effectiveness for cyanoacrylate tissue adhesives.

POTENTIAL RISK	**REGULATORY CONTROL**
Clinical adverse events:	
Dehiscence	Clinician Training; Product Labeling Special Controls: ASTM standard test methods for tension and wound closure strength properties
Infection	Clinician Training; Product Labeling
Eye bonding	Clinician Training; Product Labeling
Erythema	Clinician Training; Product Labeling
Allergic reaction; chemical reaction (vomiting/temperature	Clinician Training; Product Labeling
Granuloma & fat necrosis, necrosis	Clinician Training; Product Labeling
Patient picked off adhesive	Clinician Training; Product Labeling

POTENTIAL RISK	REGULATORY CONTROL
Wound drainage, no infection	Clinician Training; Product Labeling
Product Issues:	
Applicator broken	General Controls: QSR regulations; nonconforming product, corrective and preventive action
Applicator malfunction	General Controls: QSR regulations; nonconforming product, corrective and preventive action
Fumes caused chemical burns	Clinician Training; Product Labeling Special Controls: Biocompatibility testing requirements outlined in guidance document General Controls: QSR regulations, MAUDE reporting
Vial broke and cut finger	Clinician Training; Product Labeling General Controls; QSR regulations, packaging design/testing
Viscosity of tubes different	General Controls: QSR regulations, quality control testing, nonconforming product Special Controls; viscosity testing outlined in FDA guidance document
Blister package compromised	General Controls; QSR regulations, packaging design/testing
Distribution of unapproved product	General Controls; QSR regulations, distribution

10.0 REPRESENTATIVE UNFAVORABLE INFORMATION

21CFR860.123(a)(7)

Unfavorable information has been cited in Section 7.0 Safety/Effectiveness of Tissue Adhesives (published and PMA-approved data) and Section 8.0 Risks to Health of Tissue Adhesives (MDR/MAUDE and Safety Alert database searches) and are identified as risks of the device.

11.0 SUMMARY OF NEW INFORMATION

21CFR860.123(a)(8)

All of the information referred to within this petition is publicly available. The "new" information is the summarization of the published literature regarding cyanoacrylate tissue adhesive medical devices. All other information referred to within this petition is already known to the FDA through MDR/MAUDE databases, weekly FDA Enforcement Reports, and the PMA Summaries of Safety and Effectiveness for the two FDA approved tissue adhesive devices.

12.0 COPIES OF SOURCE DOCUMENTATION

21CFR860.123(a)(9)

Copies of source documentation have not been provided for the following reasons:

- Literature review: copies of the cited literature articles have not been provided due to copyright laws. Should the FDA desire copies of the attached articles, the petitioner would be pleased to provide the petitioner's copies of requested articles.

- Approved-PMA SSE's for Tissue Adhesives: Copies of the Summary of Safety and Effectiveness from the two FDA-approved PMAs for tissue adhesives have not been provided as these documents are readily available to the FDA. In addition, since the PMA approval of one of these devices (DermaBond P9600052) occurred greater than six years ago, the PMA and associated documents are available to the FDA for review and consideration in support of this petition for reclassification in accordance with Section 216 of the Food and Drug Administration Modernization Act of 1997 (FDAMA) and FDA's guidance document "*Guidance on Section 216 of the Food and Drug Modernization Act of 1997*", dated August 9, 2000.

- MDR/MAUDE database search: copies of the individual MDR/MAUDE reports have not been provided as these are readily available to the FDA.

- Safety Alert reports: copies of the individual Safety Alert reports have not been provided as these are readily available to the FDA.

- ASTM Test Standards: copies of the ASTM test standards have not been provided due to copy right laws. Should the FDA desire copies of the ASTM Test Standards for tissue adhesives, the petitioner would be pleased to provide the petitioner's copies of requested standards

13.0 FINANCIAL CERTIFICATION

21CFR860.123(a)(10)

This section is not applicable as the petitioner did not sponsor any of the clinical investigations cited in this petition, thus the petitioner has not entered into any financial arrangements with the clinical investigators for the conduct of these studies.

The petitioner certifies that none of the clinical investigators identified in the published articles have a proprietary interest in the petitioner's company, which is privately owned.

ATTACHMENT A: SUPPLEMENTAL DATA SHEET

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

SUPPLEMENTAL DATA SHEET

FORM APPROVED: OMB NO. 0910-0138
EXPIRATION DATE: January 31, 2003
(See OMB Statement on Page 2)

Panel Recommendation

1. GENERIC TYPE OF DEVICE
Tissue Adhesive For Soft Tissue Adhesive

2. ADVISORY PANEL
General and Plastic Surgery Device Panel

3. IS DEVICE AN IMPLANT (21 CFR 860.3)?
☐ Yes ☒ No

4. INDICATIONS FOR USE IN THE DEVICE'S LABELING
Tissue adhesives are indicated for the closure of topical skin incisions including laparoscopic incisions and trauma-induced lacerations in areas of low skin tension. Tissue adhesives may be used in conjunction with, but not in place of, subcuticular sutures.

5. IDENTIFICATION OF ANY RISKS TO HEALTH PRESENTED BY DEVICE
General
Review of a) the literature, b) PMA Summary of Safety and Effectiveness documents for two PMA-approved products (P960052 and P010002), c) FDA MDR/MAUDE databases, and d) FDA Safety Alert database revealed that the most common risks associated with the use of tissue adhesives include: inadvertant eye bonding, dehiscence, infection, allergic reaction, erythema and edema. With the exception of the inadvertant eye bonding, all of these events are relatively rare and depend upon the type of incision/laceration being closed (e.g., lacerations are more likely to exhibit infection than surgical incisions). All of these events have historicaly been included in tissue adhesive labeling and the petitioner suggests that continuing this practice will provide reasonable assurance of the safe and effective performance of the devices.

6. RECOMMENDED ADVISORY PANEL CLASSIFICATION ANDPRIORITY

Classification II Priority (Class II or III Only) _____

7. IF DEVICE IS AN IMPLANT, OR IS LIFE-SUSTAINING OR LIFE-SUPPORTING AND HAS BEEN CLASSIFIED INA CATEGORY OTHER THAN CLASS III, EXPLAIN FULLY, THE REASONS FOR THE LOWER CLASSIFICATION WITH SUPPORTING DOCUMENTATION AND DATA
Not applicable

8. SUMMARY OF INFORMATION, INCLUDING CLINICAL EXPERIENCE OR JUDGMENT, UPON WHICH CLASSIFICATION RECOMMENDATION IS BASED
Review of a) the literature, b) PMA Summary of Safety and Effectiveness documents for two PMA-approved products (P960052 and P010002), c) FDA MDR/MAUDE databases, and d) FDA Safety Alert database revealed that the most common risks associated with the use of tissue adhesives include: inadvertant eye bonding, dehiscence, infection, allergic reaction, erythema and edema. Other device/product issues identified were very rare and included applicator issues, viscosity issues, packaging issues and distribution of unapproved product. The petitioner believes that since a) the risk of significant clinical adverse events when using tissue adhesives is low; b) the benefits include effective wound closure, faster closure time, improved cosmesis, less-invasive/less-tissue trauma, no secondary dressing, and no suture/staple removal; and c) the risk of field issues is extremely low, the application of General Controls, including Premarket Notification Procedures (21CFR807.81) which require the establishment of substantial equivalence to an already-cleared predicate and compliance with the Quality System Regulations (21CFR820), and Special Controls, including use of recognized standards and a guidance document, will be adequate to provide reasonable assurance of safety and effectiveness for tissue adhesives.

9. IDENTIFICATION OF ANY NEEDED RESTRICTIONS ON THE USE OF THE DEVICE *(e.g., special labeling, banning, or prescription use)*

For prescription use only

10. IF DEVICE IS RECOMMENEDED FOR CLASS I, RECOMMEND WHETHER FDA SHOULD EXEMPT IT FROM

Justification / Comments

☐ a. Registration / Device Listing _____

☐ b. Premarket Notification _____

☐ c. Records and Reports _____

☐ d. Good Manufacturing Practice _____

11. IF DEVICE IS RECOMMENDED FOR CLASS II, RECOMMEND WHETHER FDA SHOULD EXEMPT IT FROM PREMARKET NOTIFICATION

☐ a. Exempt

☒ b. Not Exempt

Justifications/Comments Premarket Notification procedures will ensure consistent product testing and performance to predicate products

12. EXISTING STANDARDS APPLICABLE TO THE DEVICE, DEVICE SUBASSEMBLIES *(Components)* OR DEVICE MATERIALS *(Parts and Accessories)*

ASTM F2255-05 Standard Test Method for Strength Properties of Tissue Adhesives in Lap-Shear by Tension Loading
ASTM F2256-05 Standard Test Method for Strength Properties of Tissue Adhesives in T-Peel by Tension Loading
ASTM F2258-05 Standard Test Method for Strength Properties of Tissue Adhesives in Tension
ASTM F2458-05 Standard Test Method for Wound Closure Strength of Tissue Adhesives and Sealants

13. COMPLETE THIS FORM PURSUANT TO 21 CFR PART 860 AND SUBMIT TO:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Health and Industry Programs (HFZ-215)
1350 Piccard Drive
Rockville, MD 20850

OMB STATEMENT

Public reporting burden for this collection of information is estimated to average 1-2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration, (HFZ-215)
2094 Gaither Road
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to , a collection of information unless it displays a currently valid OMB control number.

ATTACHMENT B: CLASSIFICATION QUESTIONNAIRE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE --- FOOD AND DRUG ADMINISTRATION

GENERAL DEVICE CLASSIFICATION QUESTIONNAIRE

FORM APPROVED: OMB NO. 0910-0138
EXPIRATION DATE: January 31, 2003
(See OMB Statement on Page 2)

PANEL MEMBER / PETITIONER
Regulatory & Clinical Research Institute, Inc.

DATE
12/30/05

GENERIC TYPE OF DEVICE
Tissue Adhesive for Soft Tissue Approximation

CLASSIFICATION RECOMMENDATION
II

1. IS THE DEVICE LIFE-SUSTAINING OR LIFE-SUPPORTING ?	☐ YES ☒ NO	Go to Item 2.
2. IS THE DEVICE FOR A USE WHICH IS OF SUBSTANTIAL IMPORTANCE IN PREVENTING IMPAIRMENT OF HUMAN HEALTH ?	☐ YES ☒ NO	Go to Item 3.
3. DOES THE DEVICE PRESENT A POTENTIAL UNREASONABLE RISK OF ILLNESS OR INJURY ?	☐ YES ☒ NO	Go to Item 4.
4. DID YOU ANSWER "YES" TO ANY OF THE ABOVE 3 QUESTIONS ?	☐ YES ☒ NO	If "Yes," go to Item 6. If "No," go to Item 5.
5. IS THERE SUFFICIENT INFORMATION TO DETERMINE THAT GENERAL CONTROLS ARE SUFFICIENT TO PROVIDE REASONABLE ASSURANCE OF SAFETY AND EFFECTIVENESS ?	☐ YES ☒ NO	If "Yes," Classify in Class I. If "No," go to Item 6.
6. IS THERE SUFFICIENT INFORMATION TO ESTABLISH *SPECIAL CONTROLS* IN ADDITION TO *GENERAL CONTROLS* TO PROVIDE REASONABLE ASSURANCE OF SAFETY AND EFFECTIVENESS ?	☒ YES ☐ NO	If "Yes," Classify in Class II and go to Item 7. If "No," Classify in Class III.
7. IF THERE IS SUFFICIENT INFORMATION TO ESTABLISH *SPECIAL CONTROLS* TO PROVIDE REASONABLE ASSURANCE OF SAFETY AND EFFECTIVENESS IDENTIFY BELOW THE SPECIAL CONTROL(S) NEEDED TO PROVIDE SUCH REASONABLE ASSURANCE. FOR CLASS II. ☒ Guidance Document ☒ Performance Standard(s) ☐ Device Tracking ☐ Testing Guidelines ☐ Other *(Specify)*		
8. IF A REGULATORY PERFORMANCE STANDARD IS NEEDED TO PROVIDE REASONABLE ASSURANCE OF THE SAFETY ANDEFFECTIVENESS OF A CLASS II OR III DEVICE, IDENTIFY THE PRIORITY FOR ESTABLISHING SUCH A STANDARD. ☒ Low Priority ASTM performance standards already exist ☐ Medium Priority _____ ☐ High Priority _____ ☐ Not Applicable _____		
9. FOR A DEVICE RECOMMENDED FOR RECLASSIFICATION INTO CLASS II, SHOULD HE RECOMMENDED REGULATORY PERFORMANCE STANDARD BE IN LACE BEFORE THE RECLASSIFICATION TAKES EFFECT ?	☐ YES ☐ NO ☒ NOT Applicable	
10. FOR A DEVICE RECOMMENDED FOR CLASSIFICATION / RECLASSIFICATION INTO CLASS III, IDENTIFY THE PRIORITY FOR REQUIRING PREMARKET APPROVAL APPLICATION (PMA) SUBMISSIONS. ☐ Low Priority _____ ☐ Medium Priority _____ ☐ High Priority _____ ☐ Not Applicable _____		

11. IDENTIFY THE NEEDED RESTRICTION(S)

☒ Only upon the written or oral authorization of a practitioner licensed by law to administer or use the device

☐ Use only by persons with specific training or experience in its use

☐ Use only in certain facilities

☐ Other *(Specify)*

13. COMPLETE THIS FORM PURSUANT TO 21 CFR PART 860 AND SUBMIT TO:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Health and Industry Programs (HFZ-215)
1350 Piccard Drive
Rockville, MD 20850

OMB STATEMENT

Public reporting burden for this collection of information is estimated to average 1-2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
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Rockville, MD 20850

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ATTACHMENT C: LITERATURE SEARCH RESULTS

Table 1: Literature Search Criteria

Search Word	Limits	Number of Articles Found	Number of Relevant Articles	Number of Unique Articles	Number of Articles Selected for In-Depth Analysis	Number of Applicable Articles Determined to support the Effectiveness Discussion of this Petition
Cyanoacrylate	Human English	1409 (111 reviews)	193	193	144	113
Butylcyanoacrylate	Human English	524 (32 reviews)	65	3	3	3
Octycyanoacrylate	Human English	42 (5 reviews)	38	1	1	1
Indermil	Human English	12 (0 reviews)	10	1	1	1
Dermabond	Human English	70 (4 reviews)	44	2	2	1
Cyanoacrylate Tissue Adhesive	Human English	1220 (87 reviews)	133	1	1	0
Cyanoacrylate Tissue Sealant	Human English	5 (0 reviews)	0			
Cyanoacrylate Wound Closure	Human English	97 (6 reviews)	67	0		
Cyanoacrylate Skin Closure	Human English	63 (6 reviews)	46	0		
Absorbable Tissue Adhesive	Human English	81 (5 reviews)	8	0		
Cyanoacrylate Medical Adhesive	Human English	78 (8 reviews)	19	0		
Cyanoacrylate + Adverse Events	Human English	7 (0 reviews)	2	0		
Butylcyanoacrylate + Adverse Events	Human English	2 (0 reviews)	0			
Octycyanoacrylate + Adverse Events	Human English	0				
Indermil + Adverse Events	Human English	0				
Dermabond + Adverse Events	Human English	3	1	0		
Cyanoacrylate Safety and Effectiveness	Human English	9	0			
Nerac Search		128	87	11	2	2

Table 2: Literature on Wound Closure

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
5	Applebaum JS et al	Prospective	Traumatic lacerations	143	TCA	Finding: "tissue bonding is a quick, efficient, and painless method of closure for lacerations."
7	Barnett P et al	Prospective Randomized	Pediatric lacerations	163 (TCA=83 Suture-80)	TCA vs. sutures	Closure Time - 0-2min(TCA) 6-10min(suture) p<0.001
12	Blondeel PN et al	Prospective Randomized	Long surgical incisions (>4cm)	209 (106=high viscosity TCA 103=commercially available TCA)	Octyl TCA vs. commercially available octyl TCA	Closure Time - OCA = S/c or Deep dermal
17	Bruns TB et al	Randomized	Pediatric lacerations	83 (TCA = 42 suture = 41)	Octyl TCA vs. sutures/staples	Closure Time - TCA=2.9 min Suture=5.8min (p=<0.01)
18	Bruns TB et al	Prospective Randomized	Pediatric lacerations	61 (TCA = 30 suture = 31)	TCA vs. sutures	Closure Time - TCA=7 min Suture=17min
22	Canonico S et al	Prospective	Stripping of greater saphenous vein	18	Butyl TCA	Closure Time - mean time to close 117 sec
28	Dalvi A, Faria M, Pinto A.	Retrospective	Planned general surgery (incision length 3-17cm)	TCA = 30 Suture = 25	TCA vs. sutures	Closure Time - 30-45sec(TCA)
35	Elmasalme FN et al	Retrospective Review	Small incisions and lacerations in pediatric pts	3274 surgery 2650 lacerations	Butyl TCA (histoacryl)	*cuts short anesthesia time by up to
37	Farion K et al	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples/ adhesive strips	Closure Time - decreased procedure time and less pain
38	Farion K et al	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples/ adhesive strips	Closure Time - decreased procedure time and less pain
42	Gallemore RP et al		Eye socket reconstruction	1	TCA	TCA is simpler and quicker than suturing a mucous membrane graft
43	Gennari R et al	Prospective Randomized	Breast surgery	133 (TCA=69 suture=64)	Octyl TCA (Dermabond) vs. sutures	Closure Time - P<0.01 significance
46	Gosain AK, Lyon VB.	Review	adhesion of soft tissue	NA	Octyl TCA (Dermabond)	Closure Time - significantly decreased time of repair with TCA vs. sutures
47	Greene D et al .	Prospective controlled	Blepharoplasty			Closure Time - 8min(TCA) 7min(Suture)
50	Harold KL et al	Prospective Randomized	Laparoscopic trocar	48 pts (137 wounds) (TCA=40 suture=49 tape=48)	Octyl TCA vs. suture vs. tape	Closure Time - 34.7±24.5sec each wound (TCA) 43.1±21.4sec(sutures) 33.4±20.8sec (tape): sutures significantly longer than TCA or tape
55	Jallali N et al	Prospective Randomized	Laparoscopic chole	25 pts (51 wounds closed with suture and 48 wounds closed with TCA)	Octyl TCA (Dermabond) vs. sutures	Closure Time - 165sec (TCA) 356sec(control); P=0.03

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
61	King ME, Kinney AY.	Review	NA	NA	NA	faster, less painful more economical than suturing
65	Maartense S et al	Prospective Randomized	Laparoscopic trocar	140 (TCA=48 suture=50 tape=42)	Octyl TCA vs. suture vs. tape	Closure Time - 33sec(TCA) 65sec(sutures)
66	Magee WP Jr et al	Retrospective	Cleft lip repair	64	Octyl TCA vs. suture vs. tape	shorter operative time, formation of a protective barrier, simplified incision care, no need for suture removal, improved scar outcome
69	Matin SF.	Prospective Randomized	Laparoscopic port	92 (TCA=50, suture= 42)	Octyl TCA vs. suture	Closure Time - 2.5min (TCA) 6min(sutures)
70	Mattick A et al	Randomized	Pediatric laceration repair	60 (30 in each group)	Octyl TCA vs. steristrips	Closure Time - individuals performing procedure judged TCA to be more difficult to apply
72	Maw JL et al	Prospective comparison with blinded assessment	Head and neck incisions	TCA = 24 Suture = 26	Octyl TCA vs. subcuticular suture	Closure Time - 29.7secs (TCA) 289.0secs(sutures): p<0.0001
76	Nahas FX et al	Prospective	Body contouring Mammoplasty & abdominal surgery	37 (1 side of body treated with TCA other treated with sutures)	Octyl TCA (Dermabond) vs. subcuticular sutures	Closure Time - 2min(TCA), 4min25sec(control - abdo sutures) 7min45sec(control - mamo sutures)
79	Ong CC et al	Prospective Randomized	Pediatric surgical incisions	59 (TCA=26 suture=33)	Octyl TCA vs. subcuticular suture	Closure Time - 181±62secs(TCA), 161±45secs(sutures) p=0.68. This was reported as nonsignificant
80	Osmond MH et al	Cost-minimization analysis	NA	NA	sutures vs. TCA	TCA is the preferred method of closure of pediatric facial lacerations because it is the most efficient and is preferred by pts.
86	Petratos PB et al	Prospective	Circumcision	10 (5 in each group)	Octyl TCA+ suture vs. suture	Closure Time - TCA shorter vs. suture P<0.001
89	Quinn J et al	Prospective Randomized	Pediatric facial lacerations	81 (TCA=37 Suture=38)	TCA vs. sutures	TCA is a faster and less painful method of repair
92	Resch KL, Hick JL.	Retrospective and concurrent chart review	Pediatric ER	100	Octyl TCA (Dermabond)	Closure Time - reduced from 106min to 69min on average (P<0.0001)
94	Rogerson L et al	Prospective	Perineal repair	20	n-butyl TCA (Indermil)	The advantages are a quick and painless skin closure which with suturing can be uncomfortable.
95	Rosin D et al	Prospective	Laparoscopic	100 pts (250 wound sites)	TCA	Glue application was easy and quick.
100	Sebesta MJ, Bishoff JT	Prospective Randomized	Laparoscopic trocar sites		Octyl TCA vs. subcuticular sutures	Closure Time: 3.7min(TCA) 14min(Suture)
101	Shamiyeh A et al	Prospective Randomized	Phlebectomy	79 (TCA=26, suture=28, tape=25)	Octyl TCA vs. suture vs. tape	Closure Time - tapes<OCA<sutures

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
107	Singer AJ et al	Prospective Randomized	Laceration and incision closure	814 wounds (TCA=406 Std=408)	Octyl TCA vs. std of care	Closure Time -2.9min (TCA) 5.2min(std) P=<.001
110	Switzer EF et al	Prospective Randomized	Inguinal hernia repair	46 (TCA=24 suture=22)	Octyl TCA vs. subcuticular sutures	Closure Time -155sec(TCA) 286sec(suture) P=<0.001
113	Toriumi DM et al	Prospective Randomized	Facial plastic surgery	111 (TCA = 49 Suture = 51)	Octyl TCA vs. sutures	Closure Time - 55secs(TCA) 3min47secs(Suture)
114	Trott AT.	Editorial	NA	NA	NA	CTA significantly less painful; in surgery total anesthesia time reduced; inflammatory responses between TCA and sutures = no difference

Table 3: Literature on Dehiscence

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
3	Alio JL et al	Controlled	Cataract		TCA+suture vs. suture	No complications reported.
4	Amiel GE et al	Retrospective	General surgery	1098	n-butyl TCA	Dehiscence - occurred in only 1.1%
14	Bowen ML, Selinger M.	Prospective controlled	Episiotomy closure	62 (TCA = 32 suture = 30)	TCA vs. sutures	No wound dehiscence reported
18	Bruns TB et al	Prospective Randomized	Pediatric lacerations	61 (TCA = 30 suture = 31)	TCA vs. sutures	Dehiscence - no occurrence in either group
22	Canonico S et al	Prospective	Stripping of Greater saphenous vein	18	Butyl TCA	Dehiscence - no occurrence reported
24	Cheng W, Saing H.	Prospective Randomized	Circumcision		Butyl-TCA v suture	Dehiscence - no significant difference
25	Coulthard P et al	Review	8 RCTs analyzed	630	Tape vs. TCAs	Dehiscence - no significant difference
26	Craven NM, Telfer NR.	Pilot then Prospective	Skin grafting	21 (TCA=13 Suture=8)	Butyl TCA vs. suture	Dehiscence - none reported
37	Farion K et al	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples / adhesive strips	Dehiscence - statistically significant risk differences were found favoring std wound care
38	Farion K et al	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples / adhesive strips	Dehiscence - increased risk when pooling all studies
40	Ferlise VJ et al	Retrospective chart review	Inguinal	52 incisions (TCA=25 suture=27)	Octyl TCA vs. suture	Dehiscence - none reported
43	Gennari R et al	Prospective Randomized	Breast surgery	133 (TCA=69 suture=64)	Octyl TCA (Dermabond) vs. sutures	Dehiscence - no reported difference
50	Harold KL et al	Prospective Randomized	Laparoscopic trocar	48 pts (137 wounds) (TCA=40 suture=49 tape=48)	Octyl TCA vs. suture vs. tape	Dehiscence - octyl TCA inferior to suture
51	Helbling C, Schlumpf R.	Prospective Randomized	Inguinal hernia repair	46 (TCA=24 suture=22)	Butyl TCA vs. suture	No adhesive complications seen
55	Jallali N et al	Prospective Randomized	Laparoscopic chole	25 pts (51 wounds closed with suture and 48 wounds closed with TCA)	Octyl TCA (Dermabond) vs. sutures	Dehiscence - no significant difference
65	Maartense S et al	Prospective Randomized	Laparoscopic trocar	140 (TCA=48 suture=50 tape=42)	Octyl TCA vs. suture vs. tape	Dehiscence - no significant difference
69	Matin SF.	Prospective Randomized	Laparoscopic port	92 (TCA=50, suture= 42)	Octyl TCA vs. suture	Dehiscence - no significant difference

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
76	Nahas FX et al	Prospective	Body contouring Mammoplasty & abdominal surgery	37 (1 side of body treated with TCA other treated with sutures)	Octyl TCA (Dermabond) vs. subcuticular sutures	Dehiscence - no significant differences reported
84	Pachulski R et al	Retrospective Review	Cardiac	585 (TCA=125 suture=335)	Octyl TCA vs. suture	Dehiscence - none reported
90	Qureshi A et al	Prospective	General gastrointestinal surgery	102	n-butyl TCA	1/102 pts had small superficial skin dehiscence; no wound infections; overall complication rate was 1.2%. "safe and reliable method of general abdominal wound closure"
92	Resch KL, Hick JL.	Retrospective and concurrent chart review	Pediatric ER	100	Octyl TCA (Dermabond)	Only 3/100 had complications(1 was dehiscence) Parents preferred TCA to sutures Closure Time - reduced from 106min to 69min on average (P<0.0001)
95	Rosin D et al	Prospective	Laparoscopic	100 pts (250 wound sites)	TCA	Only one infection, 2 dehiscence reported. Cosmesis were excellent and pt satisfaction was high as no suture removal. Glue application was easy and quick.
98	Saxena AK, Willital GH.	Prospective Randomized	Pediatric extremity lacerations	64 (32 in each group)	Octyl TCA vs. sutures	Dehiscence - 2 occurred in adhesive group but closed w/o adverse outcome
99	Schonauer F et al		Pediatric wound closure	56	Butyl TCA	Dehiscence - none reported
100	Sebesta MJ, Bishoff JT	Prospective Randomized	Laparoscopic trocar sites		Octyl TCA vs. subcuticular sutures	Dehiscence - no reported difference
101	Shamiyeh A et al	Prospective Randomized	Phlebectomy	79 (TCA=26, suture=28, tape=25)	Octyl TCA vs. suture vs. tape	Dehiscence - no significant difference
102	Shorr N et al	Prospective	Eyelid skin grafts	18	Butyl TCA	Dehiscence - no incidences reported
107	Singer AJ et al	Prospective Randomized	Laceration and incision closure	814 wounds (TCA=406 Std=408)	Octyl TCA vs. std of care	Dehiscence - no significant difference
108	Singer AJ et al	Review	5 RCTs analyzed	NA	Octyl TCA vs. sutures	Dehiscence - no significant difference
109	Sinha S et al	Prospective Randomized	Hand surgery		n-butyl TCA vs. suture	Dehiscence - no significant difference
115	Turkaslan T et al	Prospective	Cleft palate	15	Butyl TCA	Dehiscence - none reported No AEs reported
116	van den Ende ED et al	Prospective Randomized	Pediatric groin incisions	100 (50 in each group)	Butyl TCA vs. suture	Dehiscence - butyl TCA inferior to sutures
119	Yavuzer R et al	Correspondence	Breast surgery	10	Octyl and Butyl TCA	No cases of wound dehiscence reported during follow-up (1yr)

Table 4: Literature on Wound Cosmesis

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
4	Amiel GE et al	Retrospective	General surgery	1098	n-butyl TCA	Cosmesis - satisfaction high with a score of 4.73 out of 5 (94.6%)
7	Barnett P et al	Prospective Randomized	Pediatric lacerations	163 (TCA=83 Suture-80)	TCA vs. sutures	Cosmesis - no difference reported
10	Bernard L et al	Prospective comparison with blinded assessment	Excisional wounds	42 (28 suture/24 TCA)	OCA vs. suture	Cosmesis - conventional sutures reported to be superior
16	Brown V.	Randomized	Pediatric lacerations	61 (32 completed f/u - TCA=17 suture=15)	TCA vs. sutures	Cosmesis - at 2 months TCA was reported to be superior No differences in complications
17	Bruns TB et al	Randomized	Pediatric lacerations	83 (TCA = 42 suture = 41)	Octyl TCA vs. sutures/staples	Cosmesis - no significant difference
18	Bruns TB et al	Prospective Randomized	Pediatric lacerations	61 (TCA = 30 suture = 31)	TCA vs. sutures	Cosmesis - TCA assessed to be as good as or better than suture as evaluated by 2 physicians Parents assessment of pain felt by child in TCA was less but not significantly different
22	Canonico S et al	Prospective	Stripping of Greater saphenous vein	18	Butyl TCA	Cosmesis - pts found that this was a very acceptable procedure for cosmetic results and because no dressing was necessary
24	Cheng W, Saing H.	Prospective Randomized	Circumcision		Butyl-TCA v suture	Cosmesis - no significant difference
25	Coulthard P et al	Review	8 RCTs analyzed	630	Tape vs. TCAs	Cosmesis - no significant difference
26	Craven NM, Telfer NR.	Pilot then Prospective	Skin grafting	21 (TCA=13 Suture=8)	Butyl TCA vs. suture	Cosmesis - excellent in all cases (TCA)
28	Dalvi A, Faria M, Pinto A.	Retrospective	Planned general surgery (incision length 3-17cm)	TCA = 30 Suture = 25	TCA vs. sutures	Cosmesis - linear scar (TCA) cross hatching (suture)
31	Eaglstein WH, Sullivan T.	Review	NA	NA	review of cyanoacrylates	Cosmesis - equivalent or superior to suturing
37	Farion K et al	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples / adhesive strips	Cosmesis - no significant difference
38	Farion K et al	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples / adhesive strips	Cosmesis - no significant difference
40	Ferlise VJ et al	Retrospective chart review	Inguinal	52 incisions (TCA=25 suture=27)	Octyl TCA vs. suture	Cosmesis - identical between groups
43	Gennari R et al	Prospective Randomized	Breast surgery	133 (TCA=69 suture=64)	Octyl TCA (Dermabond) vs. sutures	Cosmesis - no reported difference
45	Goktas N et al	Prospective randomized	Adult lacerations	92	TCA vs. suture	Cosmesis - no significant difference

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
46	Gosain AK, Lyon VB.	Review	adhesion of soft tissue	NA	Octyl TCA (Dermabond)	Cosmesis - no reported difference between TCA and sutures; rated less painful by pts undergoing repair of cutaneous lacerations
47	Greene D et al .	Prospective controlled	Blepharoplasty			Cosmesis - no significant difference; pts preferred glue
48	Hall LT, Bailes JE	Retrospective Review	Lumbar and Cervical Neurosurgery	200	Octyl TCA	Dermabond save to use in lumbar/cervical neurosurgeries. 1/200 had an infection. Pts able to shower, no suture/staple removal. Pt response = positive
50	Harold KL et al	Prospective Randomized	Laparoscopic trocar	48 pts (137 wounds) (TCA=40 suture=49 tape=48)	Octyl TCA vs. suture vs. tape	Cosmesis - Octyl TCA inferior to suture
52	Holger JS et al	Prospective Randomized	Facial lacerations	150 (TCA=49 absorbable sutures=49 non-absorbable suture=47)	TCA vs. absorbable sutures/non-absorbable sutures	Cosmesis - no clinically important differences
53	Hollander JE, Singer AJ.	Prospective Randomized	Facial lacerations	124 (TCA=33 Suture=61)	Octyl TCA vs. sutures	Cosmesis - both groups are equivalent - physician learning curve not a factor.
55	Jallali N et al	Prospective Randomized	Laparoscopic chole	25 pts (51 wounds closed with suture and 48 wounds closed with TCA)	Octyl TCA (Dermabond) vs. sutures	Cosmesis - no significant difference
58	Keng TM, Bucknall TE.		Groin incisions		Butyls-TCA vs. subcuticular sutures	Cosmesis - TCA significantly better cosmesis
61	King ME, Kinney AY.	Review	NA	NA	NA	Cosmesis - no significant difference between sutures and TCA
65	Maartense S et al	Prospective Randomized	Laparoscopic trocar	140 (TCA=48 suture=50 tape=42)	Octyl TCA vs. suture vs. tape	Cosmesis - TCAs significantly better than tape
66	Magee WP Jr et al	Retrospective	Cleft lip repair	64	Octyl TCA vs. suture vs. tape	shorter operative time, formation of a protective barrier, simplified incision care, no need for suture removal, improved scar outcome
69	Matin SF.	Prospective Randomized	Laparoscopic port	92 (TCA=50, suture= 42)	Octyl TCA vs. suture	Cosmesis - no significant difference
70	Mattick A et al	Randomized	Pediatric laceration repair	60 (30 in each group)	Octyl TCA vs. steristrips	Cosmesis - no significant difference
71	Mattick A.	Review	Pediatric lacerations	NA	butyl TCA (dermabond) with histoacryl and steristrips	no significant difference in cosmesis between Dermabond and steristrips

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
72	Maw JL et al	Prospective comparison with blinded assessment	Head and neck incisions	TCA = 24 Suture = 26	Octyl TCA vs. subcuticular suture	Cosmesis - no significant difference
73	McKinley SH, Yen MT.	Retrospective review	External Dacryocystorhinostomy (closing cutaneous incisions)	21	Octyl TCA	TCA applied w/out complications, all pts had excellent wound closure, no infections noted, 1 pt had dehiscence, one had hypertrophic scar formation. Deemed safe, quick, does not compromise wound integrity, provides aesthetic result and potentially safer and more convenient
75	Morton RJ et al	Prospective evaluation	Scalp wounds	50 wounds	Butyl TCA	only 1/50 did not achieve complete healing at review; advantages include speed and ease of application, painless, does not require local anesthesia, no return visit required
76	Nahas FX et al	Prospective	Body contouring Mammoplasty & abdominal surgery	37 (1 side of body treated with TCA other treated with sutures)	Octyl TCA (Dermabond) vs. subcuticular sutures	Cosmesis - no significant differences reported
77	Nouri K et al	Vignette	Dehiscence of surgical wounds	1	Octyl TCA	Octyl TCA used to close surgical wound (dehiscence) instead of another surgery. Healed with good cosmesis. Advantages, reduced pain and anxiety, no follow-up visit, less expensive.
79	Ong CC et al	Prospective Randomized	Pediatric surgical incisions	59 (TCA=26 suture=33)	Octyl TCA vs. subcuticular suture	Cosmesis - equally good cosmesis
83	Ozturan O et al	Prospective Randomized	Colmellular incision (rhinoplasty)	101 (TCA=34 suture-67)	Butyl-TCA vs. suture	Cosmesis - trend towards better cosmesis with TCA
84	Pachulski R et al	Retrospective Review	Cardiac	585 (TCA=125 suture=335)	Octyl TCA vs. suture	Cosmesis - both groups achieved adequate results
86	Petratos PB et al	Prospective	Circumcision	10 (5 in each group)	Octyl TCA+ suture vs. suture	Cosmesis - optimal wound healing reported in all groups - no scarring in TCA
88	Quinn J et al	Prospective Randomized	Traumatic lacerations	136 (TCA=68 Suture=68)	TCA vs. sutures	Cosmesis - no differences noted in the cosmetic outcomes (long-term study - 1yr)
89	Quinn J et al	Prospective Randomized	Pediatric facial lacerations	81 (TCA=37 Suture=38)	TCA vs. sutures	Cosmesis - no significant difference
95	Rosin D et al	Prospective	Laparoscopic	100 pts (250 wound sites)	TCA	Cosmesis were excellent and pt satisfaction was high as no suture removal.
97	Santibanez-Gallerani A et al	Report	NA	20 wounds	Octyl TCA	No tissue damage, decrease in wound strength or associated discoloration/fuzziness onto skin, esthetic results were considered good to excellent using new fine-tip applicator

#	Author	Study Type	Surgery Type	# of Patients	Comparison	Results
98	Saxena AK, Willital GH.	Prospective Randomized	Pediatric extremity lacerations	64 (32 in each group)	Octyl TCA vs. sutures	Cosmesis - no significant difference
101	Shamiyeh A et al	Prospective Randomized	Phlebectomy	79 (TCA=26, suture=28, tape=25)	Octyl TCA vs. suture vs. tape	Cosmesis - no significant difference
102	Shorr N et al	Prospective	Eyelid skin grafts	18	Butyl TCA	Cosmesis - acceptable
103	Simon HK et al	Prospective Randomized	Pediatric lacerations	61 (TCA=30 Sutures=31)	TCA vs. sutures	Cosmesis - comparable if not better outcome for TCA at 2 months: at one year they were comparable
104	Simon HK et al	Retrospective analysis	Facial lacerations from a prospective randomized study	TCA = 30 Suture = 31	TCA vs. sutures	Cosmesis - no significant difference (TCA may be the preferred method of cutaneous closure for facial lacerations oriented against Langer's lines.)
106	Singer AJ et al	Prospective Randomized	Laceration repair	TCA = 63 Suture = 61	Octyl TCA vs. standard wound closure	Cosmesis - both groups have similar cosmetic appearance at 3-months
107	Singer AJ et al	Prospective Randomized	Laceration and incision closure	814 wounds (TCA=406 Std=408)	Octyl TCA vs. std of care	Cosmesis - no significant difference
108	Singer AJ et al	Review	5 RCTs analyzed	NA	Octyl TCA vs. sutures	Cosmesis - no significant difference
109	Sinha S et al	Prospective Randomized	Hand surgery		n-butyl TCA vs. suture	Cosmesis - no significant difference
110	Switzer EF et al	Prospective Randomized	Inguinal hernia repair	46 (TCA=24 suture=22)	Octyl TCA vs. subcuticular sutures	Cosmesis - no significant difference (however suture group scored better 4.2 vs. 3.88)
112	Toriumi DM, Bagal AA.	Information	NA	NA	NA	effective method for closure of facial lacerations
113	Toriumi DM et al	Prospective Randomized	Facial plastic surgery	111 (TCA = 49 Suture = 51)	Octyl TCA vs. sutures	Cosmesis - OCA significantly improved cosmesis score
116	van den Ende ED et al	Prospective Randomized	Pediatric groin incisions	100 (50 in each group)	Butyl TCA vs. suture	Cosmesis - butyl TCA inferior to sutures
118	Wang MY et al	Prospective	Neurosurgical operations	102 (142 incisions)	octyl TCA	of 102 pts only 1 had poor cosmetic result - no other pt complaints regarding wound care or cosmesis.
119	Yavuzer R et al	Correspondence	Breast surgery	10	Octyl and Butyl TCA	no cases of wound dehiscence, infection or unacceptable scars during follow-up (1yr)
120	Zafar F et al	Short Note	Circumcision	60	Butyl TCA (histoacryl)	Cosmesis - excellent at 2weeksNo incidence of wound breakdown (only 1 infection reported) no AEs reported. Quick and easy to use over suturing
121	Zempsky WT et al	Prospective Randomized	Facial Lacerations	97 (TCA=49 steristrips=48)	Octyl TCA vs. Steristrips	Cosmesis - no significant difference

Table 5: Tissue Adhesive Literature Review

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
1	No authors listed	Cyanoacrylate tissue adhesive and facial lacerations. BMJ. 1989 Nov 11;299(6709):1217-8.	1989	Letter	General surgery	43 (TCA=22 Control=21)	TCA with traditional closure methods	TCA applied by nurses - found it's use was easy to learn and it was a preferable option for many wounds
2	No authors listed	DERMABOND topical skin adhesive. Int J Trauma Nurs. 1999 Jan-Mar;5(1):29-31.	1999					*Not able to review – article not able to be located*
3	Alio JL et al	Use of cyanoacrylate tissue adhesive in small-incision cataract surgery. Ophthalmic Surg Lasers. 1996 Apr;27(4):270-4	1996	Controlled	Cataract		TCA+suture vs. suture	at postop Stigmatism less in TCA+suture group at 12 weeks both groups the same. No complications reported.
4	Amiel GE et al	Use of N-butyl-2-cyanoacrylate in elective surgical incisions—longterm outcomes. J Am Coll Surg. 1999 Jul;189(1):21-5.	1999	Retrospective	General surgery	1098	n-butyl TCA	**Dehiscence** - occurred in only 1.1% **Cosmesis** - satisfaction high with a score of 4.73 out of 5 (94.6%) **AE –** 5.5% of pts reported redness or tenderness at incision site; 0.5% had swelling at site.
5	Applebaum JS et al	The use of tissue adhesion for traumatic laceration repair in the emergency department. Ann Emerg Med. 1993 Jul;22(7):1190-2.	1993	Prospective	Traumatic lacerations	143	TCA	71 pts (98.6%) treated stated that they would choose tissue bonding for convenience, comfort - only one preferred suturing. Finding: "tissue bonding is a quick, efficient, and painless method of closure for lacerations." **AE**: Infectious complications were cited on 3 occasions.
6	Atkinson P.	Tissue adhesive with adhesive strips for wound closure. Emerg Med J. 2003 Sep;20(5):498.	2003	Letter	NA	NA	use of TCA with adhesive strips	Wounds can be closed using adhesive strips along with TCA effectively
7	Barnett P et al	Randomized trial of histoacryl blue tissue adhesive glue versus suturing in the repair of pediatric lacerations. J Pediatric Child Health. 1998 Dec;34(6):548-50.	1998	Prospective Randomized	Pediatric lacerations	163 (TCA=83 Suture-80)	TCA vs. sutures	**Closure Time** - 0-2min(TCA) 6-10min(suture) $p<0.001$ **Cosmesis** - no difference reported Drs and nurses rated glue as less painful but children rated the pain the same ($p=0.24$) **AE**: no difference between groups in amount of redness, dehiscence or discharge.

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
8	Barto W.	Randomized study of the effectiveness of closing laparoscopic trocar wounds with octylcyanoacrylate, adhesive papertape or poliglecaprone (Br J Surg 2002; 89: 1370-1375). Br J Surg. 2003 Mar;90(3):369.	2002	Randomized				*Not able to review*
9	Becker C	Sewing up 'liquid stitches'; Dermabond ad campaign aims straight at consumer Modern Healthcare 2002 Volume 32	2002	Comment on dressing	NA	NA	Octyl TCA	Downside - "it may not be appropriate for all types of wounds or skin services"
10	Bernard L et al	A prospective comparison of octyl cyanoacrylate tissue adhesive (dermabond) and suture for the closure of excisional wounds in children and adolescents. Arch Dermatol. 2001 Sep;137(9):1177-80.	2001	Prospective comparison with blinded assessment	Excisional wounds	42 (28 suture/24 TCA)	OCA vs. suture	**Cosmesis** - conventional sutures reported to be superior **AE** – no infections reported
11	Bhalla RK, Lesser TH.	Simple, painless, cosmetic closure of endaural incisions. J Laryngol Otol. 2003 Jan;117(1):67-8.	2003	Short Communication	Endaural incisions	NA	NA	TCA is a simple, safe and cosmetically equivocal method of closing ear incisions.
12	Blondeel PN et al	Closure of long surgical incisions with a new formulation of 2-octylcyanoacrylate tissue adhesive versus commercially available methods. Am J Surg. 2004 Sep;188(3):307-13.	2004	Prospective Randomized	Long surgical incisions (>4cm)	209 (106=high viscosity TCA 103=commercially available TCA)	Octyl TCA vs. commercially available octyl TCA	**Closure Time** - OCA = S/c or Deep dermal **AE** – wound infection more common in control group but not statistically significant. Incidence of erythema and other indicators of acute inflammation were similar between groups.
13	Borley NR, Mortensen NJ.	Topical adhesive as a wound dressing for elective abdominal surgery. Ann R Coll Surg Engl. 2001 Jul;83(4):285-6.	2001	Comment on dressing	Abdominal surgery	NA	Octyl TCA (Dermabond)	Dressing ideal because: provides additional support (adherent to wound edges), sealed/flexible/water resistant membrane over incision, does not interfere with stoma or drain site dressings, avoids risk of fluid accumulation in skin folds, maintains visibility of wound, requires no maintenance
14	Bowen ML, Selinger M.	Episiotomy closure comparing enbucrilate tissue adhesive with conventional sutures. Int J Gynaecol Obstet. 2002 Sep;78(3):201-5.	2002	Prospective controlled	Episiotomy closure	62 (TCA = 32 suture = 30)	TCA vs. sutures	Pain scores did not differ No wound dehiscence reported

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
15	Branfield AS.	Use of tissue adhesives in sport? A new application in international ice hockey. Br J Sports Med. 2004 Feb;38(1):95-6; discussion 96.	2004	Prospective	Facial lacerations as a result of Hockey games	6	TCA only	Results: dermabond quick to apply (less than 5min). No added covering required. Advantages listed same as article by Bruns TB and Worthingtom JM.
16	Brown V.	Laceration repair with tissue adhesive in children. J Fam Pract. 1997 May;44(5):445-6.	1997	Randomized	Pediatric lacerations	61 (32 completed f/u - TCA=17 suture=15)	TCA vs. sutures	**Cosmesis** - at 2 months TCA was reported to be superior **AE** - No differences in complications no adverse inflammation was reported.
17	Bruns TB et al	A new tissue adhesive for laceration repair in children. J Pediatr. 1998 Jun;132(6):1067-70.	1998	Randomized	Pediatric lacerations	83 (TCA = 42 suture = 41)	Octyl TCA vs. sutures/staples	**Closure Time** - TCA=2.9 min Suture=5.8min (p=<0.01) **Cosmesis** - no significant difference Parents assessment of pain felt by child in TCA was less but not significantly different **AE**: TCA – 1 wound infection..
18	Bruns TB et al	Laceration repair using a tissue adhesive in a children's emergency department. Pediatrics. 1996 Oct;98(4 Pt 1):673-5	1996	Prospective Randomized	Pediatric lacerations	61 (TCA = 30 suture = 31)	TCA vs. sutures	**Dehiscence** - no occurrence in either group **Closure Time** - TCA=7 min Suture=17min **Cosmesis** - TCA assessed to be as good as or better than suture as evaluated by 2 physicians Parents assessment of pain felt by child in TCA was less but not significantly different **AE**: TCA – 1 wound infection..
19	Bruns TB, Worthington JM.	Using tissue adhesive for wound repair: a practical guide to dermabond. Am Fam Physician. 2000 Mar 1;61(5):1383-8.	2000	Review of Dermabond	NA	NA	NA	Advantages of TCA vs. sutures: max bonding strength @ 2.5min, equivalent in strength to healed tissue @ 7days postop, needles not required (no anesthetic needed), faster repair time, better acceptance by patients, water resistant, removal of sutures not required.
20	Burchett N.	Cyanoacrylate tissue adhesive. Arch Emerg Med. 1991 Jun;8(2):155-6.	1991	Letter/Case Study	fixation of pre-tibial flap lacerations	3 case studies	TCA vs. steristrips	None
21	Calnan CD.	Cyanoacrylate dermatitis. Contact Dermatitis. 1979 May;5(3):165-7.	1979					*Not able to review – article not able to be located.*

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
22	Canonico S et al	Sutureless skin closure in varicose vein surgery: preliminary results. Dermatol Surg. 2001 Mar;27(3):306-8.	2001	Prospective	Stripping of Greater saphenous vein	18	Butyl TCA	**Dehiscence** - no occurrence reported **Closure Time** - mean time to close 117 sec **Cosmesis** - pts found that this was a very acceptable procedure for cosmetic results and because no dressing was necessary
23	Charters A.	Wound glue: a comparative study of tissue adhesives. Accid Emerg Nurs. 2000 Oct;8(4):223-7.	2000	Prospective, nonblinded	Lacerations	63	Indermil, Liquiband, Dermabond	Liquiband - average pain score was 0.1 whereas Dermabond was 0.97; nurses reported that Liquiband was the "best tissue adhesive in terms of closure and ease of use". Indermil was the only TCA to report 10% success
24	Cheng W, Saing H.	A prospective randomized study of wound approximation with tissue glue in circumcision in children. J Pediatric Child Health. 1997 Dec;33(6):515-6.	1997	Prospective Randomized	Circumcision		Butyl-TCA v suture	**Dehiscence** - no significant difference **Cosmesis** - no significant difference
25	Coulthard P et al	Tissue adhesives for closure of surgical incisions. Cochrane Database Syst Rev. 2004;(2):CD004287.	2004	Review	8 RCTs analyzed	630	Tape vs. TCAs	**Dehiscence** - no significant difference **Cosmesis** - no significant difference **AE:** no significant difference
26	Craven NM, Telfer NR.	An open study of tissue adhesive in full-thickness skin grafting. J Am Acad Dermatol. 1999 Apr;40(4):607-11.	1999	Pilot then Prospective	Skin grafting	21 (TCA=13 Suture=8)	Butyl TCA vs. suture	**Dehiscence** - none reported **Cosmesis** - excellent in all cases (TCA)
27	Cuschieri A.	Tissue adhesives in endosurgery. Semin Laparosc Surg. 2001 Mar;8(1):63-8.	2001					*Not able to review – article not able to be located.*
28	Dalvi A, Faria M, Pinto A.	Non-suture closure of wound using cyanoacrylate. J Postgrad Med. 1986 Apr;32(2):97-100.	1986	Retrospective	Planned general surgery (incision length 3-17cm)	TCA = 30 Suture = 25	TCA vs. sutures	**Closure Time** - 30-45sec(TCA) **Cosmesis** - linear scar (TCA) cross hatching (suture) **AE**: "wound infection has been shown to be more in suture technique"
29	de Blanco LP.	Lip suture with isobutyl cyanoacrylate. Endod Dent Traumatol. 1994 Feb;10(1):15-8.	1994	Case Study	Lip sutures	2	Butyl TCA	Able to use in dental/lip situations. Advantage - hemostatis, no delay in wound healing and repair

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
30	Doraiswamy NV et al	Which tissue adhesive for wounds? Injury. 2003 Aug;34(8):564-7.	2003	Prospective	Pediatric lacerations	51 (17 in each group)	Dermabond, Histoacryl, Indermil	Parents preferred TA to suturing or steristrips. No difference in gluing effect, application not easy due to movement of head
31	Eaglstein WH, Sullivan T.	Cyanoacrylates for skin closure. Dermatol Clin. 2005 Apr;23(2):193-8.	2005	Review	NA	NA	review of cyanoacrylates	**Cosmesis** - equivalent or superior to suturing
32	Eaglstein WH et al	A liquid adhesive bandage for the treatment of minor cuts and abrasions. Dermatol Surg. 2002 Mar;28(3):263-7.	2002	Prospective Randomized	Minor cuts and abrasions	162 (81 in each group)	Octyl TCA or bandaid	Safe and easy to use - controlled bleeding, stayed on wounds well, pts found it superior to the bandaid in terms of protection during daily activities, no dressing changes required.
33	Eiferman RA, Snyder JW.	Antibacterial effect of cyanoacrylate glue. Arch Ophthalmol. 1983 Jun;101(6):958-60.	1983	Case Study	Corneal perforations	2	antibacterial effect of Histoacryl	ineffective against gram (-) microorganisms but effective against gram (+) strains
34	Ellis DA, Shaikh A.	The ideal tissue adhesive in facial plastic and reconstructive surgery. J Otolaryngol. 1990 Feb;19(1):68-72.	1990	Retrospective Review	Facial plastic and reconstructive surgery	Fibrin Glue = 23 TCA = 108	Fibrin glue (Tisseel) vs. n-butyl TCA (Histoacryl)	TCA group had good results in 100%: Fibrin glue had 81% good results No postop complications were seen in the healing of the wounds – no instances of infection.
35	Elmasalme FN et al	Use of tissue adhesive in the closure of small incisions and lacerations. J Pediatr Surg. 1995 Jun;30(6):837-8.	1995	Retrospective Review	Small incisions and lacerations in pediatric pts	3274 surgery 2650 lacerations	Butyl TCA (histoacryl)	*cuts short anesthesia time by up to *local anesthesia not required *of the 3274 only 12 failures due to leaking into wound *of the 2650 there were 36 failures due to infection
36	England RJ et al	Does indermil glue improve success rates in myringoplasty? Interim analysis of a prospective trial. Rev Laryngol Otol Rhinol (Bord). 2000;121(2):91-3.	2000	Prospective	Myringoplasty (ear)	15	Butyl TCA	effective in ear graft fixations, not ototoxic,
37	Farion K et al	Tissue adhesives for traumatic lacerations in children and adults. Cochrane Database Syst Rev. 2002;(3):CD003326.	2002	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples/ adhesive strips	**Dehiscence** - statistically significant risk differences were found favoring std wound care **Closure Time** - decreased procedure time and less pain **Cosmesis** - no significant difference

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38	Farion K et al	Tissue adhesives for traumatic lacerations: a systematic review of randomized controlled trials. Acad Emerg Med. 2003 Feb;10(2):110-8.	2003	Review	8 RCTs reviewed	NA	TCA vs. sutures/staples/ adhesive strips	**Dehiscence** - increased risk when pooling all studies **Closure Time** - decreased procedure time and less pain **Cosmesis** - no significant difference
39	Farouk R et al	Preliminary experience with butyl-2-cyanoacrylate adhesive in tension-free inguinal hernia repair. Br J Surg. 1996 Aug;83(8):1100.	1996	Note	Hernia repair	21	use of TCA to fix mesh and close external oblique	The use of TCA has no risk of periostitis, muscle ischemia or accidental injure of vessels. Closure time is rapid without risk of injury to pt or surgeon and the adhesive acts as a sterile dressing
40	Ferlise VJ et al	Use of cyanoacrylate tissue adhesive under a diaper. BJU Int. 2001 May;87(7):672-3.	2001	Retrospective chart review	Inguinal	52 incisions (TCA=25 suture=27)	Octyl TCA vs. suture	**Dehiscence** - none reported **Cosmesis** - identical between groups **AE**: no instances of infection
41	Fisher AA.	Reactions to cyanoacrylate adhesives: "instant glue". Cutis. 1985 Jan;35(1):18, 20, 22 passim.	1985	NA	NA	NA		background information on skin reactions due to TCA
42	Gallemore RP et al	Use of isobutyl cyanoacrylate tissue adhesive to stabilize mucous membrane grafts in total socket reconstruction. Ophthal Plast Reconstr Surg. 1999 May;15(3):210-2.	1999		Eye socket reconstruction	1	TCA	TCA is simpler and quicker than suturing a mucous membrane graft
43	Gennari R et al	A prospective, randomized, controlled clinical trial of tissue adhesive (2-octylcyanoacrylate) versus standard wound closure in breast surgery. Surgery. 2004 Sep;136(3):593-9.	2004	Prospective Randomized	Breast surgery	133 (TCA=69 suture=64)	Octyl TCA (Dermabond) vs. sutures	**Dehiscence** - no reported difference **Closure Time** - P<0.01 significance **Cosmesis** - no reported difference **AE –** "several pts in the suture group exhibited increased inflammation and erythema around incision site, whereas TCA caused less tissue reaction. No instances of infection in either group.
44	Gerrard C et al	Biological tissue adhesive for multiple use in the accident and emergency department. J Accid Emerg Med. 2000 Sep;17(5):341-3.	2000	Bench Testing	Not human study- bench testing of strength and microbial properties of cyanoacrylate		na	TCA shows no deterioration in strength over time and there is no evidence of microbial contamination of the glue over 28 days

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45	Goktas N et al	Comparison of tissue adhesive and suturing in the repair of lacerations in the emergency department. Eur J Emerg Med. 2002 Jun;9(2):155-8.	2002	Prospective randomized	Adult lacerations	92	TCA vs. suture	**Cosmesis** - no significant difference
46	Gosain AK, Lyon VB.	The current status of tissue glues: part II. For adhesion of soft tissues. Plast Reconstr Surg. 2002 Nov;110(6):1581-4.	2002	Review	adhesion of soft tissue	NA	Octyl TCA (Dermabond)	**Closure Time** - significantly decreased time of repair with TCA vs. sutures **Cosmesis** - no reported difference between TCA and sutures; rated less painful by pts undergoing repair of cutaneous lacerations
47	Greene D et al .	Efficacy of octyl-2-cyanoacrylate tissue glue in blepharoplasty. A prospective controlled study of wound-healing characteristics. Arch Facial Plast Surg. 1999 Oct-Dec;1(4):292-6	1999	Prospective controlled	Blepharoplasty			**Closure Time** - 8min(TCA) 7min(Suture) **Cosmesis** - no significant difference; pts preferred glue
48	Hall LT, Bailes JE	Using Dermabond for Wound Closure in Lumbar and Cervical Neurosurgical Procedures OperNeuros Jan 2005(56); 147-150	2005	Retrospective Review	Lumbar and Cervical Neurosurgery	200	Octyl TCA	Dermabond safe to use in lumbar/cervical neurosurgeries. 1/200 had an infection. Pts able to shower, no suture/staple removal. Pt response = positive Only one pt had a wound infection and one pt had transient incisional erythema
49	Hallock GG.	Expanded applications for octyl-2-cyanoacrylate as a tissue adhesive. Ann Plast Surg. 2001 Feb;46(2):185-9.	2001	Prospective Review	NA	92 pts (102 encounters)	Octyl TCA	Off label use discussion.
50	Harold KL et al	Optimal closure method of five-millimeter trocar sites. Am J Surg. 2004 Jan;187(1):24-7.	2004	Prospective Randomized	Laparoscopic trocar	48 pts (137 wounds) (TCA=40 suture=49 tape=48)	Octyl TCA vs. suture vs. tape	**Dehiscence** - octyl TCA inferior to suture **Closure Time** - 34.7±24.5sec each wound (TCA) 43.1±21.4sec (sutures) 33.4±20.8sec (tape): sutures significantly longer than TCA or tape **Cosmesis** - Octyl TCA inferior to suture
51	Helbling C, Schlumpf R.	Sutureless Lichtenstein: first results of a prospective randomized clinical trial. Hernia. 2003 Jun;7(2):80-4. Epub 2003 Jan 30.	2003	Prospective Randomized	Inguinal hernia repair	46 (TCA=24 suture=22)	Butyl TCA vs. suture	No adhesive complications seen

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52	Holger JS et al	Cosmetic outcomes of facial lacerations repaired with tissue-adhesive, absorbable, and nonabsorbable sutures. Am J Emerg Med. 2004 Jul;22(4):254-7.	2004	Prospective Randomized	Facial lacerations	150 (TCA=49 absorbable sutures=49 non-absorbable suture=47)	TCA vs. absorbable sutures/non-absorbable sutures	**Cosmesis** - no clinically important differences **AE**: 1 wound infection reported in suture group.
53	Hollander JE, Singer AJ.	Application of tissue adhesives: rapid attainment of proficiency. Stony Brook Octylcyanoacrylate Study Group. Acad Emerg Med. 1998 Cot's(10):1012-7.	1998	Prospective Randomized	Facial lacerations	124 (TCA=33 Suture=61)	Octyl TCA vs. sutures	**Cosmesis** - both groups are equivalent - physician learning curve not a factor.
54	Jailbait M.	Topical adhesive as a wound dressing for elective abdominal surgery. Ann R Coll Surg Engl. 2002 May;84(3):221; author reply 221.	2002					*Not able to review – article not able to be located.*
55	Jallali N et al	A prospective randomized trial comparing 2-octyl cyanoacrylate to conventional suturing in closure of laparoscopic cholecystectomy incisions. J Laparoendosc Adv Surg Tech A. 2004 Aug;14(4):209-11.	2004	Prospective Randomized	Laparoscopic chole	25 pts (51 wounds closed with suture and 48 wounds closed with TCA)	Octyl TCA (Dermabond) vs. sutures	**Dehiscence** - no significant difference **Closure Time** - 165sec (TCA) 356sec(control); P=0.03 **Cosmesis** - no significant difference
56	Jourdan IC, Bailey ME.	Initial experience with the use of N-butyl 2-cyanoacrylate glue for the fixation of polypropylene mesh in laparoscopic hernia repair. Surg Laparosc Endosc. 1998 Aug;8(4):291-3.	1998	Prospective	Hernia repair	6 (7 incisions)	use of TCA to fix mesh during laparoscopic repair	Mesh successfully fixed with glue; no complications; at f/u pts were comfortable; no evidence of recurrence.
57	Kamer FM, Joseph JH.	Histoacryl. Its use in aesthetic facial plastic surgery. Arch Otolaryngol Head Neck Surg. 1989 Feb;115(2):193-7.	1989	Historical Review	Facial plastic surgery	100	Butyl TCA	safe, reliable, and cost-effective alternative to conventional wound closure techniques
58	Keng TM, Bucknall TE.	A clinical trial of tissue adhesive (histoacryl) in skin closure of groin wounds. Med J Malaysia. 1989 Jun;44(2):122-8.	1989		Groin incisions		Butyls-TCA vs. subcuticular sutures	**Cosmesis** - TCA significantly better cosmesis

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59	Kilic A, Ozdengil E.	Skin graft fixation by applying cyanoacrylate without any complication. Plast Reconstr Surg. 2002 Jul;110(1):370-1.	2002	Letter	Skin grafts	NA		TCA can be used effectively in skin grafts because it is rapid and suture-free. No side effects because applied to healthy skin, cheaper materials, no need to remove stitches.
60	Kim BS et al	N-butyl cyanoacrylate glue embolization of splenic artery aneurysms. J Vasc Interv Radiol. 2004 Jan;15(1 Pt 1):91-4.	2004					*Not able to review – article not able to be located.*
61	King ME, Kinney AY.	Tissue adhesives: a new method of wound repair. Nurse Pract. 1999 Oct;24(10):66, 69-70, 73-4.	1999	Review	NA	NA	NA	faster, less painful more economical than suturing **Cosmesis** - no significant difference between sutures and TCA
62	Labas P et al	Pancreatic duct occlusion with acrylic glue after pancreas resection. Przegl Lek. 2003;60(12):789-91.	2003	Retrospective review	Pancreatic resections	61	NA	use of TCA in the main duct is safe and effective
63	Lee KW et al	An alternate technique to close neurosurgical incisions using octylcyanoacrylate tissue adhesive. Pediatr Neurosurg. 1999 Aug;31(2):110-4.	1999	Technical note	facial lacerations	2 case studies	review of cyanoacrylates	Use of TCA eliminates the need for post-of dressing, dressing changes and visit for suture removal
64	Liebelt EL.	Current concepts in laceration repair. Curr Opin Pediatr. 1997 Oct;9(5):459-64.	1997					*Not able to review – article not able to be located.*
65	Maartense S et al	Randomized study of the effectiveness of closing laparoscopic trocar wounds with octylcyanoacrylate, adhesive papertape or poliglecaprone. Br J Surg. 2002 Nov;89(11):1370-5.	2002	Prospective Randomized	Laparoscopic trocar	140 (TCA=48 suture=50 tape=42)	Octyl TCA vs. suture vs. tape	**Dehiscence** - no significant difference **Closure Time** - 33sec(TCA) 65sec(sutures) **Cosmesis** - TCAs significantly better than tape **AE –** wound infection highest in TCA group (10%) However no statistical difference between groups.
66	Magee WP Jr et al	Use of octyl-2-cyanoacrylate in cleft lip repair. Ann Plast Surg. 2003 Jan;50(1):1-5.	2003	Retrospective	Cleft lip repair	64	Octyl TCA vs. suture vs. tape	shorter operative time, formation of a protective barrier, simplified incision care, no need for suture removal, improved scar outcome, no allergic reactions were reported.
67	Malyon AD et al	Use of tissue glue in field situations. J R Army Med Corps. 1999 Jun;145(2):78-9.	1999					*Not able to review – article not able to be located.*

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68	Martin-Garcia RF et al	Octyl-2-cyanoacrylate liquid bandage as a wound dressing in facial excisional surgery: results of an uncontrolled pilot study. Dermatol Surg. 2005 Jun;31(6):670-3.	2005	Uncontrolled pilot study	Facial excisional surgery	20 pts	Octyl TCA	pilot study proved to be safe and effective in wound dressing Only one AE reported: no signs of infection, poor wound healing, or allergic reaction on remaining wounds. Three pts reported mild transient erythema.
69	Matin SF.	Prospective randomized trial of skin adhesive versus sutures for closure of 217 laparoscopic port-site incisions. J Am Coll Surg. 2003 Jun;196(6):845-53.	2003	Prospective Randomized	Laparoscopic port	92 (TCA=50, suture= 42)	Octyl TCA vs. suture	**Dehiscence** - no significant difference **Closure Time** - 2.5min (TCA) 6min(sutures) **Cosmesis** - no significant difference **AE**: TCA- 5 pts had a wound infection, Suture – 3 pts had a wound infection
70	Mattick A et al	A randomized, controlled trial comparing a tissue adhesive (2-octylcyanoacrylate) with adhesive strips (Steristrips) for pediatric laceration repair. Emerg Med J. 2002 Sep;19(5):405-7.	2002	Randomized	Pediatric laceration repair	60 (30 in each group)	Octyl TCA vs. steristrips	**Closure Time** - individuals performing procedure judged TCA to be more difficult to apply **Cosmesis** - no significant difference
71	Mattick A.	Use of tissue adhesives in the management of pediatric lacerations. Emerg Med J. 2002 Sep;19(5):382-5.	2002	Review	Pediatric lacerations	NA	butyl TCA (dermabond) with histoacryl and steristrips	no significant difference between the Dermabond and Histoacryl no significant difference in cosmesis between Dermabond and steristrips
72	Maw JL et al	A prospective comparison of octylcyanoacrylate tissue adhesive and suture for the closure of head and neck incisions J Otolaryngol. 1997 Feb;26(1):26-30.	1997	Prospective comparison with blinded assessment	Head and neck incisions	TCA = 24 Suture = 26	Octyl TCA vs. subcuticular suture	**Closure Time** - 29.7secs (TCA) 289.0secs(sutures): $p<0.0001$ **Cosmesis** - no significant difference **AE**: no differences in complications between the two groups
73	McKinley SH, Yen MT.	Octyl-2-cyanoacrylate tissue adhesive in external dacryocystorhinostomy. Ophthal Plast Reconstr Surg. 2005 May;21(3):197-200.	2005	Retrospective review	External Dacryocystorhinostomy (closing cutaneous incisions)	21	Octyl TCA	TCA applied w/out complications, all pts had excellent wound closure, no infections noted, 1 pt had dehiscence, one had hypertrophic scar formation. Deemed safe, quick, does not compromise wound integrity, provides aesthetic result and potentially safer and more convenient

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74	Mizrahi S et al	Use of tissue adhesives in the repair of lacerations in children. J Pediatr Surg. 1988 Apr;23(4):312-3.	1988					*Not able to review – article not able to be located.*
75	Morton RJ et al	The use of histoacryl tissue adhesive for the primary closure of scalp wounds. Arch Emerg Med. 1988 Jun;5(2):110-2.	1988	Prospective evaluation	Scalp wounds	50 wounds	Butyl TCA	only 1/50 did not achieve complete healing at review; advantages include speed and ease of application, painless, does not require local anesthesia, no return visit required
76	Nahas FX et al	The use of tissue adhesive for skin closure in body contouring surgery. Aesthetic Plast Surg. 2004 May-Jun;28(3):165-9. Epub 2004 Jul 30.	2004	Prospective	Body contouring Mammoplasty & abdominal surgery	37 (1 side of body treated with TCA other treated with sutures)	Octyl TCA (Dermabond) vs. subcuticular sutures	**Dehiscence** - no significant differences reported **Closure Time** - 2min(TCA), 4min25sec(control - abdo sutures) 7min45sec(control - mamo sutures) **Cosmesis** - no significant differences reported None of the cases presented local inflammatory reactions.
77	Nouri K et al	Octyl-2-cyanoacrylate use for defect closure after wound dehiscence. Arch Dermatol. 2004 Dec;140(12):1541-2.	2004	Vignette	Dehiscence of surgical wounds	1	Octyl TCA	Octyl TCA used to close surgical wound (dehiscence) instead of another surgery. Healed with good cosmesis. Advantages, reduced pain and anxiety, no follow-up visit, less expensive.
78	Nowobilski W et al	Lichtenstein inguinal hernioplasty using butyl-2-cyanoacrylate versus sutures. Preliminary experience of a prospective randomized trial. Eur Surg Res. 2004 Nov-Dec;36(6):367-70.	2004	Prospective Randomized	Hernia repair	46	Butyl TCA vs. suture	TCA group had significantly lower pain score post op. Cost of both procedures was comparable
79	Ong CC et al	Comparing wound closure using tissue glue versus subcuticular suture for pediatric surgical incisions: a prospective, randomized trial. Pediatr Surg Int. 2002 Sep;18(5-6):553-5. Epub 2002 Jun 14.	2002	Prospective Randomized	Pediatric surgical incisions	59 (TCA=26 suture=33)	Octyl TCA vs. subcuticular suture	**Closure Time** - 181±62secs(TCA), 161±45secs(sutures) p=0.68. This was reported as nonsignificant **Cosmesis** - equally good cosmesis **AE**: no pts reported any rash, wound infection or dehiscence.
80	Osmond MH et al	Economic comparison of a tissue adhesive and suturing in the repair of pediatric facial lacerations. J Pediatr. 1995 Jun;126(6):892-5	1995	Cost-minimization analysis	NA	NA	sutures vs. TCA	TCA is the preferred method of closure of pediatric facial lacerations because it is the most efficient and is preferred by pts.

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81	Osmond MH et al	A randomized, clinical trial comparing butylcyanoacrylate with octylcyanoacrylate in the management of selected pediatric facial lacerations. Acad Emerg Med. 1999 Mar;6(3):171-7.	1999	Prospective Randomized	Pediatric facial lacerations	47 in each group	Octyl TCA vs. Butyl TCA	no significant difference between the two groups
82	Ozkan KU et al	Wound approximation with tissue glue in circumcision. Int J Urol. 2005 Apr;12(4):374-7	2005					*Not able to review – article not able to be located.*
83	Ozturan O et al	Butylcyanoacrylate tissue adhesive for columellar incision closure. J Laryngol Otol. 2001 Jul;115(7):535-40.	2001	Prospective Randomized	Colmellular incision (rhinoplasty)	101 (TCA=34 suture-67)	Butyl-TCA (LiquiBand) vs. suture	**Cosmesis** - trend towards better cosmesis with TCA
84	Pachulski R et al	Cardiac device implant wound closure with 2-octyl cyanoacrylate. J Interv Cardiol. 2005 Jun;18(3):185-7.	2005	Retrospective Review	Cardiac	585 (TCA=125 suture=335)	Octyl TCA vs. suture	**Dehiscence** - none reported **Cosmesis** - both groups achieved adequate results **AE**: TCA group had only 1 AE (infections) whereas Suture group had 9 (5 allergy, 3 cellulitis, 1 infection).
85	Perron AD et al	The efficacy of cyanoacrylate-derived surgical adhesive for use in the repair of lacerations during competitive athletics. Am J Emerg Med. 2000 May;18(3):261-3.	2000	Prospective observational	Lacerations during athletic events	32 lacerations (28 hockey players)	Octyl TCA (Dermabond)	31 lacerations were good/excellent 1 was acceptable due to superficial dehiscence
86	Petratos PB et al	Evaluation of octylcyanoacrylate for wound repair of clinical circumcision and human skin incisional healing in a nude rat model. J Urol. 2002 Feb;167(2 Pt 1):677-9.	2002	Prospective	Circumcision	10 (5 in each group)	Octyl TCA+ suture vs. suture	**Closure Time** - TCA shorter vs. suture P<0.001 **Cosmesis** - optimal wound healing reported in all groups - no scarring in TCA
87	Quinn J et al	A randomized trial comparing octylcyanoacrylate tissue adhesive and sutures in the management of lacerations. JAMA. 1997 May 21;277(19):1527-30.	1997	Prospective Randomized	Lacerations	136(TCA=68 Suture=68)	Octyl TCA vs. sutures	No difference in mean visual analog cosmesis score; no difference in wound evaluation scores; TCA was a faster method of wound repair.
88	Quinn J et al	Tissue adhesive versus suture wound repair at 1 year: randomized clinical trial correlating early, 3-month, and 1-year cosmetic outcome. Ann Emerg Med. 1998 Dec;32(6):645-9.	1998	Prospective Randomized	Traumatic lacerations	136 (TCA=68 Suture=68)	Octyl TCA (Dermabond) vs. sutures	**Cosmesis** - no differences noted in the cosmetic outcomes (long-term study - 1yr)

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89	Quinn J et al	A randomized, controlled trial comparing a tissue adhesive with suturing in the repair of pediatric facial lacerations. Ann Emerg Med. 1993 Jul;22(7):1130-5.	1993	Prospective Randomized	Pediatric facial lacerations	81 (TCA=37 Suture=38)	TCA (Histoacryl) vs. sutures	TCA is a faster and less painful method of repair **Cosmesis** - no significant difference **AE**: TCA – 1 pt had an infection and 1 pt had erythema; Suture – 1 pt had an infection and 4 pts reported erythema.
90	Qureshi A et al	n-Butyl cyanoacrylate adhesive for skin closure of abdominal wounds: preliminary results. Ann R Coll Surg Engl. 1997 Nov;79(6):414-5.	1997	Prospective	General gastrointestinal surgery	102	n-butyl TCA	of 102 pts only 1 had small superficial skin dehiscence; no wound **infections**; overall complication rate was 1.2%. "safe and reliable method of general abdominal wound closure"
91	Rajimwale A et al	Octyl-2-cyanoacrylate as a routine dressing after open pediatric urological procedures. J Urol. 2004 Jun;171(6 Pt 1):2407-8.	2004	Prospective	Pediatric urological procedures	146 (200 incisions)	Octyl TCA	All but 1 pt had satisfactory response to appearance of scar Dermabond is a safe and effective barrier that provides water resistance- no need for dressing
92	Resch KL, Hick JL.	Preliminary experience with 2-octylcyanoacrylate in a pediatric emergency department. Pediatr Emerg Care. 2000 Oct;16(5):328-31.	2000	Retrospective and concurrent chart review	Pediatric ER	100	Octyl TCA (Dermabond)	**AE -** Only 3/100 had complications(1 was dehiscence and 2 were wound infections) Parents preferred TCA to sutures **Closure Time** - reduced from 106min to 69min on average (P<0.0001)
93	Roberts AC.	The tissue adhesive indermil and its use in surgery. Acta Chir Plast. 1998;40(1):22-5.	1998	Review	NA	NA	NA	90% of pts would prefer wound closure by an adhesive in relation to traditional sutures.
94	Rogerson L et al	Preliminary experience with twenty perineal repairs using Indermil tissue adhesive. Eur J Obstet Gynecol Reprod Biol. 2000 Feb;88(2):139-42.	2000	Prospective	Perineal repair	20	n-butyl TCA (Indermil)	The advantages are a quick and painless skin closure which with suturing can be uncomfortable.
95	Rosin D et al	Closure of laparoscopic trocar site wounds with cyanoacrylate tissue glue: a simple technical solution. J Laparoendosc Adv Surg Tech A. 2001 Jun;11(3):157-9.	2001	Prospective	Laparoscopic	100 pts (250 wound sites)	TCA	Only one **infection**, 2 **dehiscence** reported. Cosmesis were excellent and pt satisfaction was high as no suture removal. Glue application was easy and quick.

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96	Samuel PR et al	The use of Indermil (n-butyl cyanoacrylate) in otorhinolaryngology and head and neck surgery. A preliminary report on the first 33 patients. J Laryngol Otol. 1997 Jun;111(6):536-40.	1997	Prospective	Otolaryngial, head, neck	33	Butyl TCA	not reported in abstract
97	Santibanez-Gallerani A et al	Improved esthetic results with fine-tip Dermabond application technique. J Craniofac Surg. 2004 Sep;15(5):890-2.	2004	Report	NA	20 wounds	Octyl TCA	No tissue damage, decrease in wound strength or associated discoloration/fuzziness onto skin, esthetic results were considered good to excellent using new fine-tip applicator
98	Saxena AK, Willital GH.	Octylcyanoacrylate tissue adhesive in the repair of pediatric extremity lacerations. Am Surg. 1999 May;65(5):470-2.	1999	Prospective Randomized	Pediatric extremity lacerations	64 (32 in each group)	Octyl TCA vs. sutures	**Dehiscence** - 2 occurred in adhesive group but closed w/o adverse outcome **Cosmesis** - no significant difference **AE**: Suture– 1 wound infection, non in the TCA group.
99	Schonauer F et al	Use of Indermil tissue adhesive for closure of superficial skin lacerations in children. Minerva Chir. 2001 Aug;56(4):427-9.	2001		Pediatric wound closure	56	Butyl TCA	**Dehiscence** - none reported
100	Sebesta MJ, Bishoff JT	Octylcyanoacrylate skin closure in laparoscopy. JSLS. 2004 Jan-Mar;8(1):9-14.	2004	Prospective Randomized	Laparoscopic trocar sites		Octyl TCA vs. subcuticular sutures	**Dehiscence** - no reported difference **Closure Time** - 3.7min(TCA) 14min(Suture)
101	Shamiyeh A et al	Prospective randomized blind controlled trial comparing sutures, tape, and octylcyanoacrylate tissue adhesive for skin closure after phlebectomy. Dermatol Surg. 2001 Oct;27(10):877-80.	2001	Prospective Randomized	Phlebectomy	79 (TCA=26, suture=28, tape=25)	Octyl TCA vs. suture vs. tape	**Dehiscence** - no significant difference **Closure Time** - tapes<OCA<sutures **Cosmesis** - no significant difference **AE**: no wound infections reported
102	Shorr N et al	Histoacryl closure of eyelid skin grafts. Ophthal Plast Reconstr Surg. 1991;7(3):190-3.	1991	Prospective	Eyelid skin grafts	18	Butyl TCA	**Dehiscence** - no incidences reported **Cosmesis** - acceptable **AE**: no incidences of wound infection reported
103	Simon HK et al	Long-term appearance of lacerations repaired using a tissue adhesive. Pediatrics. 1997 Feb;99(2):193-5.	1997	Prospective Randomized	Pediatric lacerations	61 (TCA=30 Sutures=31)	TCA vs. sutures	**Cosmesis** - comparable if not better outcome for TCA at 2 months: at one year they were comparable

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
104	Simon HK et al	Lacerations against Langer's lines: to glue or suture? J Emerg Med. 1998 Mar-Apr;16(2):185-9.	1998	Retrospective analysis	Facial lacerations from a prospective randomized study	TCA = 30 Suture = 31	TCA vs. sutures	**Cosmesis** - no significant difference (TCA may be the preferred method of cutaneous closure for facial lacerations oriented against Langer's lines.)
105	Singer AJ et al	Evaluation of a new high-viscosity octylcyanoacrylate tissue adhesive for laceration repair: a randomized, clinical trial. Acad Emerg Med. 2003 Oct;10(10):1134-7.	2003	Randomized	Laceration repair	84 (42 in each group)	Octyl TCA (low vs. high viscosity)	high-viscosity less likely to migrate into wound **AE**: no incidences of wound infection reported in either group
106	Singer AJ et al	Prospective, randomized, controlled trial of tissue adhesive (2-octylcyanoacrylate) vs standard wound closure techniques for laceration repair. Stony Brook Octylcyanoacrylate Study Group. Acad Emerg Med. 1998 Feb;5(2):94-9.	1998	Prospective Randomized	Laceration repair	TCA = 63 Suture = 61	Octyl TCA vs. standard wound closure	**Cosmesis** - both groups have similar cosmetic appearance at 3-months **AE**: TCA – 1 pt had an infection (at 5-10 dys)
107	Singer AJ et al	Closure of lacerations and incisions with octylcyanoacrylate: a multicenter randomized controlled trial. Surgery. 2002 Mar;131(3):270-6.	2002	Prospective Randomized	Laceration and incision closure	814 wounds (TCA=406 Std=408)	Octyl TCA vs. std of care	**Dehiscence** - no significant difference **Closure Time** -2.9min (TCA) 5.2min(std) P=<.001 **Cosmesis** - no significant difference **AE**: 12 infections treated (TCA=9, Suture=3) There was no difference between groups in the proportion of infected wounds. Less OCA treated wounds were erythematous than wounds treated with sutures (18% vs 36%).
108	Singer AJ et al	A review of the literature on octylcyanoacrylate tissue adhesive. Am J Surg. 2004 Feb;187(2):238-48.	2004	Review	5 RCTs analyzed	NA	Octyl TCA vs. sutures	**Dehiscence** - no significant difference **Cosmesis** - no significant difference
109	Sinha S et al	A single blind, prospective, randomized trial comparing n-butyl 2-cyanoacrylate tissue adhesive (Indermil) and sutures for skin closure in hand surgery. J Hand Surg [Br]. 2001 Jun;26(3):264-5.	2001	Prospective Randomized	Hand surgery		n-butyl TCA vs. suture	**Dehiscence** - no significant difference **Cosmesis** - no significant difference **AE**: no infection reported and no adverse wound outcomes reported

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
110	Switzer EF et al	Subcuticular closure versus Dermabond: a prospective randomized trial. Am Surg. 2003 May;69(5):434-6.	2003	Prospective Randomized	Inguinal hernia repair	46 (TCA=24 suture=22)	Octyl TCA vs. subcuticular sutures	**Closure Time** -155sec(TCA) 286sec(suture) P=<0.001 **Cosmesis** - no significant difference (however suture group scored better 4.2 vs. 3.88) *based on study, authors did not feel that dermabond was an acceptable alternative to subcuticular sutures for hernia repair*
111	Taravella MJ, Chang CD.	2-Octyl cyanoacrylate medical adhesive in treatment of a corneal perforation. Cornea. 2001 Mar;20(2):220-1.	2001					*Not able to review – article not able to be located.*
112	Toriumi DM, Bagal AA.	Cyanoacrylate tissue adhesives for skin closure in the outpatient setting. Otolaryngol Clin North Am. 2002 Feb;35(1):103-18, vi-vii.	2002	Information	NA	NA	NA	effective method for closure of facial lacerations
113	Toriumi DM et al	Use of octyl-2-cyanoacrylate for skin closure in facial plastic surgery. Plast Reconstr Surg. 1998 Nov;102(6):2209-19.	1998	Prospective Randomized	Facial plastic surgery	111 (TCA = 49 Suture = 51)	Octyl TCA vs. sutures	**Closure Time** - 55secs(TCA) 3min47secs(Suture) **Cosmesis** - OCA significantly improved cosmesis score
114	Trott AT.	Cyanoacrylate tissue adhesives. An advance in wound care. JAMA. 1997 May 21;277(19):1559-60.	1997	Editorial	NA	NA	NA	CTA significantly less painful; in surgery total anesthesia time reduced; inflammatory responses between TCA and sutures = no difference
115	Turkaslan T et al	Use of adhesives in cleft palate surgery: a new flap fixation technique. J Craniofac Surg. 2005 Jul;16(4):719-22.	2005	Prospective	Cleft palate	15	Butyl TCA	**Dehiscence** - none reported **AE** - None reported
116	van den Ende ED et al	Adhesive bonds or percutaneous absorbable suture for closure of surgical wounds in children. Results of a prospective randomized trial. J Pediatr Surg. 2004 Aug;39(8):1249-51.	2004	Prospective Randomized	Pediatric groin incisions	100 (50 in each group)	Butyl TCA (Indermil) vs. suture	**Dehiscence** - butyl TCA inferior to sutures **Cosmesis** - butyl TCA inferior to sutures **AE**: TCA-4pts had an infection, Suture-2pts had an infection
117	Vargas G, Reger TB.	An alternative to sutures. Medsurg Nurs. 2000 Apr;9(2):83-5.	2000	Review	NA	NA	Octyl (dermabond)	Octylcyanoacrylate is a versatile skin adhesive. Convenient and feasible in use to warrant further investigation.

#	Author	Title/Citation	Year	Study Type	Surgery Type	# of Patients	Comparison	Results
118	Wang MY et al	A prospective analysis of the use of octylcyanoacrylate tissue adhesive for wound closure in pediatric neurosurgery. Pediatr Neurosurg. 1999 Apr;30(4):186-8.	1999	Prospective	Neurosurgical operations	102 (142 incisions)	octyl TCA	of 102 pts only 1 had poor cosmetic result - no other pt complaints regarding wound care or cosmesis.
119	Yavuzer R et al	Using tissue adhesives for closure of periareolar incisions in breast reduction surgery. Plast Reconstr Surg. 2003 Jul;112(1):337.	2003	Correspondence	Breast surgery	10	Octyl and Butyl TCA	**AE**: no cases of wound dehiscence, infection or unacceptable scars during follow-up (1yr)
120	Zafar F et al	Sutureless circumcision. Br J Surg. 1993 Jul;80(7):859.	1993	Short Note	Circumcision	60	Butyl TCA (histoacryl)	**Cosmesis** - excellent at 2 weeks. No incidence of wound breakdown (only 1 infection reported) no **AE**s reported. Quick and easy to use over suturing
121	Zempsky WT et al	Randomized controlled comparison of cosmetic outcomes of simple facial lacerations closed with Steri Strip Skin Closures or Dermabond tissue adhesive. Pediatr Emerg Care. 2004 Aug;20(8):519-24.	2004	Prospective Randomized	Facial Lacerations	97 (TCA=49 steristrips=48)	Octyl TCA vs. Steristrips	**Cosmesis** - no significant difference **AE** - Wound complication rates were similar between groups (P=0.06). TCA had 1 reported wound infection, 6 reported wound dehiscence. Suture had no wound infection and 1 wound dehiscence.

ATTACHMENT D: TISSUE ADHESIVE REFERENCES

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ATTACHMENT E: MDR/MAUDE SAFETY INFORMATION

Table 6: Summary of MDR/MAUDE Data for Product Code MPN

Report Type		Total	Percent (%)
Eye Bonded		**176**	**60%**
Dehiscence		**42**	**14.2%**
Infection		**39**	**13.2%**
Allergic Reaction		**8**	**2.7%**
Erythema		**7**	**2.4%**
Infection & Dehiscence		**2**	**0.7%**
Product Issue:		**13**	**4.4%**
	Applicator Broken	1	7.7%
	Applicator Malfunction	1	7.7%
	Chemical Rx - Vomiting and Temperature	1	7.7%
	Fumes caused chemical burns	2	15.4%
	Product Sterility Compromised	1	7.7%
	Vial Broke and Cut Finger	6	46.2%
	Viscosity of Tubes Different	1	7.7%
Other:		**9**	**3.0%**
	Granuloma & Fat Necrosis	2	22.2%
	Necrosis	1	11.1%
	Patient picked off adhesive	1	11.1%
	Wound drainage - no infection	1	11.1%
	Unknown	4	44.4%
Total:		**296**	**100%**

Table 7: Summary of Events Related to the Product or Adverse Event

Report Type	Total	%	Product Problem Report	%	Adverse Event Report	%	Note
Eye Bonded	**176**	60.0%	51	29.0%	123	69.9%	2 reported as not product related but no notation for AE
Dehiscence	**42**	14.2%	1	2.4%	41	97.6%	
Infection	**39**	13.2%	2	5.1%	37	94.9%	
Allergic Reaction	**8**	2.7%	7	87.5%	1	12.5%	1 reported as not product related but no notation for AE
Erythema	**7**	2.4%	7	100%	0	--	
Infection & Dehiscence	**2**	0.7%	2	100%	0	--	
Product Issue:	**13**	4.4%	6	46.2%	7	53.8%	
Other:	**9**	3.0%	7	70%	2	20%	1 reported as not product related but no notation for AE
Total:	**296**		**133**	**44.9%**	**159**	**53.7%**	

Table 8: Summary of Events by Product

Report Type	n	%	Dermabond	%	Indermil	%	Unknown	%
Eye Bonded	176	60.0	176	60.9	0	0.0	0	0.0
Dehiscence	42	14.2	41	14.2	1	25.0	0	0.0
Infection	39	13.2	38	13.1	0	0.0	1	33.3
Allergic Reaction	8	2.7	6	2.1	2	50.0	0	0.0
Erythema	7	2.4	7	2.4	0	0.0	0	0.0
Infection & Dehiscence	2	0.7	2	0.7	0	0.0	0	0.0
Product Issue:	13	4.4	12	4.2	0	0.0	1	33.3
Other	9	3.0	7	2.4	1	25	1	33.3
Total:	**296**	**100%**	**289 (97.7%)**		**4 (1.4%)**		**3 (1.0%)**	

Table 9: Adverse Event Reports Listed Chronologically for Cyanoacrylate Tissue Adhesives

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
1	Dermabond	Closure Medical	Eye bonded	2/8/1999	Yes	No
2	Dermabond	Closure Medical	Eye bonded	2/18/1999	Yes	No
3	Dermabond	Closure Medical	Eye bonded	2/19/1999	Yes	No
4	Dermabond	Closure Medical	Eye bonded	3/8/1999	No	Yes
5	Dermabond	Closure Medical	Eye bonded	3/8/1999	No	Yes
6	Dermabond	Closure Medical	Eye bonded	3/8/1999	No	Yes
7	Dermabond	Closure Medical	Eye bonded	3/10/1999	No	Yes
8	Dermabond	Closure Medical	Eye bonded	3/10/1999	No	Yes
9	Dermabond	Closure Medical	Eye bonded	3/10/1999	No	Yes
10	Dermabond	Closure Medical	Eye bonded	3/10/1999	No	Yes
11	Dermabond	Closure Medical	Eye bonded	3/17/1999	No	Yes
12	Dermabond	Closure Medical	Eye bonded	3/17/1999	No	
13	Dermabond	Closure Medical	Eye bonded	3/17/1999	No	Yes
14	Dermabond	Closure Medical	Eye bonded	3/17/1999	No	Yes
15	Dermabond	Closure Medical	Eye bonded	3/27/1999	Yes	No
16	Dermabond	Closure Medical	Eye bonded	4/7/1999	No	Yes
17	Dermabond	Closure Medical	Eye bonded	4/22/1999	No	Yes
18	Dermabond	Closure Medical	Eye bonded	5/11/1999	No	Yes
19	Dermabond	Closure Medical	Eye bonded	5/11/1999	No	Yes
20	Dermabond	Closure Medical	Eye bonded	5/11/1999	No	Yes
21	Dermabond	Closure Medical	Eye bonded	5/14/1999	No	Yes
22	Dermabond	Closure Medical	Eye bonded	5/14/1999	No	Yes
23	Dermabond	Closure Medical	Eye bonded	5/14/1999	No	Yes
24	Dermabond	Closure Medical	Eye bonded	5/24/1999	No	Yes
25	Dermabond	Closure Medical	Eye bonded	5/24/1999	No	Yes
26	Dermabond	Closure Medical	Eye bonded	6/2/1999	No	Yes
27	Dermabond	Closure Medical	Eye bonded	6/2/1999	No	Yes
28	Dermabond	Closure Medical	Eye bonded	6/2/1999	No	Yes
29	Dermabond	Closure Medical	Eye bonded	6/3/1999	No	Yes
30	Dermabond	Closure Medical	Eye bonded	6/3/1999	No	Yes
31	Dermabond	Closure Medical	Eye bonded	6/3/1999	No	Yes
32	Dermabond	Closure Medical	Eye bonded	6/8/1999	No	Yes
33	Dermabond	Closure Medical	Eye bonded	6/9/1999	No	Yes
34	Dermabond	Closure Medical	Eye bonded	6/17/1999	No	Yes
35	Dermabond	Closure Medical	Eye bonded	6/24/1999	No	Yes
36	Dermabond	Closure Medical	Eye bonded	6/24/1999	No	Yes
37	Dermabond	Closure Medical	Eye bonded	6/28/1999	No	Yes
38	Dermabond	Closure Medical	Eye bonded	6/28/1999	No	Yes

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
39	Dermabond	Closure Medical	Eye bonded	6/28/1999	No	Yes
40	Dermabond	Closure Medical	Eye bonded	7/23/1999	Yes	No
41	Dermabond	Closure Medical	Eye bonded	7/23/1999	No	Yes
42	Dermabond	Closure Medical	Eye bonded	8/16/1999	No	Yes
43	Dermabond	Closure Medical	Eye bonded	8/16/1999	No	Yes
44	Dermabond	Closure Medical	Eye bonded	8/16/1999	No	Yes
45	Dermabond	Closure Medical	Eye bonded	8/16/1999	No	Yes
46	Dermabond	Closure Medical	Eye bonded	8/17/1999	No	Yes
47	Dermabond	Closure Medical	Eye bonded	8/17/1999	No	Yes
48	Dermabond	Closure Medical	Eye bonded	8/17/1999	No	Yes
49	Dermabond	Closure Medical	Eye bonded	8/18/1999	No	Yes
50	Dermabond	Closure Medical	Eye bonded	8/18/1999	No	Yes
51	Dermabond	Closure Medical	Eye bonded	8/18/1999	No	Yes
52	Dermabond	Closure Medical	Eye bonded	8/18/1999	No	Yes
53	Dermabond	Closure Medical	Eye bonded	9/1/1999	No	Yes
54	Dermabond	Closure Medical	Eye bonded	9/1/1999	No	Yes
55	Dermabond	Closure Medical	Eye bonded	9/8/1999	No	Yes
56	Dermabond	Closure Medical	Eye bonded	9/8/1999	No	Yes
57	Dermabond	Closure Medical	Eye bonded	9/15/1999	No	Yes
58	Dermabond	Closure Medical	Eye bonded	9/15/1999	No	Yes
59	Dermabond	Closure Medical	Eye bonded	9/27/1999	No	Yes
60	Dermabond	Closure Medical	Eye bonded	10/7/1999	No	Yes
61	Dermabond	Closure Medical	Eye bonded	10/7/1999	No	Yes
62	Dermabond	Closure Medical	Eye bonded	10/14/1999	No	Yes
63	Dermabond	Closure Medical	Eye bonded	10/21/1999	No	Yes
64	Dermabond	Closure Medical	Eye bonded	11/12/1999	No	Yes
65	Dermabond	Closure Medical	Eye bonded	11/12/1999	No	Yes
66	Dermabond	Closure Medical	Eye bonded	11/19/1999	No	Yes
67	Dermabond	Closure Medical	Eye bonded	11/19/1999	No	Yes
68	Dermabond	Closure Medical	Eye bonded	11/19/1999	No	Yes
69	Dermabond	Closure Medical	Eye bonded	11/19/1999	No	Yes
70	Dermabond	Closure Medical	Eye bonded	12/8/1999	No	Yes
71	Dermabond	Closure Medical	Eye bonded	12/8/1999	No	Yes
72	Dermabond	Closure Medical	Eye bonded	12/15/1999	No	Yes
73	Dermabond	Closure Medical	Eye bonded	12/15/1999	No	Yes
74	Dermabond	Closure Medical	Eye bonded	12/21/1999	No	Yes
75	Dermabond	Closure Medical	Eye bonded	1/3/2000	No	Yes
76	Dermabond	Closure Medical	Eye bonded	1/6/2000	No	Yes
77	Dermabond	Closure Medical	Eye bonded	1/21/2000	No	Yes
78	Dermabond	Closure Medical	Eye bonded	2/7/2000	No	Yes

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
79	Dermabond	Closure Medical	Eye bonded	2/16/2000	No	Yes
80	Dermabond	Closure Medical	Eye bonded	2/18/2000	No	Yes
81	Dermabond	Closure Medical	Eye bonded	2/18/2000	No	Yes
82	Dermabond	Ethicon	Unable to squeeze product from applicator	2/29/2000	No	Yes
83	Dermabond	Closure Medical	Eye bonded	3/1/2000	No	Yes
84	Dermabond	Closure Medical	Eye bonded	3/7/2000	No	Yes
85	Dermabond	Closure Medical	Eye bonded	3/7/2000	Yes	No
86	Dermabond	Closure Medical	Wound dehiscence	4/3/2000	Yes	No
87	Dermabond	Closure Medical	Wound dehiscence	4/3/2000	Yes	No
88	Dermabond	Closure Medical	Wound dehiscence	4/3/2000	Yes	No
89	Dermabond	Closure Medical	Wound re-opened	4/7/2000	Yes	No
90	Dermabond	Closure Medical	Wound became red & swollen	4/7/2000	Yes	No
91	Dermabond	Closure Medical	Eye bonded	4/7/2000	Yes	No
92	Dermabond	Closure Medical	Eye bonded	4/7/2000	No	Yes
93	Dermabond	Closure Medical	Eye bonded	4/7/2000	No	Yes
94	Dermabond	Closure Medical	Eye bonded	4/7/2000	No	Yes
95	Dermabond	Closure Medical	Eye bonded	4/28/2000	No	Yes
96	Dermabond	Closure Medical	Laceration swell after 4 days	5/10/2000	Yes	No
97	Dermabond	Closure Medical	Patient picked off adhesive	5/11/2000	Yes	No
98	Dermabond	Closure Medical	Eye bonded	5/18/2000	No	Yes
99	Dermabond	Closure Medical	Eye bonded	5/22/2000	No	Yes
100	Dermabond	Closure Medical	Incision redden after application	5/22/2000	Yes	No
101	Dermabond	Closure Medical	Allergic Reaction	5/25/2000	Yes	No
102	Dermabond	Closure Medical	Eye bonded	6/2/2000	No	Yes
103	Dermabond	Closure Medical	Eye bonded	6/2/2000	No	Yes
104	Dermabond	Closure Medical	Eye bonded	6/16/2000	No	Yes
105	Dermabond	Closure Medical	Eye bonded	6/16/2000	No	Yes
106	Dermabond	Closure Medical	Eye bonded	6/22/2000	No	Yes
107	Dermabond	Closure Medical	Eye bonded	6/30/2000	No	Yes
108	Dermabond	Closure Medical	Eye bonded	7/6/2000	No	Yes
109	Dermabond	Closure Medical	Eye bonded	7/12/2000	No	Yes
110	Dermabond	Closure Medical	Eye bonded	7/12/2000	No	Yes
111	Dermabond	Closure Medical	Eye bonded	7/12/2000	No	Yes
112	Dermabond	Closure Medical	Eye bonded	8/4/2000	No	Yes
113	Dermabond	Closure Medical	Eye bonded	8/4/2000	No	Yes
114	Dermabond	Closure Medical	Eye bonded	8/24/2000	No	Yes
115	Dermabond	Closure Medical	Eye bonded	8/24/2000	No	Yes
116	Dermabond	Closure Medical	Eye bonded	8/24/2000	No	Yes
117	Dermabond	Closure Medical	Wound dehiscence	8/29/2000	Yes	No

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
118	Dermabond	Closure Medical	Wound dehiscence	8/29/2000	Yes	No
119	Dermabond	Closure Medical	Wound dehiscence	8/29/2000	Yes	No
120	Dermabond	Closure Medical	Wound re-opened	8/30/2000	Yes	No
121	Dermabond	Closure Medical	Infection and dehiscence	8/30/2000	Yes	No
122	Dermabond	Closure Medical	Infection and dehiscence	8/30/2000	Yes	No
123	Dermabond	Closure Medical	Eye bonded	8/30/2000	No	Yes
124	Dermabond	Closure Medical	Eye bonded	9/22/2000	No	Yes
125	Dermabond	Closure Medical	Eye bonded	9/22/2000	No	Yes
126	Dermabond	Ethicon	Fingers lacerated by glass from ampule	11/16/2000	No	Yes
127	Dermabond	Ethicon	Glass penetrated tubing - cut dr finger	12/12/2000	No	Yes
128	Dermabond	Closure Medical	Eye bonded	1/23/2001	No	Yes
129	Dermabond	Closure Medical	Eye bonded	1/23/2001	No	Yes
130	Dermabond	Closure Medical	Eye bonded	1/23/2001	No	Yes
131	Dermabond	Closure Medical	Eye bonded	2/8/2001	No	Yes
132	Dermabond	Closure Medical	Eye bonded	2/8/2001	No	Yes
133	Dermabond	Closure Medical	Eye bonded	2/8/2001	No	Yes
134	Dermabond	Closure Medical	Wound re-opened	2/20/2001	Yes	No
135	Dermabond	Closure Medical	Eye bonded	2/27/2001	No	Yes
136	Dermabond	Closure Medical	Wound re-opened	4/4/2001	Yes	No
137	Dermabond	Closure Medical	Wound re-opened	4/4/2001	Yes	No
138	Dermabond	Closure Medical	Wound re-opened	4/4/2001	Yes	No
139	Dermabond	Closure Medical	Wound re-opened	4/4/2001	Yes	No
140	Dermabond	Closure Medical	Wound re-opened	4/4/2001	Yes	No
141	Dermabond	Closure Medical	Eye bonded	4/17/2001	No	Yes
142	Dermabond	Closure Medical	Eye bonded	4/27/2001	No	Yes
143	Dermabond	Closure Medical	Eye bonded	4/27/2001	No	Yes
144	Dermabond	Closure Medical	Wound dehisced	5/11/2001	Yes	No
145	Dermabond	Closure Medical	Eye bonded	6/13/2001	No	Yes
146	Dermabond	Closure Medical	Wound dehiscence	6/27/2001	Yes	No
147	Dermabond	Closure Medical	Eye bonded	6/27/2001	No	Yes
148	Dermabond	Closure Medical	Wound dehiscence	6/27/2001	Yes	No
149	Dermabond	Closure Medical	Wound dehiscence	6/27/2001	Yes	No
150	Dermabond	Closure Medical	Allergic Reaction	6/27/2001	Yes	No
151	Dermabond	Closure Medical	Eye bonded	7/2/2001	No	Yes
152	Dermabond	Closure Medical	Eye bonded	7/6/2001	No	Yes
153	Dermabond	Closure Medical	Allergic Reaction	7/17/2001	Yes	Yes
154	Dermabond	Closure Medical	Wound re-opened	7/17/2001	Yes	No
155	Dermabond	Closure Medical	Wound dehisced	8/3/2001	Yes	No
156	Dermabond	Closure Medical	Eye bonded	8/10/2001	Yes	No
157	Dermabond	Closure Medical	Eye bonded	8/10/2001	No	Yes

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
158	Dermabond	Closure Medical	Wound dehisced	8/20/2001	Yes	No
159	Dermabond	Closure Medical	Wound dehisced	8/20/2001	Yes	No
160	Dermabond	Ethicon	Wound dehiscence	9/12/2001	Yes	No
161	Dermabond	Closure Medical	Eye bonded	9/14/2001	Yes	No
162	Dermabond	Closure Medical	Eye bonded	11/13/2001	No	Yes
163	Dermabond	Closure Medical	Abscess developed	12/3/2001	Yes	No
164	Dermabond	Closure Medical	Eye bonded	12/3/2001	No	Yes
165	Dermabond	Closure Medical	Wound infection	1/10/2002	Yes	No
166	Dermabond	Closure Medical	Wound infection	1/10/2002	Yes	No
167	Dermabond	Closure Medical	Wound infection	1/10/2002	Yes	No
168	Dermabond	Closure Medical	Wound infection	1/10/2002	Yes	No
169	Dermabond	Closure Medical	Wound infection	1/10/2002	Yes	No
170	Dermabond	Closure Medical	Wound infection	1/10/2002	Yes	No
171	Dermabond	Ethicon	Staph infection due to contamination	1/17/2002	No	Yes
172	Dermabond	Ethicon	Eye bonded	1/25/2002	Yes	No
173	Dermabond	Closure Medical	Wound dehisced	2/13/2002	Yes	No
174	Dermabond	Closure Medical	Eye bonded	2/13/2002	No	Yes
175	Dermabond	Closure Medical	Eye bonded	2/13/2002	No	Yes
176	Dermabond	Closure Medical	Eye bonded	2/13/2002	No	Yes
177	Dermabond	Closure Medical	Eye bonded	2/27/2002	No	Yes
178	Dermabond	Closure Medical	Allergic Reaction	3/5/2002	Yes	No
179	Dermabond	Closure Medical	Infection	3/5/2002	Yes	No
180	Dermabond	Closure Medical	Infection	3/5/2002	Yes	No
181	Dermabond	Closure Medical	Infection	3/7/2002	Yes	No
182	Dermabond	Closure Medical	Eye bonded	3/11/2002	No	
183	Dermabond	Closure Medical	Infection	3/18/2002	Yes	No
184	Dermabond	Closure Medical	Eye bonded	3/22/2002	No	Yes
185	Dermabond	Closure Medical	Unknown	4/25/2002	Yes	No
186	Dermabond	Closure Medical	Glass from inner vial penetrated outer vial - cut dr.	5/8/2002	No	Yes
187	Dermabond	Closure Medical	Pain & swell around incision	5/8/2002	Yes	No
188	Dermabond	Closure Medical	Wound dehisced	5/28/2002	Yes	No
189	Dermabond	Closure Medical	Infection	6/19/2002	Yes	No
190	Dermabond	Closure Medical	Infection	6/19/2002	Yes	No
191	Dermabond	Closure Medical	Eye bonded	7/1/2002	Yes	No
192	Dermabond	Closure Medical	Infection	7/23/2002	Yes	No
193	Dermabond	Closure Medical	Wound re-opened	7/23/2002	Yes	No
194	Dermabond	Closure Medical	Glass perforated ampoule - cut finger	7/24/2002	No	Yes
195	Dermabond	Closure Medical	Infection - Pseudomonas Aerugionsa	7/26/2002	Yes	No
196	Dermabond	Closure Medical	Eye bonded	8/1/2002	Yes	No

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
197	Dermabond	Closure Medical	Chemical Reaction causing vomiting and temp	8/22/2002	Yes	No
198	Dermabond	Closure Medical	Eye bonded	8/29/2002	Yes	No
199	Dermabond	Closure Medical	Eye bonded	8/29/2002	Yes	No
200	Dermabond	Closure Medical	Eye bonded	9/3/2002	Yes	No
201	Dermabond	Closure Medical	Eye bonded	9/4/2002	Yes	No
202	Dermabond	Closure Medical	Eye bonded	9/16/2002	Yes	No
203	Dermabond	Closure Medical	Periareolar Abscess	9/26/2002	Yes	No
204	Dermabond	Closure Medical	Inflammation of incision	9/26/2002	Yes	No
205	Dermabond	Closure Medical	Infection	9/26/2002	Yes	No
206	Dermabond	Closure Medical	Eye bonded	10/16/2002	Yes	No
207	Dermabond	Closure Medical	Glass perforated ampoule - cut finger	10/18/2002	Yes	No
208	Dermabond	Closure Medical	Eye bonded	10/22/2002	Yes	No
209	Dermabond	Closure Medical	Eye bonded	10/22/2002	Yes	No
210	Dermabond	Closure Medical	Eye bonded	10/22/2002	Yes	No
211	Dermabond	Closure Medical	Eye bonded	10/29/2002	Yes	No
212	Dermabond	Closure Medical	Wound re-opened	11/5/2002	Yes	No
213	Dermabond	Closure Medical	Eye bonded	11/5/2002	Yes	No
214	Dermabond	Closure Medical	Possible Infection	11/14/2002	Yes	No
215	Dermabond	Closure Medical	Wound re-opened	11/14/2002	Yes	No
216	Dermabond	Closure Medical	Erythematous Reaction	12/13/2002	Yes	No
217	Dermabond	Closure Medical	Eye bonded	12/19/2002	Yes	No
218	Dermabond	Closure Medical	Dehiscence	12/19/2002	Yes	No
219	Dermabond	Closure Medical	Eye bonded	1/28/2003	Yes	No
220	Dermabond	Closure Medical	Infection	1/31/2003	Yes	No
221	Dermabond	Closure Medical	Infection	2/10/2003	Yes	No
222	Dermabond	Closure Medical	Wound re-opened	2/27/2003	Yes	No
223	Dermabond	Closure Medical	Wound re-opened	3/19/2003	Yes	No
224	Dermabond	Closure Medical	Wound re-opened	3/19/2003	Yes	No
225	Dermabond	Closure Medical	Wound re-opened	3/19/2003	Yes	No
226	Dermabond	Closure Medical	Eye bonded	4/3/2003	Yes	No
227	Dermabond	Closure Medical	Eye bonded	4/11/2003	Yes	No
228	Dermabond	Closure Medical	Eye bonded	4/25/2003	Yes	No
229	Dermabond	Closure Medical	Vial broke and cut finger	5/16/2003	Yes	No
230	Dermabond	Closure Medical	Allergic Reaction	5/28/2003	Yes	No
231	Dermabond	Closure Medical	Wound re-opened	6/23/2003	Yes	No
232	Dermabond	Closure Medical	Wound re-opened	6/25/2003	Yes	No
233	Dermabond	Closure Medical	Dehiscence	6/25/2003	Yes	No
234	Unknown	Unknown	Applicator broken	7/16/2003	No	Yes
235	Dermabond	Closure Medical	Eye bonded	7/17/2003	Yes	No

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
236	Indermil	Tyco Health	Body rejecting device	8/13/2003	No	
237	Dermabond	Closure Medical	Fumes cased chemical burns	8/21/2003	Yes	No
238	Dermabond	Ethicon	Drainage with spurapubic wound	8/22/2003	No	Yes
239	Dermabond	Closure Medical	Eye bonded	9/9/2003	Yes	No
240	Dermabond	Closure Medical	Eye bonded	9/10/2003	Yes	No
241	Dermabond	Closure Medical	Incision re-opened	9/15/2003	Yes	No
242	Dermabond	Closure Medical	Eye bonded	9/26/2003	Yes	No
243	Dermabond	Closure Medical	Wound Dehiscence	10/2/2003	Yes	No
244	Dermabond	Closure Medical	Eye bonded	10/2/2003	Yes	No
245	Dermabond	Closure Medical	Eye bonded	10/2/2003	Yes	No
246	Indermil	Loctite Ltd	Foreign body reaction	10/7/2003	Yes	No
247	Dermabond	Closure Medical	Eye bonded	10/31/2003	Yes	No
248	Dermabond	Closure Medical	Eye bonded	11/25/2003	Yes	No
249	Indermil	Tyco Health	Necrosis	11/26/2003	Yes	No
250	Dermabond	Closure Medical	Eye bonded	12/11/2003	Yes	No
251	Dermabond	Closure Medical	Fumes cased chemical burns	12/23/2003	Yes	No
252	Dermabond	Closure Medical	Wound drainage - no infection	12/23/2003	Yes	No
253	Dermabond	Closure Medical	Eye bonded	12/23/2003	Yes	No
254	Dermabond	Closure Medical	Eye bonded	1/1/2004	Yes	No
255	Dermabond	Closure Medical	Eye bonded	1/1/2004	Yes	No
256	Dermabond	Closure Medical	Infection	1/22/2004	Yes	No
257	Dermabond	Closure Medical	Infection	3/2/2004	Yes	No
258	Dermabond	Closure Medical	Infection	3/2/2004	Yes	No
259	Dermabond	Closure Medical	Eye bonded	3/26/2004	Yes	No
260	Dermabond	Ethicon	Viscosity of tubes different	4/16/2004	No	Yes
261	Dermabond	Closure Medical	Infection	4/26/2004	Yes	No
262	Dermabond	Closure Medical	Eye bonded	6/2/2004	Yes	No
263	Dermabond	Closure Medical	Eye bonded	6/4/2004	Yes	No
264	Unknown	United States Surgical	Unknown	6/15/2004	No	
265	Dermabond	Closure Medical	Infection	7/13/2004	Yes	No
266	Dermabond	Closure Medical	Eye bonded	7/13/2004	Yes	No
267	Dermabond	Closure Medical	Eye bonded	7/19/2004	Yes	No
268	Dermabond	Closure Medical	Infection	7/30/2004	Yes	No
269	Dermabond	Closure Medical	Eye bonded	8/11/2004	Yes	No
270	Indermil	Indermil	Wound Dehiscence	9/13/2004	No	Yes
271	Dermabond	Closure Medical	Unknown	9/28/2004	Yes	No
272	Dermabond	Closure Medical	Unknown	10/1/2004	Yes	No
273	Dermabond	Closure Medical	Product Sterility Compromised	11/9/2004	Yes	No
274	Dermabond	Closure Medical	Infection	11/23/2004	Yes	No

	Product Brand Name	Manufacturer	Event Description	Date FDA Received	Adverse Event?	Product Problem?
275	Dermabond	Closure Medical	Eye bonded	1/24/2005	Yes	No
276	Dermabond	Closure Medical	Eye bonded	2/21/2005	Yes	No
277	Dermabond	Closure Medical	Infection	2/21/2005	Yes	No
278	Unknown	Outside Vendor	Infection	2/24/2005	Yes	No
279	Dermabond	Closure Medical	Allergic Reaction	3/3/2005	Yes	No
280	Dermabond	Closure Medical	Eye bonded	3/14/2005	Yes	No
281	Dermabond	Closure Medical	Infection	4/28/2005	Yes	No
282	Dermabond	Closure Medical	Infection	4/28/2005	Yes	No
283	Dermabond	Closure Medical	Granuloma & Fat Necrosis	5/17/2005	Yes	No
284	Dermabond	Closure Medical	Granuloma & Fat Necrosis	5/17/2005	Yes	No
285	Dermabond	Closure Medical	Erythema	5/25/2005	Yes	No
286	Dermabond	Closure Medical	Eye bonded	6/30/2005	Yes	No
287	Dermabond	Closure Medical	Wound Breakdown	8/4/2005	Yes	No
288	Dermabond	Closure Medical	Infection	8/16/2005	Yes	No
289	Dermabond	Closure Medical	Infection	8/16/2005	Yes	No
290	Dermabond	Closure Medical	Infection	8/25/2005	Yes	No
291	Dermabond	Closure Medical	Febrile Reaction	8/25/2005	Yes	No
292	Dermabond	Closure Medical	Eye bonded	9/9/2005	Yes	No
293	Dermabond	Closure Medical	Pseudomonas Infection	9/19/2005	Yes	No
294	Dermabond	Closure Medical	Pseudomonas Infection	9/19/2005	Yes	No
295	Dermabond	Closure Medical	Infection	9/19/2005	Yes	No
296	Dermabond	Closure Medical	Infection	9/19/2005	Yes	No