

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

### I. GENERAL INFORMATION

Device Generic Name: Topical Tissue Adhesive

Device Trade Name: Indermil™ Tissue Adhesive

Sponsor's Name and Address:  
United States Surgical, a division of Tyco Healthcare Group, LP.  
150 Glover Ave.  
Norwalk, CT 06856

Premarket Approval Application  
(PMA) Number: P010002

Date of Panel Recommendation: None.

Date of GMP Inspection: November 7, 2001

Date of Notice of Approval  
To the Applicant: May 22, 2002

### II. INDICATIONS FOR USE

Indermil™ tissue adhesive is indicated for the closure of topical skin incisions including laparoscopic incisions, and trauma-induced lacerations 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.

### III. DEVICE DESCRIPTION

Indermil™ is a sterile, liquid topical tissue adhesive composed of *n*-Butyl-2-Cyanoacrylate monomer. Indermil™ tissue adhesive is supplied in a 0.5g single patient use, plastic ampule. Each ampule is sealed within a foil packet so the exterior of the ampule is also sterile. Indermil™ remains liquid until exposed to water or water-containing substances/ tissue, after which it cures (polymerizes) and forms a film that bonds to the underlying surface.

### IV. CONTRAINDICATIONS

Indermil™ tissue adhesive is not to be applied to subdermal layers of tissue. The polymerized adhesive is not absorbed by tissues and may elicit a foreign body reaction.

The tissue adhesive is not to be applied to any internal organs, blood vessels, nerve tissue, mucosal surfaces or mucocutaneous junctions, areas with dense natural hair, or within the conjunctival sac of the eye.

The tissue adhesive is not to be applied to the surface of the eye. If the eye is bonded closed, release eyelashes with warm water by covering with a wet pad. The adhesive will bond to eye protein and will cause periods of weeping which will help to release the adhesive. Keep the eye covered until the adhesive is no longer adhered to the surface of the eye -- usually within 1 to 3 days. Do not force the eye open.

The tissue adhesive is not to be applied to wounds subject to high skin tension, or on areas of increased skin tension such as the elbows, knees, or knuckles. The tissue adhesive is not to be used in areas of skin excision.

The tissue adhesive is not to be applied to wounds that show evidence of infection or gangrene.

The tissue adhesive is not to be used on patients with known preoperative systemic infections, uncontrolled diabetes, or diseases or conditions that are known to interfere with the wound healing process.

The tissue adhesive is not to be used on patients with a known hypersensitivity to cyanoacrylate or formaldehyde.

## **V. WARNINGS AND PRECAUTIONS**

Refer to device labeling for a list of the warnings and precautions.

## **VI. ALTERNATE PRACTICES AND PROCEDURES**

Skin wounds can be closed utilizing various medical devices in order to maintain tissue apposition during the critical phase of wound healing. The most commonly utilized device is the non-absorbable monofilament suture. The sutures remain in place for approximately 7-10 days, at which time the patient returns to have the sutures removed. Similarly, metal skin staples are utilized in the same fashion as sutures, requiring a return visit for staple removal. Adhesive tapes have also been used to hold skin wound edges together. In addition, another commercially available tissue adhesive has been utilized to maintain approximation of skin wound edges caused by surgical incisions or traumatic lacerations.

## **VIII. MARKETING HISTORY**

Indermil™ was first issued a Product License in the United Kingdom on September 28, 1993. Indermil™ was granted the CE Mark in accordance with the European Medical Device Directive (93/42/EEC) on December 12, 1995. Since that time, Indermil™ has been sold throughout the European Union and Switzerland, as well as the following international markets: Australia, Canada, Colombia, Mexico, Hungary, Slovakia, Taiwan, Thailand, India, Israel and Saudi Arabia.



Indermil™ has not been withdrawn from marketing for any reason relating to the safety or effectiveness of the device.

## **IX. SUMMARY OF PRECLINICAL STUDIES**

Preclinical studies were performed to evaluate the safety and effectiveness of Indermil™ tissue adhesive in both the laboratory and in animal models.

### STUDIES ON THE SAFETY OF INDERMIL™: BIOCOMPATIBILITY STUDIES

Based on the categorization of medical devices by nature of body contact and duration of contact described in the ISO 10993-1, Indermil™ is considered a *Surface-contacting device (ISO 10993-1, sect. 4.1.2)* with a prolonged contact duration of *> 24 hours to 30 days (ISO 10993-1, sect. 4.2)*. Based on the information that is known about the safety of butylcyanoacrylates, and the characteristics and intended use of Indermil™, the following biocompatibility tests were performed to evaluate its safety:

- Cytotoxicity
- Sensitization
- Irritation
- Genotoxicity

The tests performed used an alternate formulation of Indermil™, referred to as LID-1187A that differed only slightly in the amount of SO<sub>2</sub> (sulfur dioxide) and stabilizer. Cytotoxicity, Sensitization, and Irritation tests required by International Organization for Standardization (ISO) 10993-1: Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing (1997) were repeated for the specification used during the Clinical Trials and maintained to the present time. All testing was conducted in accordance with Good Laboratory Practice Standards.

The test results demonstrate that Indermil™ was found to be non-cytotoxic to L929 cells when evaluated as a saline or MEM extract. In addition, Indermil™ did not cause delayed contact hypersensitivity in the guinea pig, when assessed using the Guinea Pig Maximization test. Indermil™ was not considered to be an irritant to either intact or abraded skin, when evaluated in rabbits. Lastly, Indermil™ was considered to be non-mutagenic in strains of *Salmonella Typhimurium* and non-clastogenic in cultured human lymphocytes. In conclusion, biocompatibility testing demonstrates that Indermil™ does not raise any significant biocompatibility concerns.

### STUDIES ON THE EFFICACY OF INDERMIL™: IN VITRO AND IN VIVO TESTING

#### **In Vitro Studies Comparing Shear Strength and Fixture Times of Adhesives**

To evaluate the efficacy of Indermil™ adhesive, batteries of studies were performed first in the laboratory to evaluate the ability of the adhesive to polymerize rapidly with adequate strength to perform as indicated. Fixture time tests were performed with both 70% hospital

grade and 99.96% laboratory grade isopropyl alcohol. Inclusion of samples cleaned with both 70% and 99.96% isopropyl alcohol was done to assess the effect of surface water on fixture time and shear strength.

Performance studies on samples cleaned with 70% Isopropyl alcohol, demonstrate that the Indermil™ tissue adhesive was equivalent, in terms of fixture time, when compared to a legally-marketed medical device. The legally-marketed device yielded higher shear strength than Indermil™.

Performance studies were also done to evaluate the fixture times of Indermil™ and a legally-marketed device on ABS fixtures pre-cleaned with 99.96% Isopropyl alcohol. The results show that the Indermil™ tissue adhesive was faster in terms of fixture time when compared with the other device. The Indermil™ tissue adhesive was slightly lower in shear strength to the other device.

While there is no direct correlation between the in-vivo wound strength and the in-vitro lap shear strength, these studies suggested that Indermil™ tissue adhesive would provide the necessary strength during wound healing to proceed to a clinical trial.

#### **In Vivo Wound Security and Wound Healing Strength of Indermil™ compared to an n-octylecyanoacrylate or wound closure tape:**

Full-thickness skin incisions were made on the backs of 84 rats and closed with Indermil™, another legally-marketed device for tissue closure, or wound closure tape. The rats were divided into three groups. Each rat received two paravertebral incisions. Group One (N = 36) received Indermil™ on one incision and the legally-marketed device on the other incision. Group Two (N = 36) received Indermil™ on one incision and Steri-Strips™ on the other incision. Group Three (N = 12) served as a control group and received Steri-Strips™ on both incisions. Wound security and wound healing strengths were determined at closure and again after 1 and 2 weeks. Initially all wound strength was provided by the closure devices. After 1 week, strength was provided by wound healing, and the closure devices provided no additional strength. At 2 weeks, healing was not inhibited and was similar in all groups. In conclusion, Indermil™, the legally-marketed device, and wound closure tape performed similarly by providing wound security for the first week of healing and then not inhibiting the normal healing process.

#### **A Comparison of the Histological Effects of Indermil™ compared to an n-octylecyanoacrylate or wound closure tape:**

A fourteen day study was conducted to compare skin wound healing between three methods of incision closure (Indermil™, another legally-marketed device for tissue closure, and wound closure tape). Two paravertebral incisions were made into the skin of 18 rats and closed with either Indermil™, the legally-marketed device, and wound closure tape which resulted in 12 closures with each method. Four tissues closed by each method were collected at 3, 7, and 14 days after closure. Histology slides were prepared. Components of the tissue reaction to each closure method were quantified which resulted in a histopathology rating for each closure site.

The criteria for histopathology evaluation was based on eleven histopathological variables. Each variable was rated on a scale from 0 to 3, where "0" was most favorable and "3" was least favorable. Histopathology rating scores were based on the average of the quantitative scores for each of the eleven variables. Evaluation of the histopathology rating indicates that the wound closure tape had the lowest rating at all timepoints, and thus, was the least reactive of the 3 closure methods. At 7 and 14 days, but not at 3 days, Indermil™ had a lower rating than the legally-marketed device, suggesting less tissue reactivity. However, the ratings for the legally-marketed device and Indermil™ were essentially equal at 14 days, indicating that these two products were comparable at that timepoint. Each closure device provided no appreciable enhancement of the normal cellular response to healing. At no time did any specimen demonstrate a histopathology rating greater than 0.77 (where a score of 1.00 is defined as a mild reaction). Therefore, all the specimens were determined to have elicited an acceptable histological response. Indermil™ elicited a response similar to the legally-marketed device and wound closure tape.

**X. SUMMARY OF THE RESULTS OF THE CLINICAL INVESTIGATION**

A multi-center, prospective, randomized trial compared INDERMIL™ Tissue Adhesive with traditional wound closure techniques to evaluate the safety and efficacy of Indermil™. Patients were randomized to wound closure using INDERMIL™ adhesive or to the comparator group where alternative wound closure techniques (suture, staples, and adhesive strips) were applied. A record was kept of the type, size and other characteristics of the wound. The clinical course of wound healing was assessed at specified intervals during the 3 month observation period. Each wound was evaluated for wound healing, cosmetic appearance, and/or general condition at 24 hrs, 1-2 weeks post treatment, and at 3 months post treatment. Wound healing complications were noted as they appeared.

The trial was designed to compare the safety and efficacy of INDERMIL™ to traditional skin closure methods (sutures, staples, clips, and adhesive strips). Patients with surgical incisions or lacerations of 8 cm or less were treated and assessed for complications (dehiscence, infection, skin irritation), time to wound closure, and cosmesis (cosmetic appearance of the wound after 3 months). One thousand ninety-two (1,092) patients were randomized in 24 centers in the US and Europe. These patients had a total of two thousand three hundred four (2,304) wounds that could be evaluated. Patients were assessed at 24 hours after the procedure or at the time of discharge and at 1-2 weeks for complications. They were assessed at 3 months following the treatment for cosmesis. Complications at 1-2 weeks and cosmesis at 3 months were primary endpoints. Cosmesis was not assessed at the 1-2 week interval.

The study population included patients who presented for simple skin closure of wounds equal to or less than 8 cm. Patients or their legal representative had to sign informed consent and agree to return for follow-up visits. Patients were excluded if the tissue adhesive might come into contact with blood vessels, had wounds under tension or over joints, had known preoperative systemic infections or infections of the site, had uncontrolled diabetes, or had diseases or conditions that are known to interfere with the wound healing process.

**PATIENT ACCOUNTING, DEMOGRAPHICS, AND WOUND CHARACTERISTICS**

A total of 1092 patients were randomized into the study from 24 sites. Of the 1092 patients, 556 (50.9%) were randomized to the INDERMIL™ group, and 536 to the control group (49.1%). The 12 sites that had 40 or more patients accounted for 83% of the patients studied.

Table 2 contains between-group comparisons of characteristics of the randomly selected wounds.

Table 2:  
Summary of Patient Accounting, Demographics, and Wound Characteristics

	<i>No Subcuticular Sutures</i>		<i>With Subcuticular Sutures</i>	
	Indermil™	Control	Indermil™	Control

<b>Accounting</b>					
N, patients enrolled		346	326	210	210
N, patients treated		346	326	210	210
N, wounds treated		925	820	281	278
N, patients, control device: suture/strips/staples **			294 / 32 / 18		126 / 20 / 83
N, wounds, control device: suture/strips/staples**			741 / 107 / 40		185 / 24 / 90
Patients completed:					
	24 hour	98.6%	98.5%	99.5%	99.0%
	7-14 days	92.5%	87.7%	94.3%	93.8%
	80 – 120 days	83.2%	79.4%	91.4%	88.5%
<b>Patient Demographics</b>					
Age	0 - 4y	3.5%	4.6%	0.0%	1.9%
	5 - 18y	9.5%	6.4%	2.4%	0.5%
	19 – 60y	64.7%	67.8%	54.1%	52.9%
	>60y	22.3%	21.2%	43.5%	44.7%
Race	White	80.1%	81.3%	85.2%	88.6%
	Black	8.4%	8.9%	5.2%	6.7%
	Asian	1.2%	0.6%	0.0%	0.0%
	Hispanic	8.7%	5.8%	7.6%	3.3%
	Other	1.7%	3.4%	1.9%	1.4%
<b>Wound Characteristics</b>					
Length in cm	mean	1.5*	1.7	4.3	4.5
Depth in cm	mean	1.5	1.5	1.5	1.4
Width in cm	mean	0.5	0.5	0.6	0.6
Class	Clean	66.8%	64.7%	87.9%	88.5%
	Clean-contaminated	31.4%	33.9%	11.7%	10.4%
	Contaminated	1.8%	1.2%	0.4%	0.7%
	Dirty	0.0%	0.2%	0.0%	0.4%
Incisions		88.2%	87.9%	96.4%	95.7%
Lacerations		11.8%	12.1%	3.6%	4.3%
<b>Use of Anesthesia</b>					
General		137 (40%)	121 (37%)		
Local only		121 (35%)*	196 (60%)		
None		88 (25%)	9 (3%)		

\* Differences between Indermil and Control were statistically significant ( $p < 0.05$ ).

\*\* Several patients/ wounds were treated with more than one control device.

The data show that the only statistically significant between-group difference in the physical size of the wounds was in mean wound length in the No Subcuticular Suture Group (NSS). There were no between-group differences in numbers of patients enrolled; numbers of control devices between NSS and With Subcuticular Suture (WSS); numbers of patients completed at each time period; age; race; in the classification of the wound as clean, clean-

contaminated, contaminated, or dirty; the use of anesthesia; or in the frequency with which subcutaneous sutures were used for closure.

Clinical characteristics of the sample are detailed in Table 3, both for the entire study population and by treatment arm. The table also contains data on vital signs such as heart rate and blood pressure. Entries are percentages or mean  $\pm$  standard deviation.

Table 3:  
Clinical Parameters

Variable	Entire sample	INDERMIL™ group	Control group	P-value
Age years	47.7 $\pm$ 20	47.4 $\pm$ 21	48.0 $\pm$ 20	0.589
Male gender	52.1%	51.8%	52.5%	0.813
Body mass index (kg/m <sup>2</sup> )	26.7 $\pm$ 5.7	26.7 $\pm$ 5.7	26.7 $\pm$ 5.6	0.994
Body temperature (°F)	97.8 $\pm$ 0.9	97.8 $\pm$ 0.9	97.8 $\pm$ 1.0	0.947
Heart rate (beats/min.)	76.4 $\pm$ 13	76.0 $\pm$ 13	76.6 $\pm$ 14	0.560
Systolic blood pressure mm/Hg	132 $\pm$ 22	132 $\pm$ 22	132 $\pm$ 22	0.833
Diastolic blood pressure mm/Hg	76.5 $\pm$ 12	76.2 $\pm$ 13	76.8 $\pm$ 12	0.459
Respiration rate breaths/min	16.7 $\pm$ 2.8	16.9 $\pm$ 2.7	16.7 $\pm$ 2.9	0.776

<sup>1</sup>Generated by chi square test after collapsing Asians and Hispanics into the "Other" category.

#### PATIENT ACCOUNTING OR DISPOSITION

Of the 1092 patients who entered the study, 171 (15.6%) discontinued participation prematurely. The premature discontinuation rate was 13.8% in the INDERMIL™ group and 17.5% in the control group. Table 4 contains a summary of the reasons for premature discontinuation. Because there was sometimes more than one reason for discontinuation, the individual reasons add up to more than the total number of premature discontinuations. The data indicate that the most common reasons for premature discontinuation were non-compliance (60.2%), the inability of the investigator to locate the patient (20.5%), and voluntary withdrawal (12.9%). For the purposes of this study, noncompliance was the category that was used for dropouts who failed to return for the final cosmesis evaluation at 3 months despite efforts to bring them in for follow-up (in accordance with the protocol).

Table 4:  
Reasons for Premature Discontinuation of Study Participation

Reason for dropping out	All dropouts (N = 171)	INDERMIL™ group (N = 77)	Control group (N = 94)
Voluntary withdrawal	12.9% (N = 22)	9.1% (n = 7)	16.0% (N = 15)

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Non compliance*	60.2% (N = 103)	59.7% (N = 46)	60.6% (N = 57)
Unable to locate patient	20.5% (N = 35)	27.3% (N = 21)	14.9% (N = 14)
Adverse event	4.7% (N = 8)	3.9% (N = 3)	5.3% (N = 5)
Patient died	3.5% (N = 6)	5.2% (N = 4)	2.1% (N = 2)
Terminated for other reasons	7.6% (N = 13)	2.6% (N = 2)	11.7% (N = 11)

\* Noncompliance was reason given when patients failed to return for final follow-ups.

Reasons for premature discontinuation were similar in the two groups with the exception that “inability to locate the patient” was a more common problem in the INDERMIL™ group (27.3%) than in the control group (14.9%). There were a total of 6 deaths, 4 in the INDERMIL™ group and 2 in the control group. No deaths were device related. There was no evidence of between-group differences for any variables.

## STUDY RESULTS

### VII. ADVERSE EFFECTS

The following adverse events were reported in a prospective, multicenter, randomized study of 1,092 patients and 2,304 wound. The control group received sutures, staples, and adhesive strips.

Table 1:  
Clinical Study Adverse Reactions

<i>Adverse Reactions observed at 10-14 days, per wound evaluated</i>	<i>No Subcuticular Sutures (NSS)</i>		<i>With Subcuticular Sutures (WSS)</i>	
	Indermil™	Control	Indermil™	Control
N, patients treated	346	326	210	210
N, wounds treated	925	820	281	278
<i>Dehiscence (Overall)**</i>	30/853 (3.5%)*	9/709 (1.3%)	4/253 (1.6%)	2/257 (0.8%)
<i>Not requiring treatment</i>	28/853 (3.2%)*	6/709 (0.9%)	3/253 (1.2%)	1/257 (0.4%)
<i>Requiring treatment</i>	2/853 (0.2%)	3/709 (0.4%)	1/253 (0.4%)	1/257 (0.4%)
<i>With infection</i>	2/853 (0.2%)	1/709 (0.1%)	0/253 (0.0%)	0/257 (0.0%)
<i>By wound class:</i>				
<i>Clean</i>	23/564 (4.1%)	4/436 (0.9%)	4/222 (1.8%)	2/226 (0.9%)
<i>Clean-contaminated</i>	7/273 (2.6%)	3/261 (1.1%)	0/31 (0.0%)	0/29 (0.0%)
<i>Contaminated</i>	0/16 (0.0%)	2/10 (20.0%)	none	0/2 (0.0%)
<i>Dirty</i>	none	0/2 (0.0%)	none	none
<i>Infection***</i>	5/853 (0.6%)	4/709 (0.6%)	1/253 (0.4%)	3/257 (1.2%)
<i>Acute Inflammation</i>				
Erythema	102/852 (12.0%)	85/709 (12.0%)	19/254 (7.5%)	17/256 (6.6%)
Edema	23/853 (2.7%)	18/707 (2.5%)	6/253 (2.4%)*	15/256 (5.9%)
Hypersensitivity	6/853 (0.7%)	1/706 (0.1%)	0/254 (0.0%)	2/256 (0.8%)

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Drainage	39/853 (4.6%)*	14/709 (2.0%)	7/254 (2.8%)	6/257 (2.3%)
Sinus Tracts	4/850 (0.5%)	0/705 (0.0%)	2/253 (0.8%)	1/256 (0.4%)

\* Differences between Indermil and Control were statistically significant (p< 0.05).

\*\* Dehiscence was defined as “any disruption in which the edge of the skin wound separates sufficiently to expose subcutaneous tissues”.

\*\*\* Infection was defined as “a purulent discharge from the wound, a positive culture or microbial count for pathogen that can be documented”. Only two wounds met this criteria, all other “suspected infections” were based solely on clinical observation.

There were 13 infections reported; 7 from the control group and 6 from the test group. Based on these data there was no significant difference in the rate of infections between the INDERMIL™ and control treatment groups. There was a statistically significant difference between the Indermil™ and Control groups in dehiscence rates (for both overall and wounds not requiring treatment), presence of edema for the WSS group, and presence of drainage for the NSS group. The difference between overall dehiscence rates was 3.5% in the Indermil™ group and 1.3% in the Control group for the NSS group.

The primary outcome variables of this study were Time to wound closure, Complications (primarily dehiscence), and Cosmesis. Table 5 below contains between-group comparisons of the outcome variables and of a series of additional outcome measures.

## VIII. POTENTIAL ADVERSE EFFECTS

In addition to the adverse events observed during the study, the following adverse events may occur: bonding to unintended body areas or tissues; discomfort due to heat generation; allergic reaction to the adhesive; foreign body reaction; and chronic non-healing wound.

Table 5  
Summary of Effectiveness Results Comparing Indermil™ to Sutures, Staples and Adhesive Strips

<i>Clinical Study Outcomes</i>	<i>No Subcuticular Sutures (NSS)</i>		<i>With Subcuticular Sutures (WSS)</i>	
	Indermil™	Control	Indermil™	Control
<i>Dermal Apposition</i>	823/853 (96.5%)*	700/709 (98.7%)	249/253 (98.4%)	255/257 (99.2%)
<i>Immediate: Additional Device (Adhesive strips)</i>	1/925 (0.1%)*	340/820 (41.5%)	2/281(0.7%)*	88/278 (31.6%)
<i>Cosmesis @ 3 months**</i> VAS Score, 100= (optimal)				
Mean Score				
All Wounds	88.0*	92.2	89.3	89.9
Dehisced Wounds	82.9	91.4	87.3	96.5
<i>Median Time to Close (minutes)***</i>	0.6*	1.0	1.1*	2.2

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\* Differences between Indermil and Control were statistically significant ( $p < 0.05$ ).

\*\* Cosmesis: Visual Analog Scale (VAS); 3-month actual time range = 80 – 120 days

\*\*\* Time to Close was measured from the initial apposition of wound edges to the time of closure.

With the exception of time to wound closure and cosmesis, all outcome measures reflect data collected at the 1-2 week assessments. Note that there are statistically significant differences between the Control and Indermil™ groups for Dermal Apposition (NSS), Immediate: Additional Device (NSS and WSS), Cosmesis: All Wounds (NSS), and Median Time to Close (NSS and WSS).

#### *Time to Close:*

The wounds treated with INDERMIL™ had a median time to close of 0.9 minutes (54 seconds) as compared to 1.6 minutes (1 minute 36 seconds) in the control group. This represents a statistically significant shorter time to closure for the INDERMIL™ group.

#### *Dehiscence:*

There was a statistically significant difference between the Indermil™ and Control groups in dehiscence rates (for both overall and wounds not requiring treatment), presence of edema, and presence of drainage for the NSS group. The statistically significant difference between overall dehiscence rates was 3.5% in the Indermil™ group and 1.3% in the Control group. This difference was not judged to be clinically significant.

#### *Cosmesis:*

The study data revealed that the Indermil™ group and Control group had equivalent cosmetic results as measured using a 100-point visual analog scale for dehisced wounds. There was a statistically significant difference between Indermil™ and Control groups for All Wounds in the NSS group (88.0% for Indermil vs. 92.2% for Control). The cosmesis scores are comparable from a clinical perspective.

## **XI. CONCLUSIONS DRAWN FROM THE STUDY**

The preclinical testing of biocompatibility, in-vitro and in-vivo strength, and histological effects, and the clinical trial in over 1,000 patients, provide a reasonable assurance of safety and effectiveness.

The clinical study data suggest that INDERMIL™ has a clinically comparable cosmesis to the comparator group with a clinically comparable incidence of adverse events. Indermil™ patients had a statistically higher dehiscence rate and faster time to wound closure than control patients, but these differences are not judged to be clinically significant.

## **XII. GENDER BIAS**

No selection bias because of gender was identified during the review of the submission and no significant gender differences were noted in the clinical studies. The ratio of male to female patient enrollment in the study was 52.1% male and 47.9% female and this is

reflective of the type and frequency of the wounds and their underlying distribution in the general population.

### **XIII. PANEL RECOMMENDATION**

Pursuant to section 515(c)(2) of the Food, Drug, and Cosmetic Act (the Act) as amended by the Safe Medical Devices Act of 1990 this PMA was not referred to the General and Plastic Surgery Panel and FDA advisory panel for review and recommendation. This is because the information in this PMA substantially duplicates information previously reviewed by this panel.

### **XIV. CDRH DECISION**

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.

The applicant's manufacturing facility was inspected on November 7, 2001, and was found to be in compliance with the Quality System Regulation (21 CFR 820).

FDA issued an approval order on May 22, 2002.

### **XV. APPROVAL SPECIFICATIONS**

Directions for Use: See product labeling.

Hazard to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Reactions in the labeling.

Postapproval Requirement and Restrictions: See the approval order.