

SECTION IV.

**SAFETY OF INTERGEL® SOLUTION FOR USE IN
GYNECOLOGICAL PELVIC SURGERY**

**SECTION IV.
TABLE OF CONTENTS**

1.0 INTRODUCTION..... 3

2.0 INFECTION ASSOCIATED WITH CLINICAL USE OF INTERGEL®
SOLUTION..... 3

3.0 CHANGES IN NEUTROPHIL AND WHITE BLOOD CELL NUMBER AFTER
SURGERY 4

4.0 EFFECTS ON INTERGEL® SOLUTION ON BACTERIAL PERITONITIS 14

5.0 CONCLUSIONS..... 20

6.0 REFERENCES..... 21

LIST OF TABLES

- Table 2.1 PATIENT LISTED IN THE CASE REPORT FORM AS HAVING AN INFECTION
- Table 3.1 EFFECT OF ADMINISTRATION OF INTERGEL® SOLUTION ON NUMBER OF PMNS AND WBCS POST-OPERATIVELY, DAY 3
- Table 3.2 EFFECT OF ADMINISTRATION OF LACTATED RINGERS ON PMN NUMBER POST-OPERATIVELY, DAY 3
- Table 3.3 EFFECT OF ADMINISTRATION OF INTERGEL SOLUTION ON PMN NUMBER POST-OPERATIVELY, DAY 7-28
- Table 3.4 EFFECT OF ADMINISTRATION LACTATED RINGERS ON PMN NUMBER POST-OPERATIVELY, DAY 7-28
- Table 3.5 EFFECT OF ADMINISTRATION OF INTERGEL® SOLUTION ON PMN NUMBER POST-OPERATIVELY, FINAL
- Table 3.6 EFFECT OF ADMINISTRATION OF LACTATED RINGERS ON PMN NUMBER POST-OPERATIVELY, FINAL
- Table 4.1 MEDIAN (RANGE) ABSCESS SCORE FOLLOWING IMPLANTATION OF FECAL MATTER INTO THE ABDOMINAL CAVITY STUDY NO. 93-673
- Table 4.2 ABSCESS SCORES IN INDIVIDUAL RATS TREATED WITH LACTATED RINGER'S SOLUTION, 11-DAYS POST-INFECTION STUDY NO. ETH4
- Table 4.3 ABSCESS SCORES IN INDIVIDUAL RATS TREATED WITH INTERGEL® SOLUTION, 11-DAYS POST-INFECTION STUDY NO. ETH4
- Table 4.4 EFFECT OF INTRAPERITONEAL FLUIDS ON SURVIVAL AFTER PERITONEAL INFECTION STUDY NO. ETH4

1.0 INTRODUCTION

INTERGEL® Solution, a gel consisting of 0.5% sodium hyaluronate ionically crosslinked with ferric ions, has undergone extensive evaluation for safety and efficacy in blinded, randomized, placebo-controlled clinical trials in the United States and Europe. Questions have been raised regarding (1) possible elevated infection rates and (2) elevated neutrophil counts in INTERGEL® Solution-treated subjects compared to controls, and (3) concerns about the appropriate design of a pre-clinical safety study.

Each of these issues has been re-examined in detail, including completion of a supplemental pre-clinical study conducted at the request and in accord with the design suggested by FDA. The re-examination of the clinical safety data was supported by consultation with two independent clinical experts in the field of infectious disease (John Grossman, Ph.D., M.D. and John Sever, Ph.D., M.D.). Results are provided below. In addition, the results of an infection potentiation study in rats conducted at the request of FDA are presented. Taken together, the data gathered from the pivotal clinical trial on INTERGEL® Solution, coupled with safety data from animal studies, and post-marketing experience identified no notable safety issues, and indicate that the product is safe for its intended use.

2.0 INFECTION ASSOCIATED WITH CLINICAL USE OF INTERGEL® SOLUTION

In the clinical trial conducted to support the PMA under evaluation, 10 patients who received INTERGEL® Solution (patients [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED]) and 4 patients who received lactated Ringer's solution (patients [REDACTED], [REDACTED], [REDACTED], [REDACTED]) were listed in the Case Report Form (CRF) as having an infection. Of these patients, three INTERGEL® Solution subjects and one lactated Ringer's subject was believed by the Principal Investigator (PI) to be possibly, probably, or definitely related to the device, corresponding to infection rates of 3/143 (2.1%) for INTERGEL® Solution-treated subjects and 1/138 (0.7%) for lactated Ringer's-treated subjects, as discussed below. These differences are not statistically significant. Therefore, when adjusted for unrelated infection outcomes, there is no difference in the infection rate between the INTERGEL® Solution and the control group.

A listing of the 14 patients that were "coded" in the CRF as with the term "infection" is provided below in Table 2.1, in addition to the following information: a description of the reported adverse event, and the assessment by the Principal Investigator (PI) of whether the infection was either possibly, probably, or definitely device-related. As shown in this table, 3 of the 10 infections in INTERGEL® Solution-treated patients were considered possibly related to treatment. These included a subject with a bladder infection (patient [REDACTED]), a Klebsiella wound infection and abdominal pain (patient [REDACTED]), and a post-operative infection (patient [REDACTED]). In the lactated Ringer's group, one patient had a surgical site wound infection, believed by the PI to be device-related (patient [REDACTED]).

**Table 2.1
 PATIENT LISTED IN THE CASE REPORT FORM
 AS HAVING AN INFECTION**

PATIENT NO.	ADVERSE POST-OPERATIVE EVENT	STATED BY PRINCIPAL INVESTIGATOR (PI) ON CRF TO BE DEVICE-RELATED ¹
INTERGEL®-SOLUTION TREATED SUBJECTS (n=143)		
██████	chicken pox	no
██████	pelvis infection	no
██████	bladder pain, infection	possibly
██████	Klebsiella wound infection; abdominal pain, suspected infection	possibly
██████	post-operative infection	no
██████	peritoneal fluid culture positive at time of surgery (chlamydia)	no
██████	wound abscess	no
██████	head cold	no
██████	vaginal fungal infection	no
██████	infection	possibly
Total no. Infections that could be device-related		3/143 (2.1%)*
LACTATED-RINGER'S SOLUTION-TREATED SUBJECTS (n=138)		
██████	surgical site wound infection	possibly
██████	infection	no
██████	wound infection	no
██████	vaginal mycosis	no
Total no. Infections that could be device-related		1/138 (0.7%)

*Not statistically significantly different from control

These infections were noted post-operatively in other patients (both in the lactated Ringer's solution and INTERGEL® Solution-treated groups), and in no other instance were they considered by the PI to be device-related.

In summary, there was not an increase in the observation of wound or pelvic infections associated with the use of INTERGEL® Solution (3.5% infections vs. 2.2% infections in controls). This is further supported by the data available from the marketing of INTERGEL® Solution outside of the U.S.

3.0 CHANGES IN NEUTROPHIL AND WHITE BLOOD CELL NUMBER AFTER SURGERY

During the clinical evaluation of INTERGEL® Solution, a number of patients who received INTERGEL® Solution or lactated Ringer's solution were found to have an increase in circulating white blood cells due to an effect on circulating neutrophils (polymorphonuclear neutrophils, PMNs). The magnitude of the increase was comparable between INTERGEL® Solution- or lactated Ringer's-treated subjects. Any difference in the number of patients with elevated neutrophils between the treatment groups was not

¹ On Adverse Event Case Report Form (CRF), Principal Investigator (PI) graded the event as possibly, probably, or definitely related to treatment.

associated with any significant difference in clinical outcome, assessed by any parameter post-operatively, between the INTERGEL® Solution and the control group.

Under normal circumstances, neutrophils are produced in the human bone marrow at the rate of 10^{11} cells per day (Cannistra and Griffin 1988). This process is controlled by two colony stimulating factors (Granulocyte Colony Stimulating Factor or G-CSF and Granulocyte Macrophage-CSF [GM-CSF]) that direct the production and differentiation of bone marrow progenitor cells. The rate of neutrophil differentiation can increase as much as 10-fold during states of stress (such as trauma) and infection (Cannistra and Griffin 1988).

During an inflammatory response, chemotactic factors are generated which signal the recruitment of additional neutrophils to the site of injury and/or infection. Trauma and major surgery stimulate a cascade of events that mediate the inflammatory response. Activation of the complement system and of neutrophils is an early response to surgical trauma (Wanscher et al. 1989). Agents that are stimulated by surgical trauma and influence neutrophil production, apoptosis and function include: Interleukin 1, Interleukin 6, Interleukin 8, Tumor Necrosis Factor, CSFs and bioactive lipids, such as platelet activating factor (Naito et al. 1992, Leirisalo-Repo 1994). In fact, several citations have reported a relationship between the degree of surgical trauma and the release of inflammatory mediators (Ellstrom et al. 1996, Baigrie et al. 1992, Wanscher et al. 1989, Kongsgaard et al. 1989). Further, surgical stress (particularly post-operatively) is associated with a marked increase in the level of circulating catecholamines (Oyama 1973). The alpha adrenergic catecholamines markedly enhance neutrophil numbers (Hill et al. 1975).

Induction of anesthesia alone has been shown to induce a slight increase in the number of circulating neutrophils (Cullen and van Belle 1975, Khan et al. 1995, Stanley et al. 1976, Takahara et al. 1995). The magnitude of the increase may be related to the degree of trauma induced during the surgical procedure Cullen and van Belle (1975). This may be explained by the observation that major, but not minor, surgery correlates with a reduction in neutrophil apoptosis (Kobayashi and Yamauchi 1997). In general, this post-operative modulation of neutrophil number and function has been considered a normal event. Following injury or trauma, this alteration in host responsiveness may be advantageous to the individual in the clearance of tissue debris and bacterial invaders.

Therefore, a change in neutrophil number is not unexpected, as surgical trauma and anesthesia are associated with an increase in the number of circulating neutrophils. With the exception of patient [REDACTED] who received an appendectomy and was, therefore, not appropriately excluded from the study), the level of the increase in neutrophil number above the upper range for a normal population observed in the INTERGEL® Solution-treated patients was not higher than that observed in the patients who received lactated Ringer's solution (Tables 3.1-3.6). Therefore, the observed increase in neutrophils was expected and was not greater in magnitude in the treated group over control. While a greater number of patients in the treatment group had this increase (48 patients vs. 31 patients in the 3-day post-operative group), the similar magnitude of this effect in the

control group suggests that these patients are not at increased risk over that present from anesthesia and surgery alone. Much higher levels of neutrophilia have been observed in normal volunteers administered G-CSF for mobilization (approximately 6 to 7 fold increase) without significant side effects (Liles et al. 1997). This further supports a lack of risk associated with a transient, modest increase in the level of circulating neutrophils.

In a vast majority of the patients with increased circulating neutrophils, the effect was transient and was reversed by the final visit (Tables 3.1-3.6). In the few patients in whom an increase was still observed at the final visit, these patients had baseline neutrophil levels within 10% of the upper limit of neutrophil values for that center (patients listed in Tables 3.5-3.6). Further, the increase observed for these patients at the final visit was within 10% of their baseline value. Therefore, these increases may represent normal biological variability and the response of these patients to surgery.

Because an increase in the number of patients with a normal post-operative increase in neutrophil number was noted, possible correlations of this hematological change with clinical observations, such as infection, which would affect neutrophil number and adhesion formation, and AFS score (a measure of adhesion formation) were determined. In the data set available from this pivotal clinical trial, no such correlation between increased neutrophil number and notations of infection in the CRFs, or increased adhesion formation, was observed.

Table 3.1
EFFECT OF ADMINISTRATION OF INTERGEL® SOLUTION ON NUMBER
OF PMNs AND WBCs POST-OPERATIVELY, DAY 3²

PATIENT NO.	PMN (%)	WBC (thousands/cu.mm)
[REDACTED]	75.6	9.5
[REDACTED]	81.6	11.1
[REDACTED]	83	18.4
[REDACTED]	88	12.3
[REDACTED]	89	15.1
[REDACTED]	79	6.8
[REDACTED]	75.8	6.2
[REDACTED]	81	14
[REDACTED]	84.1	14.8
[REDACTED]	75	9.4
[REDACTED]	70	9.2
[REDACTED]	77	13.8
[REDACTED]	70	9.9
[REDACTED]	69	9.8
[REDACTED]	87	12.8
[REDACTED]	82	14.5
[REDACTED]	77	6.2
[REDACTED]	77.2	11
[REDACTED]	76.4	10
[REDACTED]	85	12.5
[REDACTED]	75.4	11.6
[REDACTED]	85.4	18
[REDACTED]	78.3	12.4
[REDACTED]	81.8	8.9
[REDACTED]	78.3	12.4
[REDACTED]	82.7	11.8
[REDACTED]	80.5	11.5
[REDACTED]	82.6	8
[REDACTED]	81.5	11
[REDACTED]	74.8	3.7
[REDACTED]	78.9	9.1
[REDACTED]	80	15.5
[REDACTED]	86	19.9
[REDACTED]	78.6	9.9

² All patients on this table have PMN values that were above those expected for the upper range of normals observed in the analytical laboratory.

Table 3.1 (Continued)
EFFECT OF ADMINISTRATION OF INTERGEL® SOLUTION ON NUMBER OF PMNs AND WBCs POST-OPERATIVELY, DAY 3²

PATIENT NO.	PMN (%)	WBC (thousands/cu.mm)
[REDACTED]	77.2	7
[REDACTED]	67	7.1
[REDACTED]	65	5.6
[REDACTED]	90	9.3
[REDACTED]	73.2	7.9
[REDACTED]	75.9	7.9
[REDACTED]	88	10
[REDACTED]	85.8	10.5
[REDACTED]	78	10.1
[REDACTED]	74.7	7.1
[REDACTED]	76.2	7
[REDACTED]	80.7	9.4
[REDACTED]	79.3	5.9
[REDACTED]	75.9	11.9
TOTAL NO. PATIENTS		48

Table 3.2
EFFECT OF ADMINISTRATION OF LACTATED RINGERS ON PMN
NUMBER POST-OPERATIVELY, DAY 3³

PATIENT NO.	PMN NO. (%)	WBC NO. (thousands/ μ L)
	80.2	11.3
	83.4	9.5
	78	10.4
	74	8.8
	76	8.2
	75	8.5
	71	8.2
	71	4.8
	74	8.1
	89.3	15
	82.5	9.2
	80.7	9.2
	76.6	11.5
	88	13.3
	80	8.5
	74.1	11.6
	83	15.8
	74.1	7.7
	87	15
	82	12.2
	77.4	9.4
	76.8	12.2
	62	4.9
	61	6
	78.3	9.5
	85.5	7.5
	74.4	6.1
	64	7
	82.7	10.1
	75.3	5.7
	80	9.6
TOTAL NO. PATIENTS	31	

³ All patients on this table have PMN values that were above those expected for the upper range of normals observed in the analytical laboratory.

Table 3.3
EFFECT OF ADMINISTRATION OF INTERGEL® SOLUTION ON PMN
NUMBER POST-OPERATIVELY, DAY 7-28⁴

PATIENT NO.	PMN NO. (%)	WBC NO. (thousands/ μ L)
	77.1	15.4
	82.2	14.3
	76.9	8.6
	80	9.7
	80.7	6
	70	7.8
	72	9.1
	76	9.2
	75.3	10.2
	75	18.6
	78	10.6
	72	11
	72.4	6.9
	76.9	10.3
	74.7	8.6
	70.3	7.7
	78.9	8.4
	73	8.2
TOTAL NO. PATIENTS	18	

⁴ All patients on this table have PMN values that were above those expected for the upper range of normals observed in the analytical laboratory.

Table 3.4
EFFECT OF ADMINISTRATION OF LACTATED RINGERS ON PMN
NUMBER POST-OPERATIVELY, DAY 7-28⁵

PATIENT NO.	PMN NO. (%)	WBC NO. (thousands/ μ L)
[REDACTED]	80.6	14.7
[REDACTED]	76	4.7
[REDACTED]	68.3	8.5
[REDACTED]	71	5.5
[REDACTED]	84	12.4
[REDACTED]	78	9.2
[REDACTED]	70.8	6
[REDACTED]	76.7	6.3
[REDACTED]	66	8.7
TOTAL NO. PATIENTS	9	

⁵ All patients on this table have PMN values that were above those expected for the upper range of normals observed in the analytical laboratory.

Table 3.5
EFFECT OF ADMINISTRATION OF INTERGEL® SOLUTION ON PMN
NUMBER POST-OPERATIVELY, FINAL⁶

PATIENT NO.	PMN NO. (%)	WBC NO. (thousands/ μ L)
██████	75	9.2
██████	77	7.5
██████	72.4	6.4
██████	77.5	10.4
██████	78.4	7.7
TOTAL NO. PATIENTS	5	

⁶ All patients on this table have PMN values that were above those expected for the upper range of normals observed in the analytical laboratory.

Table 3.6
EFFECT OF ADMINISTRATION OF LACTATED RINGERS ON PMN
NUMBER POST-OPERATIVELY, FINAL⁷

PATIENT NO.	PMN NO. (%)	WBC NO. (thousands/ μ L)
	69	6.8
TOTAL NO. PATIENTS	1	

⁷ The patient on this table had a PMN value that was above that expected for the upper range of normals observed in the analytical laboratory.

4.0 EFFECTS ON INTERGEL® SOLUTION ON BACTERIAL PERITONITIS

The clinical data described above are consistent with the animal data obtained with the INTERGEL® Solution administered at clinically relevant concentrations. As part of the preclinical safety studies of devices for adhesion prevention, the potentiation of infection caused by implantation of fecal material into the abdomen was evaluated in a model described by Onderdonk et al. (1974). Peritonitis was induced by implanting a double-walled gelatin capsule containing a mixture of cecal contents from hamburger-fed rats, peptone yeast broth, glucose and barium sulfate. Prior to closure of the wound, the assigned test material was applied to the area surrounding the capsule. The animals were observed daily for 11 days for signs of morbidity and mortality. Those that died during the observation period were necropsied to confirm the presence of acute bacterial infection. Those that survived the acute infection were euthanized 11 days following surgery and examined for transcutaneous palpability of the abscesses. Upon opening, the presence of splenomegaly was recorded and abscess formation at the liver, spleen, abdominal wall, retrohepatic gutter, colonic gutter, bowel, and omentum was graded by two separate observers in a blinded randomized manner based on a 5-point scale.⁸

INTERGEL® Solution is an ionically crosslinked 0.5% HA solution that is approved in Europe for marketing for adhesion prevention in the abdominal cavity (Johns et al. 1997, Johns and diZerega 2000). Hyskon in a solution of 32% dextran 70 in a dextrose solution which is approved for use as a contrast agent for hysteroscopy, but was used as an adjuvant for adhesion prevention during the 1970s and 1980s. The mortality and abscess formation data from the first study that evaluated INTERGEL® Solution and Hyskon are presented in Table 4.1 (Study No. 93-673). Of note, although in this model, Hyskon significantly increased mortality, an increase in infection rates or infection related mortality following clinical use of Hyskon as an adhesion prevention adjuvant has not been reported.

No significant differences in mortality were observed between the surgical control group, lactated Ringer's solution treated groups, INTERGEL® Solution-treated groups, or the low-volume Hyskon treated group. In contrast, administration of high-volume Hyskon significantly increased the mortality associated with the induced bacterial peritonitis (1 survivor vs. 11 to 17 in the other groups). No significant differences in abscess scores for the liver, bowel, omentum, or "other" sites (combined scores for spleen, retrohepatic gutter, and colonic gutter) were observed between any of the groups receiving Hyskon or lactated Ringer's solution compared with surgical control. In contrast, treatment with INTERGEL® Solution (both volumes) produced significant decreases in the number of

⁸ Five-point scale: 0 = no abscesses present at site, 0.5 = one very small abscess present at site, 1 = several small abscesses present at site, 2 = medium to large abscesses present at site, and 3 = one very large abscess present at site.

Table 4.1
MEDIAN (RANGE) ABSCESS SCORE FOLLOWING IMPLANTATION OF FECAL MATTER
INTO THE ABDOMINAL CAVITY STUDY NO. 93-673

Treatment Group	No. Animals Dead (N=20 per group)	Abscess Score ⁹					
		Liver	Abdominal Wall	Bowel	Omentum	Other	Total
Surgical Control							
	5						
Mean		1.53	3.07	0.80	2.20	0.33	7.93
SD		0.62	0.57	1.17	0.54	0.87	2.24
Ringer's lactate^a							
5 mL/kg							
	3						
Mean		1.33	1.87	0.33	0.53	0.27	6.33
SD		1.19	1.31	0.70	0.50	0.68	2.39
15 mL/kg							
	5						
Mean		0.93	1.60	0.20	2.27	2.00	5.00
SD		1.12	1.25	0.75	0.68	0.65	2.45
Hyskon^b							
5 mL/kg							
	6						
Mean		0.93	0.86	0.14	2.00	0.00	3.93
SD		1.03	1.25	0.52	0.65	0.00	1.75
15 mL/kg^c							
	19	2	0	0	2	0	4
INTERGEL® Solution							
5 mL/kg							
	5						
Mean		0.93	1.00*	0.00	1.80	0.00	3.73*
SD		0.93	0.97	0.00	0.54	0.00	1.65
15mL/kg							
	9						
Mean		1.22	1.07*	0.15	2.03	0.00	4.41*
SD		0.80	0.83	0.53	0.79	0.00	1.95
^a Manufactured by Baxter. ^b Manufactured by Abbott Laboratories, Inc. ^c Abscess score data are based on one surviving animal. *Significantly different from the surgical control value, p<0.05, rank analysis.							

⁹ Five-point scale: 0 = no abscesses present at site, 0.5 = one very small abscess present at site, 1 = several small abscesses present at site, 2 = medium to large abscesses present at site, and 3 = one very large abscess present at site.

abscesses in the abdominal wall and in total abscess formation relative to the surgical control group. Further, the low volume INTERGEL® Solution group also had a significantly lower total abscess score than the low volume lactated Ringer's solution control group.

This study has recently been repeated at the request of FDA (Study No. ETH4, Effect of INTERGEL® Solution on Mortality and Abscess Formation after Intraperitoneal Infection in Rats). In this study, a model of mixed bacterial flora was used in a larger group of animals (powered to detect a difference between LD₅₀ and LD₇₅) at the clinical dose of 5 ml/kg (see Tables 4.2-4.4). Out of 60 animal per group, 22 (36.7%) of the animals treated with lactated Ringer's solution and 24 (40.0%) of the animals treated with INTERGEL® Solution died post-infection (Table 4.4). The mean overall abscess scores for the rats treated with lactated Ringer's solution (6.7 ± 0.25) and INTERGEL® Solution (6.02 ± 0.32) were similar. Therefore, no differences in mortality or abscess formation were observed in animals treated with lactated Ringer's solution compared with INTERGEL® Solution (the complete study report is attached to this document in Appendix C). The above studies showed that INTERGEL® Solution reduced or did not affect abscess formation, and did not affect mortality after infection.

Table 4.2
ABSCESS SCORES IN INDIVIDUAL RATS TREATED WITH LACTATED
RINGER'S SOLUTION, 11-DAYS POST-INFECTION STUDY NO. ETH4

ABSCESS SCORE ¹⁰				
LIVER	ABDOMINAL WALL	BOWEL	OMENTUM	OVERALL
2	2	0	2	6
3	3	0	1	7
2	3	3	3	11
0	2	1	1	4
0	4	3	0	7
3	0	1	3	7
1	2	2	3	8
0	3	2	1	6
1	2	1	2	6
0	2	4	2	8
1	2	4	3	9
0	2	0	1	3
0	3	2	3	8
1	3	2	1	7
0	2	2	1	5
1	0	2	3	6
3	0	2	3	8
0	2	3	2	7
0	2	1	2	5
0	2	2	1	5
0	3	2	0	5
2	0	2	4	7
0	3	2	1	6
0	2	4	1	7
1	2	1	2	6
2	3	0	3	8
2	4	0	1	7
1	3	2	1	7
0	4	1	1	6
2	1	1	1	5
2	1	0	4	7
0	2	2	1	5
1	0	2	3	6
0	3	2	1	6
0	2	2	3	7
3	2	0	3	8
3	3	1	3	10
0	3	3	1	7
50.8±4.5 ¹¹	49.4±4.1	53.3±4.1	46.7±4.1	57.6±3.6

¹⁰ Five-point scale: 0 = no abscesses present at site, 0.5 = one very small abscess present at site, 1 = several small abscesses present at site, 2 = medium to large abscesses present at site, and 3 = one very large abscess present at site

¹¹ These values are the mean and standard error of the mean of the ranks of the abscess scores at each site and of the overall score.

Table 4.3
ABSCESS SCORES IN INDIVIDUAL RATS TREATED WITH INTERGEL®
SOLUTION, 11-DAYS POST-INFECTION STUDY NO. ETH4

ABSCESS SCORE ¹²				
LIVER	ABDOMINAL WALL	BOWEL	OMENTUM	OVERALL
1	2	0	1	4
1	2	1	1	5
2	4	3	2	11
0	2	3	2	7
0	0	2	2	4
0	1	0	1	2
0	4	0	0	4
1	2	3	3	9
2	2	0	1	5
1	3	2	2	8
1	1	0	1	3
1	4	0	2	7
0	4	1	2	7
1	4	2	2	9
2	3	2	3	10
3	1	0	2	6
1	1	0	4	6
1	3	0	3	7
0	1	1	3	5
1	2	0	3	6
0	2	2	1	5
0	3	1	1	5
1	1	0	2	4
0	3	1	2	6
1	2	1	2	6
0	3	2	2	7
0	3	2	3	8
2	0	2	3	7
0	1	2	3	6
0	3	0	1	4
0	3	1	1	5
2	2	1	1	6
0	4	2	2	8
0	1	3	2	6
0	0	4	1	5
0	2	1	1	4
44.0±3.9 ¹³	52.7±4.3	42.7±4.5	47.1±3.9	46.8±4.5

¹² Five-point scale: 0 = no abscesses present at site, 0.5 = one very small abscess present at site, 1 = several small abscesses present at site, 2 = medium to large abscesses present at site, and 3 = one very large abscess present at site

¹³ These values are the mean and standard error of the mean of the ranks of the abscess scores at each site and of the overall score.

Table 4.4
EFFECT OF INTRAPERITONEAL FLUIDS ON SURVIVAL AFTER
PERITONEAL INFECTION STUDY NO. ETH4

GROUP	NO. DIED/TOTAL	PERCENTAGE¹⁴
Lactated Ringer's solution	22/60	36.7
INTERGEL® Solution	24/60	40.0

¹⁴ Difference is not statistically significant

5.0 CONCLUSIONS

These data demonstrate that the use of INTERGEL® Solution, at clinically relevant doses, does not lead to an increase in infections when compared to control. In addition, the low, transient increase in circulating neutrophil number that is observed in some INTERGEL® Solution-treated subjects was not associated with any significant difference in clinical outcome, assessed by any parameter post-operatively, between the INTERGEL® Solution and the control group. Furthermore, the magnitude of the increase in neutrophils in INTERGEL® Solution subjects was not greater than that observed in the controls. These observations from the clinical study are supported by the animal data presented, which show that INTERGEL® Solution reduced or did not affect abscess formation, and did not affect mortality in an animal model of bacterial peritonitis.

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