MicroLyte AG

IM-BED® BIOSCIENCES
Advanced materials for wound healing

Biocompatible and Safe per ISO 10993 Standards

The biocompatibility profile of the **Microlyte™ Ag** wound dressing was assessed in accordance with International Standard *ISO-10993: Biological Evaluations of Medical Devices.*

Method and Results

According to guidelines of ISO 10993-1, Part 1, **Microlyte™ Ag** wound dressings were classified as follows:

- **Category:** Surface device
- **Contact:** 'Skin', and 'breached or compromised surface'
- **Contact Duration:** Prolonged (24 hours to 30 days)

Based on this classification, the requisite ISO biocompatibility tests were conducted as listed in Table 1. All tests were performed by an independent CRO in accordance with the provisions of the FDA Good Laboratory Practice (GLP) Regulations, 21 CFR, Part 58 during the course of the study.

TABLE 1: Biocompatibility test results of **Microlyte™ Ag** wound dressings following ISO 10993-Part 1 guidelines

TEST	METHOD	ACCEPTANCE CRITERIA	RESULT PASS/FAIL
Cytotoxicity (MTT assay) -ISO 10993 Part 5	Extracts of test article in 1x Minimum Essential Medium (at 37°C for 24 h) were incubated with L-929 mouse fibroblast cells at 37°C for 24 hours, and percent cell viability was determined by a calorimeteric MTT assay.	If cell viability is reduced to < 70% of the reagent control extract, a cytotoxic potential exists.	≥ 95% cell viability **PASS**
Acute Systemic Toxicity Study in Mice -ISO 10993 Part 11	The test article was extracted in 0.9% sodium chloride (SC) and sesame oil (SO) at 37°C for 72 hours (extract ratio, 6 cm2: 1 mL). A single dose (50 mL/kg) of extract, or the extract vehicle was **injected intraperitoneally** into each animal (5 mice/group). Mice were observed for signs of systemic toxicity at 4, 24, 48 and 72 hours.	No test animal exhibit a significantly greater reaction than the control animals, i.e. dead, convulsions, prostration, or >2 g weight loss.	No mortality or evidence of systemic toxicity. All animals gained weight over the course of study. **PASS**
Acute Intracutaneous Reactivity Study in Rabbits - ISO 10993 Part 10	The test article was extracted in SC or SO as described above. A 0.2 mL dose of extract was **injected intracutaneously** into five separate sites on the right side of the back of each 3 animals, while the extract vehicle alone was injected on the left side. The injections sites were scored on a scale of 0 to 4 for erythema and edema at 24, 48 and 72 hours after injection.	The difference in overall mean score for erythema and edema between the test extract and corresponding control was 1.0 or less.	The difference in mean scores was 0.0 for SC extracts, and 0.2 for SO extracts. **PASS**
Maximization Sensitization Test in Guinea Pigs - ISO 10993 Part 10	Extract of test article in SC or SO (prepared as described above) were **intradermally injected and occlusively patched** to 10 test guinea pigs (per extract). The extraction vehilce (blank control) was similarly injected and patched in 5 control guinea pigs (per vehicle). **Following a recovery period (24 days)**, the test and control animals received **a challenge patch** of the appropriate test article extract or the vehicle alone. **In addition, the test article was applied** to the same animals. Patches were removed after 24 hours. All sites were scored on a scale of 0 to 3 for dermal reactions (erythema) at 24 and 48 hours after patch removal.	Grades of 1 or greater observed in the test group generally indicated sensitization, provided that grades of less than 1 were observed on the control animals.	The test article extracts and the test article showed no evidence of causing delayed dermal contact sensitization in the guinea pig. The test article was not considered a sensitizer. **PASS**
Subacute/Sub-chronic systemtic toxicity in rats -ISO 10993 Part 11	Test or control article (Telfa non-adherent cotton pads) applied to full-thickness 2 cm x 2 cm wounds on the back of rats. Articles were replaced on days 3, 7, 14, 21. Six rats per sex per group (total 24 rats) for meaningful statistical analysis of systemic toxicity parameters after 28 days on study. Dosage applied in rats was 50x exaggeration of the clinical dose received by a 50 kg man. Blood samples collected at the end of 28 days for hematologic and clinical chemistry analysis. Body weight, organ weight, organ/body weight and organ/brain weight ratios, hematology and clinical chemistry values were evaluated statistically. Male and female data were analyzed separately unless a rationale exists for combing the sexes.	Systemic tissues including the liver, spleen, both kidneys, submandibular and mesenteric lymph nodes, both adrenals, heart, thymus, lungs and bronchi, and both testes or ovaries were collected, evaluated macroscopically, fixed, sectioned, stained, and evaluated microscopically.	All wounds healed within 21 days. No difference in absolute organ weights and organ/body weight ratios between test groups. No effect on hematologic parameters and clinical chemistry parameters of blood samples. No macroscopic or microscopic tissue changes indicative of systemic toxicity. **PASS**

Conclusion

Microlyte™ Ag wound dressing is biocompatible and safe for it's intended use in management of partial and full thickness wounds including pressure ulcers, venous ulcers, diabetic ulcers, first and second degree burns, abrasions and lacerations, donor sites and surgical wounds, and debrided and grafted partial thickness wounds.