HaloGUARD™

Summary of ISO 10993 Biocompatabilty Testing and Wound Healing Studies for HaloGUARD vs. BioPatch

HaloGUARD was evaluated according to recommended ISO biocompatibility tests for safety and compared with the predicate BioPatch. Upon completion of the testing FDA requested further in-vivo testing designed to evaluate the effect both HaloGUARD and BioPatch may have on wound healing. This test is not the standard required for this type of device, but was asked for by FDA due to the presence of MDR's related to patch devices and wounds.

TABLE 1: Summary of ISO 10993 Testing Completed

Study	Test Method	HaloGUARD Results	BioPatch Results
L929 Agar Diffusion	ISO 10993-5 Tests for in-vitro Cytotoxicity	24 hours: Grade 0 48 hours: Grade 1 Non-cytotoxic	Not tested
L929 MEM Elution	ISO 10993-5 Tests for in-vitro Cytotoxicity	Moderate Biological Reactivity: Grade 3 (Scale of 0 to 4)	Severe Biological Reactivity: Grade 4 (Scale of 0 to 4)
Intracutaneous Injection Assay	ISO 10993-10 Tests for Irritation and Skin Sensitization (Irritation)	Non-irritant	Non-irritant
Systemic Toxicity Test	ISO 10993-11 Tests for Systemic Toxicity	Not systemically toxic	Not systemically toxic
Article-Mediated Rabbit-Pyrogen Assay	ISO 10993-11 Tests for Systemic Toxicity	Non-pyrogenic	Non-pyrogenic
Kligman Maximization Test	ISO 10993-10 Tests for Irritation and Skin Sensitization	Non-sensitizer	Not tested
Determination of Chemical Compounds Present In and On the Sponsor Device	ISO 10993-18 Chemical Characterization	No significant extract-able or leachable material was reported	Not tested
Full Thickness Excisional Wound Healing Study in Swine	ISO 10993-6 Tests for Local Effects After Implantation	See Tables Day 7 through Day 28 for details	

Table 1 above shows that HaloGUARD is overall sunstantially equivalent to BioPatch. What is noteworthy is that BioPatch showed severe reactivity in the cytotoxicity assay compared to HaloGUARD.

The wound healing study is a porcine model where artificial wounds are created of specific size and depth on the backs of the subject animals bi laterally along the spinal column. The wounds on one side are covered with the BioPatch and wounds on the opposite side covered with HaloGUARD. Wounds are observed for a number of characteristics once every 7 days, when a fresh patch is placed over the wound. The following tables summarize the observations made by the laboratory during the 28 day period of the study.

TABLE 2: Wound Healing Study Day 7 Evaluation Data Summary

Characteristic	Control Average[+] (Predicate Device)	Test Average[+] (Predicate Device)	Subject Device Results
Mean Wound Circumference (cm)	7.1	7.0	Substantially Equivalent
Signs of Infection*	0.0	0.0	Substantially Equivalent
Granulation Tissue*	0.0	0.0	Substantially Equivalent
Erythema*	0.5	0.5	Substantially Equivalent
Hair Regrowth*	0.0	0.0	Substantially Equivalent
Eschar Formation**	0.0	0.0	Substantially Equivalent
Estimate of Re-epithelialization*	0.0	0.0	Substantially Equivalent
Photos Taken	Yes	Yes	Substantially Equivalent

*scored as 0 = none; 1 = mild; 2 = moderate; 3 = severe
**scored as 0 = absent; 1 = present
[+]averages calculated as total observational scores divided by total sites in test or control group

TABLE 3: Wound Healing Study Day 14 Evaluation Data Summary

Characteristic	Control Average[+] (Predicate Device)	Test Average[+] (Predicate Device)	Subject Device Results
Mean Wound Circumference (cm)	6.7	7.0	Substantially Equivalent
Signs of Infection*	1.8	1.5	Substantially Equivalent
Granulation Tissue*	1.8	1.8	Substantially Equivalent
Erythema*	0.0	0.3	Substantially Equivalent
Hair Regrowth*	0.1	0.2	Substantially Equivalent
Eschar Formation**	0.6	0.6	Substantially Equivalent
Estimate of Re-epithelialization*	1.2	1.2	Substantially Equivalent
Photos Taken	Yes	Yes	Substantially Equivalent

*scored as 0 = none; 1 = mild; 2 = moderate; 3 = severe
**scored as 0 = absent; 1 = present
[+]averages calculated as total observational scores divided by total sites in test or control group

TABLE 4: Wound Healing Study Day 21 Evaluation Data Summary

Characteristic	Control Average[+] (Predicate Device)	Test Average[+] (Predicate Device)	Subject Device Results
Mean Wound Circumference (cm)	5.0	4.9	Substantially Equivalent
Granulation Tissue*	1.4	1.4	Substantially Equivalent
Signs of Infection*	0.8	0.7	13% less than Predicate
Erythema*	0.2	0.1	Substantially Equivalent
Hair Regrowth*	0.0	0.0	Substantially Equivalent
Eschar Formation**	0.8	0.8	Substantially Equivalent
Estimate of Re-epithelialization*	1.1	1.2	Substantially Equivalent
Photos Taken	Yes	Yes	Substantially Equivalent

*scored as 0 = none; 1 = mild; 2 = moderate; 3 = severe
**scored as 0 = absent; 1 = present
[+]averages calculated as total observational scores divided by total sites in test or control group

TABLE 5: Wound Healing Study Day 28 Evaluation Data Summary

Characteristic	Control Average[+] (Predicate Device)	Test Average[+] (Predicate Device)	Subject Device Results
Mean Wound Circumference (cm)	4.2	3.6	15% smaller than Predicate
Granulation Tissue*	1.8	1.8	Substantially Equivalent
Signs of Infection*	0.8	0.3	63% less than Predicate
Erythema*	0.1	0.1	Substantially Equivalent
Hair Regrowth*	0.1	0.2	Substantially Equivalent
Eschar Formation**	0.7	0.6	20% less than Predicate
Estimate of Re-epithelialization*	0.6	1.2	50% greater than Predicate
Photos Taken	Yes	Yes	Substantially Equivalent

*scored as 0 = none; 1 = mild; 2 = moderate; 3 = severe
**scored as 0 = absent; 1 = present
[+]averages calculated as total observational scores divided by total sites in test or control group

Observation Summary

Tables 2 through 5 have evaluated a number of wound healing characteritics and have indicated that by day 21, HaloGUARD showed a 63% reduction in observed signs of infection; a 15% smaller wound circumference; 20% less eschar formation and 50% greater re-epithelialization than the predicate BioPatch.

Conclusions and Design Considerations:

HaloGUARD was designed to attempt to address some of the shortcomings seen with clinical use of the BioPatch. HaloGUARD uses a softer foam with specific porosity characteristics so as to help alleviate some of the irritation issues associated with BioPatch. HaloGUARD has sustained release of CHG to ensure 7 days of release and meet 168 hour efficacy requirements, table 7 below shows the results of challenging the same location of a HaloGUARD™ patch with 10^6 CFU/ml for 7 days.

TABLE 6: Microbial Simulated Use Challenge Results (Day 7)

Microorganism Challenge Strain	Log_{10} CFU/Challenge
Staphylococcus aureus (MRSA)	6.3
Staphylococcus epidermidis (MRSE)	6.2
Vancomycin-Resistant Enterococci (VRE)	6.1
Pseudomonas aeruginosa (P. aeruginosa)	6.3
Klebsiella pneumoniae (K. pneumoniae)	6.4
Enterobacter cloacae (E. cloacae)	6.3
Candida albicans (C. albicans)	5.6
Candida tropicalis (C. tropicalis)	5.2

The results clearly indicate that there is a minimum of 5.2 log reduction even after 7 days of microbial challenge.