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Loctite Corporation
1001 Trout Brook Crossing
Rocky Hill, CT 06067

Date of Test Completion: October 31, 2003
Project Numbers: 03-3249

Certificate of Compliance
ISO 10993 Biological Tests
[INCLUSIVE OF ADDITIONAL USP PHYSICOCHEMICAL TESTING]

Test Article: Loctite 4305 Medical Device Adhesive

Lot Number: 3D067

INTRACUTANEOUS INJECTION (ISO): The purpose of this test is to evaluate the irritation potential of the test article extracts in rabbits after intracutaneous injection. Test article extract in saline, cottonseed oil, polyethylene glycol 400 and alcohol in saline did not produce a significantly greater tissue reaction than blank extract when injected intracutaneously into rabbits. Additional extracts (PEG & Alcohol in Saline) were used to cover the requirements of United States Pharmacopeia 26, National Formulary 21, 2003; Monograph <88>: Biological Reactivity Tests, *In Vivo*. Based on the criteria set forth by the protocol, the test article is considered negligible or slight irritant-conforms. *Reference: Biological Evaluation of Medical Devices - Part 10: Irritation and Delayed-type Hypersensitivity, ISO 10993-10, 2002.*

ACUTE SYSTEMIC INJECTION (ISO): The purpose of this assay is to evaluate the test article extracts for potential toxic effects as a result of single dose systemic injection in mice. Test article extracted in saline, cottonseed oil, polyethylene glycol 400 and alcohol in saline did not produce a significantly greater systemic reaction than blank extract when injected into mice. Additional extracts (PEG & Alcohol in Saline) were used to cover the requirements of United States Pharmacopeia 26, National Formulary 21, 2003; Monograph <88>: Biological Reactivity Tests, *In Vivo*. The test article did not show greater biological reactivity compared to the control material-conforms.
Reference: Biological Evaluation of Medical Devices - Part 11: Tests for Systemic Toxicity, ISO 10993-11:1993.

CYTOTOXICITY (ISO): The purpose of the MEM Elution is to determine biological reactivity of monolayer cell culture (L929) in response to the test article. The test article is considered non-cytotoxic and meets the requirements of the MEM Elution Test, ISO 10993-5.
Reference: Biological Evaluation of Medical Devices-Part 5: Tests for In Vitro Cytotoxicity, ISO 10993-5:1999.

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HEMOCOMPATIBILITY (ISO):
Hemolysis: This assay is designed to evaluate the hemolytic potential of the test article extracts. Hemolytic activity of the test article with rabbit blood indicated that the test article was non-hemolytic (<5%).
Reference: Biological Evaluation of Medical Devices - Part 4: Selection of Tests for Interactions with Blood, ISO 10993-4, 2002.

***In Vitro* Hemocompatibility Assay**: This assay is designed to ensure that the test material extract does not adversely affect the cellular components of blood. The test article was evaluated for its potential to adversely affect selected hematological parameters. The hematological parameters tested were complete blood count including platelets, hematocrit, erythrocyte indices and free plasma hemoglobin. The test article meets the requirements.
Reference: Biological Evaluation of Medical Devices - Part 4: Selection of Tests for Interactions with Blood, ISO 10993-4:2002.

IMPLANTATION TEST (ISO): The macroscopic and histological reaction of the test article, implanted in rabbit muscle for 2 weeks was not significant when compared to negative control sites-conforms.
Reference: Biological Evaluation of Medical Devices - Part 6: Tests for Local Effects After Implantation, ISO 10993-6: 1994.

PHYSICOCHEMICAL TEST (USP): This test determines the physical and chemical properties of extracts of test material. The test article passes the USP Physiocochemical Tests for plastics.
Reference: United States Pharmacopeia 26, National Formulary 21, 2003.

These studies are in conformance to all applicable laws and regulations. Specific regulatory requirements include the current Good Laboratory Practice for Nonclinical Studies (GLP), FDA, 21 CFR, Part 58.

The adhesive bonded polycarbonate lap shears utilized to approximate typical medical device applications are disassembled prior to testing in order to maximize adhesive exposure during the respective tests. All test results reflect maximum exposure of the adhesive to the various test parameters and conditions. In this manner, the adhesive test results provide a higher margin of safety when compared to the tests involving only the bondline area and thickness.

Study Director

Quality Assurance

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