

Loctite Corporation  
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Rocky Hill, CT 06067

**Date of Test Completion:** June 1, 2000  
**Project Number:** 00-1693  
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**Certificate of Compliance**  
**ISO 10993 Biological Tests**

[INCLUSIVE OF ADDITIONAL USP PHYSICOCHEMICAL TESTING]

**Test Article:** LOCTITE 4081 Instant Adhesive, Polycarbonate Bonded Lap Shears

**Lot No:** OB072

**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 23, National Formulary 18, Monograph <88>: Biological Reactivity Tests, In Vivo. Based on the criteria set forth by the protocol, the test article is considered a negligible or slight irritant-conforms.

*Reference: Biological Evaluation of Medical Devices - Part 10: Tests for Irritation and Sensitization, ISO 10993-10:1995*

**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 23, National Formulary 18, 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 Cytotoxicity: In Vitro Methods, 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 Interaction with Blood, ISO 10993-4:1992*

**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 Interaction with Blood, ISO 10993-4:1992*

**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 Physicochemical Tests for plastics.

*Reference: United States Pharmacopeia 24*

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, CFR, Part 58

The bonded lap shears 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 tests involving only the bondline area and thickness.

  
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Study Director

  
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QA Officer

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