VII. Conclusions

These studies were conducted for McGhan Medical Corporation by

to determine the potential of Patch and Overlay Assembly to compromise the immune system. In female B6C3F1 mice implanted with Patch and Overlay Assembly Test Article for 28 days, no biologically significant effects were observed on standard toxicological parameters including spleen weights, thymus weights, thymus histopathology or leukocyte number.

Overall, exposure to the Patch and Overlay Assembly did not produce significant changes in the functional ability of the immune system. Although changes were observed in B cell and T cell subset populations, the effect appears to be due to the decrease in spleen cell number observed following exposure to the Patch and Overlay Assembly. Of the cell populations evaluated, the T cell population in general and the $CD4^+$ T helper cell subpopulation in particular appeared to be the most affected. However, in the two functional assays, the IgM spleen antibody-forming cell response and the mixed leukocyte response, both of which are T cell dependent assays, no significant decrease in function was observed in the animals exposed to the Patch and Overlay Assembly Test Article. While no significant effect was observed on the natural killer cell function when evaluated on a specific activity basis, a decrease was observed in the high dose group, when the data were evaluated as total spleen activity. This decrease may, in part, be due to the decrease in spleen cell number.

The results of this comprehensive immunotoxicological evaluation demonstrate that, under the experimental conditions used, although changes in spleen cell number and spleen cell populations were observed, exposure to the Patch and Overlay Assembly Test Article did not adversely affect the functional ability of the immune system.

VIII. REFERENCES

1 Luster, M.I., Portier, C., Pait, D.C., White, K.L., Jr., Gennings, C., Munson, A.E. and Rosenthal, G.J. 1992. Risk assessment in immunotoxicology. I. Sensitivity and predictability of immune tests. *Fund. Appl. Toxicol.* 18:200-210.

2 Bradley, S.G., Munson, A.E., McCay, J.A., Brown, R.D., Musgrove, D.L., Wilson, S., Stern, M., Luster, M.I. and White, K.L., Jr. 1994. Subcronic 10 day immunotoxicity of polydimethylsiloxan (silicone) fluid, gel and elastomer and polyurethane disks in female B6C3F1 mice. *Drug and Chem. Toxicol.* 17(3):175-220.

3 Bradley, S.G., White, K.L., Jr., McCay, J.A., Brown, R.D., Musgrove, D.L., Wilson, S., Stern, M., Luster, M.I. and Munson, A.E. 1994. Immunotoxicity of 180 day exposure to polydimethylsiloxan (silicone) fluid, gel and elastomer and polyurethane disks in female B6C3F1 mice. *Drug and Chem. Toxicol.* 17(3):221-269.

4 Jerne, N.K., Henry, C., Nordin, A.A., Fuh, H., Koros, M.C. and Letkovits, I. 1974. Plaque-forming cells: Methodology and theory. *Transpl. Rev.* 18:130-191.

5 Luster, M.I., Munson, A.E., Thomas, P., Holsapple, M.P., Fenters, J., White, K.L., Jr., Lauer, L.D. and Dean, J.H. 1988. Development of a testing battery to assess chemical-induced immunotoxicity. *Fund. Appl. Toxicol.* 10:2-19.

6 Bartlett, M.S. 1937. Sub-sampling for attributes. *J. Roy. Stat. Soc. Suppl.* 4:131-135.

7 Kruskall W.H. and Wallis, W.A. 1952. Use of ranks in one-criterion variance analysis. *J. Amer. Stat. Assoc.* 47:583-621.

8 Dunnett, C.W. 1955. A multiple comparison procedure for comparing several treatments with a control. *J. Amer. Stat. Assoc.* 50:1096-1121.

9 Wilson, K.V. 1956. A Distribution Free Test of Analysis of Variance Hypothesis. *Psychol. Bull.*, 53:96-101.

10 Gross, A.J. and Clark, V.A. 1975. Gehan-Wilcoxon Test. In *Survival Distribution: Reliability Applications in Biomedical Sciences* (A.J. Gross and V.A. Clark, eds.). John Wiley & Sons, New York, p. 120-123.

11 Hollander, M. and Wolfe, D.A. 1975. Jonckheere's Test: Non-Parametric Statistics Methods (M. Hollander and D.A. Wolfe, eds.). John Wiley & Sons, New York, p. 124-129.

12 Sokal, R.R. and Rohlf, F.J. 1981. *Biometry*. Freeman, San Francisco, p. 226-231.