Flexcon® DermaFlex™ H-778 Adhesive Biocompatibility Statement

Below are the biocompatibility test results for Flexcon's DermaFlex™ H-778 adhesive, as provided by Flexcon's adhesive supplier. Flexcon's "H-778" adhesive part number is in place of the adhesive supplier's part number. "Flexcon's Adhesive Supplier" is in place of references to vendor identity.

Toxicological Assessment of "H-778" Acrylic Copolymer Solution for Skin Contact Applications

EXECUTIVE SUMMARY

"H-778" is a solvent based acrylic copolymer adhesive intended to be used in medical devices with skin contact application. According to the International Organization for Standardization (ISO) 10993-1, there are three main toxicological endpoints which need to be assessed for skin contact application: cytotoxicity, skin irritation (or intracutaneous reactivity) and sensitization. "Flexcon's Adhesive Supplier" has conducted safety testing with "H-778" and it can be concluded that the adhesive is suitable for skin contact application and is not expected to be irritating or sensitizing. Results from safety testing are described in a recent safety assessment1 and are summarized below in more details.
It must be noted that the manufacturing steps of final products incorporating "H-778" include drying steps at elevated temperatures which lead to the evaporation of solvents, residual monomers and other impurities. The concentration of such residual components in the final product depend on the particular drying process parameters which may have an impact on the toxicological properties of an adhesive and is therefore outside of "Flexcon's Adhesive Supplier's" control. It is therefore recommended to monitor the residual levels of solvents and impurities in the finished product. The solvent in which "H-778" is delivered contains toluene. If any significant amount of toluene is still present in the dried adhesive film, a consumer exposure assessment might be necessary to ensure compliance with US Regulatory Agencies including California Proposition 65.

Toxicological Evaluation

Potential for Cytotoxicity

Flexcon's "H-778" was tested[2] in vitro for cellular cytotoxicity (ISO 10993-5 Part 5) using L-929 mouse fibroblast cell cultures and the study was conducted according to Good Laboratory Practices (GLP). The cytotoxicity assay is defined by a colorimetric quantitative measurements of cell viability and proliferation. The principle of the method is based on the conversion of yellow-colored tetrazolium salt (MTT) to insoluble purple-colored formazan crystals by the action of NADPH-oxidoreductase enzymes present in viable and undamaged cells. Therefore, the intensity of the purple-colored formazan is directly proportional to cell viability. In the MTT assay, the adhesive film was extracted at a ratio of 6 cm^2: mL of Minimal Essential Medium (1X MEM) for 24 hours at 37°C and undiluted as well as diluted extracts were tested in triplicate on monolayers of L-929 mouse fibroblast cells for 24-26 hours at 37°C. Under the conditions of the study, "H-778" extracts did not cause cell toxicity, while the positive and the negative controls performed as expected. Thus, it can be concluded from this test that the adhesive "H-778" is not expected to induce cytotoxicity.

Dermal Irritation

The primary dermal irritation potential of "H-778" was determined[3] according to ISO 10993-10: 2010 (E) and conducted according to GLP. A total of 3 young and healthy New Zealand albino rabbits were administered a single dose of 2.5 cm^2 dry adhesive film and placed on two of four clipped intact skin sites of the back of each animals. The remaining two sites serves as negative control and the sites including test articles were semi-occluded for 4 hrs. The skin was observed for erythema and oedema or other evidence of dermal irritation (Primary Irritation Index (PII)) at 1 hour following the removal of the skin cover, and at 24, 48 and 72 hours. The adhesive did not produced irritation at any sites examined and the primary irritation index for the 24, 48 and 72 hours exposure was 0 (Koch, R., email communication). Therefore it can be concluded that "H-778" is not expected to be irritating in humans.
In addition, "H-778" was evaluated in several studies involving human subjects (N=24) was applied to the arm for a period of 3 weeks ('Flexcon Adhesive Supplier' Reports No. [redacted]&[redacted]) under semi-occlusive condition. Results showed that the test article was found to be slightly irritating (erythema score ranged from 1.08-1.13) immediately following patch removal.

Skin Sensitization

The sensitization potential of “H-778” was determined in a Buehler sensitization test[6] according to ISO 10993-10 and conducted according to GLP. The adhesive was applied for 6-8 hours to the intact skin under occlusive condition to ten guinea pigs, as a patch of 25 x 25 mm2 of coated adhesive. Animals were treated three times a week and for a total of nine induction treatments over a three-week period. The control article was similarly patched to five guinea pigs. After one week of rest period, both control and treated animals were challenged with one topical application of the tested adhesive film for 6-8 hours with evaluations at 24 and 48 hours post-application. The adhesive film was considered a non-skin sensitizer.

Conclusions

From a toxicological point of view “H-778” can be considered suitable for skin contact applications in accordance to ISO 10993 and based on animal and human data. However, it remains the responsibility of the manufacturer of the final finished product to monitor the residual levels of monomers and impurities resulting from its own process and evaluate the safety of the final product. It is recommended to test manufacturer specific samples of the final product for its dermatological compatibility with human volunteers.