Environmental Protection Agency § 798.4100


[50 FR 39397, Sept. 27, 1985, as amended at 54 FR 21064, May 16, 1989]

Subpart E—Specific Organ/Tissue Toxicity

§798.4100 Dermal sensitization.

(a) Purpose. In the assessment and evaluation of the toxic characteristics of a substance, determination of its potential to provoke skin sensitization reactions is important. Information derived from tests for skin sensitization serves to identify the possible hazard to a population repeatedly exposed to a test substance. While the desirability of skin sensitization testing is recognized, there are some real differences of opinion about the best method to use. The test selected should be a reliable screening procedure which should not fail to identify substances with significant allergenic potential, while at the same time avoiding false negative results.

(b) Definitions. (1) Skin sensitization (allergic contact dermatitis) is an immunologically mediated cutaneous reaction to a substance. In the human, the responses may be characterized by pruritis, erythema, edema, papules, vesicles, bullae, or a combination of these. In other species the reactions may differ and only erythema and edema may be seen.

(2) Induction period is a period of at least 1 week following a sensitization exposure during which a hypersensitive state is developed.

(3) Induction exposure is an experimental exposure of a subject to a test substance with the intention of inducing a hypersensitive state.

(4) Challenge exposure is an experimental exposure of a previously treated subject to a test substance following an induction period, to determine whether the subject will react in a hypersensitive manner.

(c) Principle of the test method. Following initial exposure(s) to a test substance, the animals are subsequently subjected, after a period of not less than 1 week, to a challenge exposure with the test substance to establish whether a hypersensitive state has been induced. Sensitization is determined by examining the reaction to the challenge exposure and comparing this reaction to that of the initial induction exposure.

(d) Test procedures. (1) Any of the following seven test methods is considered to be acceptable. It is realized, however, that the methods differ in their probability and degree of reaction to sensitizing substances.

(i) Freund’s complete adjuvant test.

(ii) Guinea-pig maximization test.

(iii) Split adjuvant technique.

(iv) Buehler test.

(v) Open epicutaneous test.

(vi) Mauer optimization test.

(vii) Footpad technique in guinea pig.

(2) Removal of hair is by clipping, shaving, or possibly by depilation, depending on the test method used.

(3) Animal selection—(i) Species and strain. The young adult guinea pig is the preferred species. Commonly used laboratory strains should be employed. If other species are used, the tester should provide justification/reasoning for their selection.

(ii) Number and sex. (A) The number and sex of animals used will depend on the method employed.

(B) The females should be nulliparous and nonpregnant.

(4) Control animals. (i) Periodic use of a positive control substance with an acceptable level of reliability for the test system selected is recommended;

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§ 798.4350 Inhalation developmental toxicity study.

(a) Purpose. In the assessment and evaluation of the toxic characteristics of an inhalable material such as a gas, volatile substance, or aerosol/particulate, determination of the potential developmental toxicity is important. The inhalation developmental toxicity study is designed to provide information on the potential hazard to the unborn which may arise from exposure of the mother during pregnancy.