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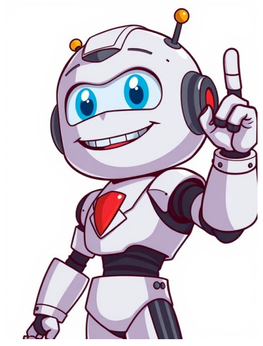

The OECD 402 test is a procedure for evaluating the hazards to human health resulting from short-term skin exposure to a chemical. According to this method, certain chemicals should not be administered above a known dose to avoid causing pain or distress through corrosive or irritating mechanisms. Some animals of the same sex are exposed dermally to the test chemical for a short period in a sequential procedure with predetermined concentrations. The initial dose is chosen so that clear signs of toxicity are expected at this concentration without leading to severe toxic effects or mortality. This OECD 402 method provides information on hazardous properties to classify chemical compounds for acute toxicity under the Globally Harmonised System of Classification and Labelling of Chemicals. Analytice offers OECD 402 testing through its network of partner laboratories, most of which have accreditation. The test can be performed under GLP (Good Laboratory Practice) conditions or without it, with both options including the preparation of an IUCLID compliant report. For more information regarding the application of the OECD 402 test in the laboratory, please contact us. ========== ========== the test material is non-toxic Information from the test data of similar compounds If information is absent then proceed for the main test For the limit test the sighting study begins at 2000 mg/Kg followed by subsequent dosing of 4 animals. ========== A study involving 5 males and 5 females, weighing between 22-28 kg, examined the effects of various doses of a test substance on skin toxicity. The testing protocol included three dose levels, with a limit test implemented to minimize animal suffering. The procedure involved administering the test substance for at least 6 hours daily, seven days a week, for 21-28 days. A satellite group was also kept for an additional 14 days to observe any potential long-term effects. Observations were made on changes in fur, skin color, eyes, mucus membranes, and weight. Clinical examinations included hematological and clinical biochemistry tests, while pathology involved a gross necropsy of adrenals, kidneys, testes, and liver. Histopathology was also conducted to assess any potential toxic effects. A total of 411 animals were used in this study, which adhered to the OECD guideline for subchronic dermal toxicity. The protocol included an acute toxicity testing phase, followed by a definition that outlined adverse effects resulting from repeated daily dermal application. The test substance was applied in graduated doses, with one dose administered per day to each group. The experiment involved 20 animals per sex, plus a satellite group of high-dose treatment, which observed extra for 28 days. Housing and feeding conditions were strictly controlled. Three dose levels were used, with a limit test implemented if skin damage occurred early in the study. If toxicity wasn't expected based on data from similar compounds, then a full study was carried out. The observation period was once daily, with animals treated for at least 6 hours daily, seven days a week, for 90 days. Clinical examinations included ophthalmological tests, hematology, and clinical biochemistry. Pathology involved a gross necropsy of adrenals, kidneys, testes, and liver, followed by histopathology to assess toxic effects. This study aimed to refine the method for assessing skin corrosion using an in vitro membrane barrier test, as outlined in OECD guideline 435. ========== The efficacy of the OECD guidelines in evaluating irritant responses was investigated. Observations showed signs of erythema and oedema at 60 minutes, and then at 24, 48 and 72 hours after patch removal. The reversibility of dermal lesions should be considered when assessing irritant responses. When responses such as alopecia (limited area), hyperkeratosis, hyperplasia and scaling persist to the end of the 14-day observation period, test substance - an irritant, OECD guideline 404, is required. The primary issue lies in the rabbits being exposed to corrosives which induce very deep wounds resulting in severe pain and distress. A comparison of data from rabbit tests and four-hour human skin patch tests for 65 substances found that 45 percent of classifications of chemical irritation potential based on animal tests were incorrect. TER (Transcutaneous Electrical Resistance Test) was introduced as a measure to identify corrosives by their ability to produce a loss of normal stratum corneum integrity and barrier function. It measures the electrical impedance of the skin, as a resistance value in kilo Ohms. The overall sensitivity of TER is 94% for a database of substances. However, TER does not provide information on skin irritation nor allows sub-categorization of corrosive substances as permitted in the Globally Harmonized Classification System (GHS). A disadvantage of TER is that neutral organics and chemicals with surface-active properties can remove skin lipids making the barrier more permeable to ions. Thus, if the TER values of test substances are less than or around 5 kΩ, the permeability can be tested using dye penetration. The Chemical Detection System (CDS) was introduced as an In Vitro Membrane Barrier Test OECD guideline-435. It uses a commercial test kit with a synthetic macromolecular bio-barrier held on a permeable barrier and includes a pH indicator dye or combination of dyes for chemical detection. Initially substance compatibility testing is carried out, using corrosive standard (NaOH), and a negative (non-corrosive) control substance should also be used. ==========The testing of chemicals, like the one being tested concurrently with the membrane barrier, helps us understand their impact on skin health. ========== This test substance's ability to cause harm is measured by how quickly it penetrates the barrier and causes damage. The time between application and penetration is used to determine corrosivity levels. ========== The study uses a human skin model, as outlined in the OECD Guideline 435, to assess the potential hazards of this chemical when applied to the skin. It also analyzes multiple endpoints, including inflammatory mediators and tissue viability. ========== The OECD 402 Acute Dermal Toxicity test is used to evaluate the short-term risks of a substance when it comes into contact with the skin. This study involves rats and follows Good Laboratory Practice regulations. The results are part of the Acute Toxicity Six-Pack tests. ========== There are two types of tests: limit tests and full tests. Limit tests quickly determine if the substance has low toxicity, while full tests provide a comprehensive assessment by establishing a dose-response relationship. Full tests are more resource-intensive but offer more detailed data for regulatory use. ========== The test article is applied to a shaved area of skin for 24 hours, with animals observed daily for at least 14 days. The weights of the animals are determined weekly, and all animals undergo a gross necropsy at the end of the study.Acute, sub acute and chronic dermal toxicity studies submitted by Gummadi Helasri (I M.Pharma) Dept. of pharmacology ========== The guideline for testing chemicals emphasizes the need to understand acute dermal toxicity, which refers to adverse effects caused by a substance after a single brief exposure through skin application over 24 hours or less. This is crucial due to scientific progress and animal welfare considerations. The test procedure involves exposing groups of female rats to the test chemical in a step-by-step manner, using fixed doses as outlined in Annex 2. The classification for each test chemical is determined based on observed outcomes. Before the experiment, animals are selected based on certain criteria such as weight, health, and skin condition. They are then housed in controlled conditions with adequate lighting, temperature, and humidity. On the day of administration, their fur is clipped from a specific area to expose their skin. The test chemical is applied uniformly over the exposed area using a porous gauze dressing and non-irritating tape. This procedure ensures that the substance comes into contact with the skin for 24 hours while minimizing irritation. The animals are observed at regular intervals, including during the first 30 minutes, every hour within the first 24 hours, daily thereafter, and even after 14 days. The observation period includes monitoring changes in skin and fur, eyes, mucous membranes, respiratory, circulatory, nervous system, somatomotor activity, and behavior patterns. Special attention is given to signs such as tremors, convulsions, salivation, diarrhoea, lethargy, sleep, and coma. During the study, individual weights of animals are recorded before and after, while all gross pathological changes are noted and microscopic examinations conducted on organs showing evidence of pathology. The test report must include information on species used, toxic response data by sex and dose, time of death or survival, effects observed at each abnormal sign, food and body weight data, haematological tests employed, and other relevant details.With relevant baseline data; clinical biochemistry tests used; necropsy findings; a detailed description of all histopathological findings; and statistical treatment of results where appropriate. Discussion and interpretation of results; conclusion. Repeated Dose Dermal Toxicity: 21/28-day Study Sub acute dermal toxicity studies; adopted: 12 May 1981; introductory parameters; solid or liquid test substance; chemical identification of test substance; purity (impurities) of test substance; solubility characteristics; pH (where appropriate); stability, including stability in vehicle when so applied – melting point/boiling point. Method Introduction, purpose, scope, relevance, application and limits of test; in the assessment and evaluation of the toxic characteristics of a chemical the determination of subchronic dermal toxicity may be carried out after initial information on toxicity has been obtained by acute testing. There is sufficient similarity between the considerations involved in the conduct of a 21-day or 28-day repeated dose dermal study to allow one guideline to cover both test durations. Principle of the test method; the test substance is applied daily to the skin in graduated doses to several groups of experimental animals, one dose per group, for a period of 21/28 days. During the period of application the animals are observed daily to detect signs of toxicity. Animals which die during the test are necropsied, and at the conclusion of the test the surviving animals are sacrificed and necropsied. DESCRIPTION OF THE TEST PROCEDURE Experimental animals; selection of species adult rat, rabbit or guinea pig may be; weights: rats, 200 to 300 g; rabbits, 2.0 to 3.0 kg; guinea pigs, 350 to 450 g. Number and sex: At least 10 animals (5 female and 5 male) with healthy skin should be used at each dose level. Housing and feeding conditions; animals should be caged individually. Temperature: 22°C (± 3°) for rodents or 20°C (± 3°) for rabbits; relative humidity: 30-70 per cent; 12 hours light, 12 hours dark cycle. Feeding: conventional laboratory diets & unlimited supply of drinking water. Test conditions; dose levels; at least three dose levels, with a control and, where appropriate, a vehicle control, should be used. Except for treatment with the test substances, animals in the control group should be handled in an identical manner to the test group subjects. The highest dose level should result in toxic effects but not produce an incidence of fatalities which would prevent a meaningful evaluation. The lowest dose level should not produce any evidence of toxicity. If application of the test substance produces severe skin irritation, the concentration may be reduced. Procedure; the animals are treated with the test substance, ideally for at least 6 hours per day on a 7-day per week basis, for a period of 21/28 days. Application on a 5-day per week basis is considered to be acceptable. Animals in a satellite group scheduled for follow-up observations should be kept for a further 14 days without treatment to detect recovery from, or persistence of, toxic effects. Observations; a careful clinical examination should be made at least once each day. Additional observations should be made daily with appropriate actions taken to minimise loss of animals to the study, e.g. necropsy or refrigeration of those animals found dead and isolation or sacrifice of weak or moribund animals. Clinical observations; haematological parameters; clinical biochemistry determination; gross necropsy; histopathology. DATA AND REPORTING DATA; individual animal data ========== Individual animal data must be provided and all data summarized in tabular forms. The test report should include species/strain used, toxic response data by sex and dose, time of death or survival to termination, toxic effects with abnormal signs observation timeline, food and body weight data, haematological tests, discussion and results interpretation, and conclusion. ==========