

Acute, Sub-acute and Chronic Toxicity Studies as per OECD Guidelines

Introduction

- Toxicity studies are conducted to evaluate the harmful effects of drugs, chemicals, and other substances on living organisms.
- OECD guidelines provide standardized procedures for conducting toxicity studies safely and scientifically.
- **These studies help determine:**
 - Safe dose levels.
 - Toxic dose levels.
 - Target organ toxicity.
 - Duration-related toxic effects.
- **Toxicity studies are commonly performed through:**
 - Oral route.
 - Dermal route.
 - Inhalational route.

Classification of Toxicity Studies

Toxicity Study Classifications



1. Acute Toxicity Study

Definition

- Acute toxicity studies evaluate toxic effects that occur after administration of a single dose or multiple doses within 24 hours.

Purpose

- **Acute toxicity studies help:**
 - Determine immediate toxic effects.
 - Estimate LD50 or toxicity category.
 - Identify target organs.

- Select dose levels for further studies.

Observation Period

- Animals are generally observed for 14 days after administration.

2. Sub-Acute Toxicity Study

Definition

- Sub-acute toxicity studies evaluate toxic effects produced by repeated administration of a substance for a short duration.

Duration

- Usually conducted for 28 days.

Purpose

- **Sub-acute studies help:**
 - Identify cumulative toxicity.
 - Detect early organ damage.
 - Determine no observed adverse effect level (NOAEL).

3. Chronic Toxicity Study

Definition

- Chronic toxicity studies evaluate toxic effects produced after long-term repeated exposure.

Duration

- **Studies may continue for:**
 - 6 months.
 - 12 months.
 - 24 months depending on study requirements.

Purpose

- **Chronic studies help detect:**
 - Delayed toxicity.
 - Organ degeneration.
 - Carcinogenicity.
 - Long-term safety.

Acute Oral Toxicity Study

OECD Guidelines

- **Common OECD guidelines include:**
 - OECD 420 (Fixed Dose Procedure).
 - OECD 423 (Acute Toxic Class Method).
 - OECD 425 (Up-and-Down Procedure).

Principle

- A single oral dose of the test substance is administered to experimental animals.
- Animals are observed for signs of toxicity and mortality.

Experimental Animals

- Usually rats or mice are used.
- Healthy young adult animals are selected.

Procedure

- Animals are fasted before dosing.
- **The test substance is administered orally using:**
 - Oral gavage.
 - Feeding needle.
- Different dose levels are selected according to guideline recommendations.

Parameters Observed

- **Observations include:**
 - Mortality.
 - Behavioral changes.
 - Tremors.
 - Convulsions.
 - Salivation.
 - Body weight changes.
 - Food and water intake.
- Gross pathological examination is performed after death or sacrifice.

Importance

- Acute oral studies help classify substances according to toxicity level.

Sub-Acute Oral Toxicity Study

OECD Guideline

- OECD 407 is used for 28-day repeated dose oral toxicity study.

Principle

- The test substance is administered orally every day for 28 days.

Procedure

- **Animals are divided into:**
 - Control group.
 - Low-dose group.
 - Medium-dose group.
 - High-dose group.
- The drug is administered daily.

Parameters Observed

- **Daily clinical observations include:**
 - Skin changes.
 - Behavioral changes.
 - Mortality.
- **Weekly observations include:**
 - Body weight.
 - Food consumption.
- **Laboratory investigations include:**
 - Hematological tests.
 - Biochemical tests.
 - Urine analysis.
- **Organs are examined histopathologically.**

Target Organs Evaluated

- **Common organs examined include:**
 - Liver.
 - Kidney.
 - Heart.
 - Brain.
 - Lungs.

Chronic Oral Toxicity Study

OECD Guideline

- OECD 452 is used for chronic toxicity studies.

Principle

- The test substance is administered orally for long durations.

Procedure

- Animals receive repeated doses for several months.
- Detailed clinical and pathological examinations are performed.

Parameters Observed

- **Parameters include:**
 - Mortality.
 - Body weight.
 - Organ weight.
 - Blood investigations.
 - Histopathology.

Importance

- **Chronic oral studies help identify:**
 - Long-term toxic effects.
 - Cumulative toxicity.
 - Carcinogenic potential.

Acute Dermal Toxicity Study

OECD Guideline

- OECD 402 is used for acute dermal toxicity testing.

Principle

- A single dose of the test substance is applied to the skin.

Procedure

- Fur is removed from the dorsal area of animals.
- The test substance is applied over the skin and covered with dressing.

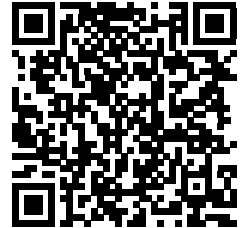


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