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**NATIONAL STANDARD OF THE
PEOPLE'S REPUBLIC OF CHINA**

GB 15193.14-2015

Replacing GB 15193.14-2003

National food safety standard -- Teratogenicity test

食品安全国家标准 致畸试验

(English Translation)

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Foreword

This standard replaces GB 15193.14-2003 "teratogenicity test." this standard compared with GB 15193.14-2003, the main changes are as follows.

- Standard name was changed to "national food safety standards teratogenicity test";
- Modify the scope;
- Increasing the content of terms and definitions, test purposes, test report and interpretation;
- Increasing the initial animal weight difference should not exceed 20% of the average weight requirement;
- Increased animal feeding requirements;
- Modify the number of pregnant mice when requested termination of the trial;

- Adds a way to establish a positive control group "with cyclophosphamide (15mg/kg body weight) on day 12 of gestation intraperitoneal injection 1 time";
- Increased maternal mortality rate shall not exceed 10% of the content;
- Increased administration of the test substance;
- Modify the traditional administration of the test substance teratogenicity test rats time;
- Increased maternal performance observed during administration of the test substance, recording the amount of water, if necessary;
- Increased for all pregnant mother visual examination;
- Amend Table 2;
- Delete the table "teratogenicity test record content," adds the need to organize the data content; statistics project and increased the net weight of Other than that, remove the ovary weight statistics;
- Increased content and information should be listed in the test report.

National Food Safety Standard Teratogenicity test

1 Scope

This standard specifies the technical requirements and test methods for animal teratogenicity tests.

This standard applies to the evaluation of the test substance teratogenic effects.

2.1 Developmental Toxicity

Individuals prenatal exposure to the test substance, and development before becoming adult (including embryo, fetal and postnatal) harmful effects occur, table Now the development of the organism structural abnormalities, altered growth, dysfunction and death.

2.2 Teratogenicity

Test substance during organogenesis caused by structural abnormalities in the offspring of a permanent nature.

2.3 Maternal toxicity

Effects of test substances cause health damage, direct or indirect parent females pregnant animals, expressed as weight reduction, dysfunction, and signs of poisoning, even death.

3 Test purposes and principles

The role of the parent subject to some hazardous substances through the placenta barrier during pregnancy, embryonic differentiation and organ development, leading to structural differences. Often, there fetal malformation. Therefore, in the conception of the animal embryo organogenesis of administration of the test substance, the substance can be detected in fetal teratogenicity effect.

Teratogenic likelihood of detecting pregnant animals after contact with the test substance caused predict human potential teratogenicity.

4.1 Instruments and Equipment

Commonly used laboratory equipment, biological microscopes, stereo microscopes, calipers, analytical balance.

4.2.1 Reagents

Formaldehyde, acetic acid, 2,4,6-nitro phenol, potassium hydroxide, glycerol, chloral hydrate, Alizarin Red.

4.2.2 The main method of reagent preparation

4.2.2.1 Alizarin Red stock solution

With 50% acetic acid as solvent alizarin red saturated liquid 5.0mL, glycerol 10.0mL, 1% chloral hydrate 60.0mL mixed, stored in a brown Bottle.

4.2.2.2 Application of Alizarin Red solution

Stock solution 3mL ~ 5mL, diluted with 10g/L ~ 20g/L of potassium hydroxide solution to 1000mL, stored in a brown bottle.

4.2.2.3 Alizarin Red solution

Alizarin Red 0.1g, potassium hydroxide 10g, distilled water 1000mL, Extemporaneous (peeling method bone staining solution).

4.2.2.4 A transparent liquid Glycerol 200mL, potassium hydroxide 10g, 790mL distilled water and mixed.

4.2.2.5 Transparent liquid B

Distilled water mixed with glycerin and other volume.

4.2.2.6 Fixative (Bouins liquid)

2,4,6-nitrophenol (saturated aqueous picric acid) 75 parts 20 parts 40% formaldehyde, 5 parts of glacial acetic acid.

5.1 Test substance

The test substance should be used in the original sample, if it can not use the original sample, the test should be treated in accordance with the principles of the test substance for proper disposal.

5.2.1 Species Selection

Experimental animals should be selected in line with GB 14922.2 and regulations. The preferred rodent rat, rabbit preferred non-rodent. If the selection of its He species should give reasons. Healthy, sexually mature males and females without mating animal weight difference when the trial began, should not exceed $\pm 20\%$ of average weight. The animal should indicate species, strain, sex, weight and weeks of age.

5.2.2 Number and sex of animals

Sexually mature males and females usually in the ratio of 1 to 1 or 1.2 mated, if not mate within 5d, males should be replaced. in order to Get enough litter to evaluate its teratogenic effects, the number of pregnant animals rats each dose level of at least 16 rabbits each dose level not less than 12 the number of pregnant animals.

5.2.3 Animal Preparation

Before the test, animals in the experimental animal room should be at least 3d ~ 5d acclimatization and quarantine observation.

5.2.4 Animal Feeding

Animal feeding conditions, drinking water, feed shall conform to GB 14925, GB 5749, GB 14924.3 and regulations. test During free access to water and food animals, pregnant animals should be caged.

5.3 Dose

The experiment included at least three dose groups, at the same time provided the vehicle control group, vehicle control group, in addition to not give the test substance, the rest were treated with dose group.

If necessary, positive control group, commonly used orally administered dose of positive control and reference enemy blight double (0.5mg/kg body weight ~ 1.0mg/kg Weight),