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

GB 15193.13-2015

Replacing GB 15193.13-2003

National food safety standard - 90 days oral toxicity test

食品安全国家标准 90天经口毒性试验

(English Translation)

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Foreword

This standard replaces GB 15193.13-2003 "30 days and 90 days feeding test." this standard compared with GB 15193.13-2003, the main changes are as follows.

--- Standard name was changed to "national food safety standards 90 days oral toxicity test";

--- Modify the "scope";

--- Added "sub-chronic toxicity", "the deleterious effects of the minimum dose observed" Defining and "satellite Unit";

- Modify the "principle";
- Added "instruments and reagents" project;
- To increase the "test" project;
- Increasing the processing requirements of the test substance;
- Modify the "animal";
- Modify the "dose group";
- Modify the "Procedure";
- Modify the administration of the test substance in the way;
- Modify the observed indicators;
- Increased body weight and food and water consumption, eye examination, urinalysis, body temperature, ECG content;
- Modify the hematological examination, blood biochemistry, pathology indicators;
- Modify the "data processing";
- Increase the results of the evaluation content;
- Increasing the project "test report";
- Added "Interpretation of Results" project.

National Food Safety Standard 90 days oral toxicity test

1 Scope

This standard specifies the experimental animals 90 days oral toxicity test methods and requirements for basic tests.

This standard applies to the evaluation of the test was sub-chronic toxicity.

2.1 Subchronic toxicity

Healthy animals in their lifetime does not exceed 10% of the time (usually rats 90d), repeat the test substance after oral exposure caused Kang damage effects.

2.2 No observed adverse effect level

Through animal experiments, the existing technical means and detection index was not observed any of the test substance-related toxic effects maximum dose.

2.3 Minimum observed adverse effect level

Under specified conditions, the test substance causing a minimal effect dose animal tissue morphology, function, growth and development, and other harmful effects.

2.4 Target organ

Organ by the test substance caused significant toxic effects of experimental animals.

2.5 Satellite Group

In toxicity studies in the design and implementation of additional group of animals, animal handling and feeding conditions and its main research similar to the test for interim or test convalescence observation and testing can also be used to observe and testing does not include other indicators and parameters in the main study.

3 Test purposes and principles

Determined within 90d oral repeated exposure caused toxic effects of the test substance, understanding the test substance dose - response relationship between target organ toxicity and Reversibility, come 90d orally minimum observed adverse effect level (LOAEL) and not observed adverse effect level (NOAEL), preliminary to determine the safety of the oral test substance, and chronic toxicity test dose, observed indicators, toxicity endpoint selection and was "tentative human health Health guidance values "provide the basis.

4.1 Instruments/Devices

Anatomy of commonly used laboratory instruments, electronic balance, biological microscope, ophthalmoscope, blood chemistry analyzers, hematology analyzers, coagulation analyzers, urine Liquid analyzers, ECG scanner, centrifuges, pathological machines.

4.2 Reagents

Formaldehyde, xylene, ethanol, hematoxylin-eosin, paraffin, thinners blood analyzer, blood chemistry analysis reagents, coagulation analyzer reagents, urine Analytical reagent (or paper) and the like.

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. will Test was incorporated into feed, drinking water or gavage administration.

5.2.1 Animal selection

Experimental animals should be selected in line with the relevant provisions of GB 14922.2 and 14922.1 of. Select has been documented on the test substance sensitive Animal species and strains, usually rodents rats preferred, the preferred non-rodent dogs (usually chosen Beagle dogs). Week-old rats Recommended no more than six weeks, weighing 50g ~ 100g. Start of the test animals of each sex differences in body weight should not exceed $\pm 20\%$ of the average weight, for not less than 20 animals in each group, male and female; if the medium-term plan to test or observe the end of the trial do observe recovery should increase the number of animals (Control and high dose increased satellite groups of 10, male and female). Dogs usually use 4 months to 6 months, puppies, not more than 9 months, at the beginning of each test gender differences in animal weight should not exceed the average weight of $\pm 20\%$, the number of animals in each group at least eight, male and female Half and half; if the test program or test the middle of an autopsy done to observe the end of the recovery period should be increased in the number of animals (control and high dose increased satellite groups 4, male and female). Sex and number of animals in the control group should be the same group with a test substance.

5.2.2 Animal Preparation

Before the test, rats in the experimental animal room should be at least 3d ~ 5d (dogs 7d ~ 14d) and adaptation to the environment quarantine observation.

5.2.3 Animal Feeding

Animal breeding conditions should be consistent with GB 14925, drinking water should be consistent with GB 5749, feed should comply with the relevant provisions of GB 14924.

During the test animals free access to water and food, animal recommend caged rat cage can also be components of sex are reared in groups, the number of animal cages (typically less per More than three) shall meet the minimum space required for experimental animals in order not to affect the free movement of animals and the animals were observed for signs appropriate. During the test each non-animal test should be less than 10% of mortality, dying animal blood biochemical tests should be carried out as far as possible, gross anatomy and disease Histopathological examination, each group of biological samples loss rate should be less than 10%.

5.3.1 Packet

The experiment included at least three doses of the test substance group, a negative (vehicle) control group, if necessary, additional untreated control group. If you need to test the medium-term to observe the blood biochemical parameters, or the end of the trial do an autopsy recovery observed in the control and high dose for an additional satellite group. In