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

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National food safety standard -- Carcinogenic test

食品安全国家标准 致癌试验

(English Translation)

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1 Scope

This standard specifies the basic technical requirements and test methods for carcinogenicity tests.

This standard applies to the evaluation of the test substance carcinogenic effect.

2.1 Carcinogenicity

Long-term repeated administration of experimental animals tumors (benign and malignant) lesions caused by the test substance.

2.2 Target organ

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

2.3 The maximum tolerated dose from 90 days oral toxicity test to determine the dose, this dose should be less than 10% weight loss in the animals in the control group, and are not generated by Non-tumor factors caused death and lead to shortened life or pathological signs of poisoning injuries.

2.4 Satellite Group

Toxicity of the design and implementation of the additional group of animals, animal handling and feeding conditions and its main research similar to the test medium 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

OK during most of the life of experimental animals, orally administered repeated carcinogenic effects caused by the test substance, to understand the incidence of cancer, the target device Carcinogenesis officer, the nature of the tumor, the tumor occurrence time and the number of tumors per animal, for predicting human exposure to the test substance and the final assessment Given that the test was able to provide the basis for the food.

4.1 Instruments and equipment

Anatomy of commonly used laboratory equipment, animal scales, electronic scales, biological microscope, biochemical analyzer, hematology analyzer, blood coagulation analyzer Instrument, urine analyzers, centrifuges, slicing machines.

4.2 Reagents

Formaldehyde, xylene, ethanol, hematoxylin-eosin, paraffin, blood dilution, chemical and biological reagents, analytical reagents coagulation, urinalysis reagent.

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 national standards and regulations (GB 14923, GB 14922.1, GB 14922.2). Should be selected from tumor Low fat animal species and strains, the choice of rats, mice, usually 6 weeks to 8 weeks. Each gender difference beginning of the test animal weight should not vary more than $\pm 20\%$ of average weight. At least 100 the number of animals per group, male and female, should be non-parous female Rat, non-pregnant rats. If the meter Mid-term test plan autopsy (satellite group), should increase the number of animals ($n =$ at least 20, male and female). Sex and number of animals in the control group should be subject the same test was set.

5.2.2 Animal Preparation

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

5.2.3 Animal Feeding

Animal feeding conditions, drinking water, feed should be in line with national standards and regulations (GB 14925, GB 5749, GB 14924.1, GB 14924.2, GB 14924.3). During the test animals free access to water and food, according to the component group sex feeding cage, cage number of animals (per general no more than three rats, mice were not more than 5) shall meet the minimum space required for experimental animals in order not to affect the freedom of movement and observe the movement of animals Signs were appropriate. During the test each non-animal test should be less than 10% of mortality, dying animal blood biochemical parameters should be possible Standard test, gross anatomy and histopathology, each biological samples loss rate should be less than 10%.

Dose group and 5.3

5.3.1 Test subjects were set up at least three groups, a negative (vehicle) control group, the control group except that no administration of the test substance, the rest were treated by the same Trial was set. If necessary, additional untreated control group.

5.3.2 The high dose should choose the maximum tolerated dose, in principle, should make the animals appear more obvious toxicity, but does not cause excess mortality;

Low dose does not cause any toxic effects; the dose should be between high-dose and low-dose, can cause mild toxic effects. General dose Group 2 spacing is appropriate to four times, no more than 10-fold.

5.4 Test period

5.4.1

Test duration is 18 months in mice, rats, 24 months, longer lifetime and lower individual rates of spontaneous tumors of animals may be appropriate extend.

5.4.2

During the test, when the number of animals the lowest dose or control group survival was only 25% at the beginning of time (male and female animals were calculated), may terminate the test. High dose group of animals was due to significant toxicity test with early death, not the trial was terminated.

5.5 Test procedure and outcome measures

5.5.1

The test is administered 5.5.1.1 according to the characteristics of the test substance and test purposes, select the test was incorporated into feed, water or orally administered. If the test was its driving Was palatability, should be given orally.

5.5.1.2

test was orally administered to the test substance is dissolved or suspended in a suitable vehicle, the preferred solvent is water. Water-insoluble test substance You can use vegetable oils (such as olive oil, corn oil, etc.), do not dissolve in water or oil test substance may be used as carboxymethyl cellulose, starch, etc. dubbed suspension or paste like. The test substance should now use the existing, data show that except for its storage solution or suspension stabilizer. Taking into account the use of solvent Media may test substance by the body absorption, distribution, metabolism and accumulation; on the test of physical and chemical properties and toxicity resulting therefrom Impact characteristics; impact on animal food intake or water intake or nutritional status. To ensure that the test substance concentration in vivo stability, daily Same period gavage once (weekly gavage 6d), during the test, the first four weeks weighed twice a week for 5 weeks to week 13 weighed weekly 1, then every 4 weeks weighed 1, weight-adjusted volume of gavage. Gavage volume generally not more than 10mL/kg body weight; as an oily liquid Body, stomach volume should not exceed 4mL/kg body weight. Each group was given the volume of the same.

5.5.1.3

incorporated into feed or drinking water test substance administered to the test substance and feed (or water) and mixed well to ensure the stability of the test substance formulation Qualitative and uniformity, without affecting the animal feeding, nutrition and water balance amount of principle. When a small amount of the test substance added to the feed, will be advised After the test was added a small amount of feed mix well, then add a certain amount of feed after mixing, so repeated 3 times to 4 times. Incorporation of the test substance feed Feed ratio generally is less than the mass fraction of 5%, if more than 5% (the maximum should not exceed 10 per cent), adjust the feed nutrient levels in the control