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

GB/T 15670.6-2017

Replacing GB/T 15670-1995

**Toxicological test methods for pesticides registration - Part 6:
Acute inhalation toxicity test**

农药登记毒理学试验方法 第6部分：急性吸入毒性试验

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1 Scope

GB/T 15670.6-2017 is the Chinese national standard on toxicological test methods for pesticides registration - part 6: acute inhalation toxicity test, in the field of agriculture. The /T suffix marks it as a recommended standard: it is not compulsory by itself, but it becomes binding as soon as a contract, a tender or a customer specification calls it up - which in practice is how most foreign buyers meet it. It was issued on 12 July 2017 by the General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China; Standardization Administration of China, and has been in force since 1 February 2018. Classification: ICS 65.100, CCS B17. This page is published from the official record of the standard held by the Chinese standards administration: the identification, the dates, the classification and the issuing body are taken from there. The clause text, the tables and the numeric limits are in the document itself, which is delivered complete in English translation.

This Part of GB/T 15670 specifies the basic principles, methods and requirements for acute inhalation toxicity test. This Part applies to the acute inhalation toxicity test conducted for pesticide registration.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

GB 14925, Laboratory animal - Requirements of environment and housing facilities
Provisions on Pesticide Registration Information (Order No. 10 of the Ministry of Agriculture
of the People's Republic of China [2007])

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1 acute inhalation toxicity The health-damaging effect that occurs when the test animal inhales a relatively high concentration of test substance (gas, vapor, aerosol or particulate matter) continuously for a short period of time (24 hours or within 24 hours, usually 4 hours).

3.2 inhaled dose The amount of test substance inhaled by the animal per unit body weight, that is, equal to a certain aerodynamic diameter (for example, 5 μm) account for 50% of the total mass or total weight of the aerosol sample, the aerodynamic equivalent diameter of the aerosol particles is the mass median aerodynamic equivalent diameter (5 μm) of the aerosol sample.

3.7 geometric standard deviation; GSD A dimensionless number used to describe the size range of aerosol particles. The smaller the geometric standard deviation, the higher the proportion of particles of similar size, that is, the better the uniformity of aerosol particles and the lower the dispersion. Usually, aerosol samples with a geometric standard deviation less than or equal to 2 are called single-phase dispersing aerosols.

3.8 inhalable diameter The aerodynamic equivalent diameter of particles that can be inhaled through the mouth and/or nose of the subject and deposited in any part of the respiratory tract. Aerosol particles with an aerodynamic equivalent diameter of less than 10 μm are usually called inhalable particles.

4 Purpose of the test

Through short-term inhalation exposure, a preliminary understanding of the acute toxicity characteristics and dose-response relationship of the test substance on test animals can be gained, to provide scientific reference for acute inhalation toxicity classification, label management and other related toxicological studies, and also to provide a basis for formulating protective measures during production and application.

5 Overview of the test

According to the physicochemical properties of the test substance, select an appropriate method to prepare it into a gas, vapor, aerosol or particulate suspension state of specific concentration, and input it into the dynamic toxicity system; randomly divide the test animals into control and different toxicity dose groups, and place them in the toxicity system

for 4 hours of exposure. After the toxicity is over, remove the test animals; carefully observe the manifestations and signs of toxic effects, death, etc. during the toxicity period and within 14 days, and perform gross autopsy on dead animals in time; at the end of the observation period, kill the animals for gross autopsy, and if diseased tissues or organs are found, conduct histopathological examination.

6.1 Test preparation

6.1.1 Test substance The test substance shall be a sample with a stable preparation process and in compliance with the quality standards, with the name, source, batch number, content (or specification), storage conditions and preparation method, etc., and a test report attached. The excipients, solvents or other media used shall be marked with the batch number, specification and manufacturer.

6.1.2 Selection and preparation of test substance vaporization or aerosol preparation method

6.1.2.1 Gaseous test substance After mixing it with air to a certain concentration through a flow meter, directly input it into the toxicity cabinet.

6.1.2.2 Low boiling point volatile liquid test substance After volatilization through air bubbling or appropriate heating, mix it with air and pass into the toxicity cabinet.

6.1.2.3 High boiling point non-volatile liquid test substance According to the physical and chemical properties of the test object, a spray method can be selected, or an aerosol generating device can be used to prepare a liquid aerosol that meets the test requirements and then mix it with a certain amount of air and input it into the toxicity cabinet.

6.1.2.4 Powdered or solid test substances Prepare the test substance into solid aerosol using an aerosol generator; mix it with a certain amount of air and introduce it into the toxicity cabinet.

6.1.3 Dynamic inhalation toxicity method Use mechanical ventilation equipment to continuously and evenly deliver air containing a certain concentration of the test substance into the toxicity cabinet, with a ventilation volume of about 12 times/h ~ 15 times/h to maintain a relatively stable toxicity concentration. Use whole-body exposure or head/nose exposure to conduct acute inhalation toxicity on animals for 4 hours. During toxicity, keep the distribution of toxicity gas in the toxicity cabinet balanced, the oxygen content not less than 19%, the CO₂ content not higher than 1%, the temperature at (22±3) °C, and the relative humidity at 30% ~ 70% (except for special circumstances, such as steam toxicity). If the toxicity not to interfere with the individual activities of the animals and the observed reactions. The animals shall be fed with regular feed and shall have free access to water.

6.1.5.3 Number and gender Each concentration group shall have at least 10 animals, 5 males and 5 females. Female animals shall be non-pregnant and nulliparous.

6.1.5.4 Inhaled dose and grouping At least 3 different concentrations of toxicity groups shall be set up, with appropriate concentration intervals between groups, so that a certain degree of toxic effect and death can occur in the test animals in each concentration group. At the same time, blank and/or corresponding excipient, solvent or other medium control groups shall be set up, and the data obtained shall be sufficient to draw a concentration-death curve and calculate the LC50 value. If the toxicity of the test substance is very low, 20 rats (half male and half female) can also be used to conduct a single dose acute inhalation toxicity test. The single acute inhalation toxicity concentration shall be 2×10^{-2} (gas test substance), 20 mg/L (liquid test substance vapor), 5 mg/L (solid or liquid test substance aerosol). If the concentration requirement cannot be reached due to the physical and chemical properties of the test substance, the test shall also be conducted at the highest concentration that the test substance can reach. When the test substance is explosive, care shall be taken to avoid using a concentration that may cause an explosion.

6.2.1 Implementation of inhalation toxicity

6.2.1.1 Balance and control of toxicity concentration Various appropriate conditions in the test preparation stage shall be used to control the toxicity concentration, inhalable diameter, etc.

6.2.1.2 Body weight measurement of toxicity animals and observation during toxicity Before the test begins, each animal shall be weighed. The time for animals to continuously inhale the test substance is 4 hours. During the toxicity process, the animals are usually in a state of fasting and water deprivation. During inhalation toxicity, attention shall be paid to observing the effects of the test substance on the respiratory system, such as respiratory irritation reactions, changes in respiratory rhythm, and changes in inhalation and exhalation patterns.

6.2.2 Test observation and inspection

6.2.2.1 Observation period After the inhalation toxicity, the test animals shall be carefully observed at least once a day for 14 consecutive days. However, the observation period is not fixed and can be adjusted according to the time of occurrence of toxic reactions and signs, as well as the length of the recovery period. If the animals show toxicity reactions and delayed death after exposure, the observation period shall be appropriately extended, and the maximum period shall not exceed 21 days.

6.2.2.2 Observation content Observe and record the clinical manifestations and signs of toxicity animals in detail, including the time of onset and recovery, the time of animal death, etc. The content of observation includes.

a) Central nervous system and neuromuscular system. abnormal posture, abnormal voice, restlessness, dullness, tremor, convulsion, paralysis, movement disorder, hypersensitivity or slowness in external response, abnormal behavior such as excessive and repeated