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PHARMACEUTICAL INDUSTRY STANDARD OF THE PEOPLE'S REPUBLIC OF CHINA

YY/T 1670.2-2025

Neurotoxicity evaluation of medical devices - Part 2: Tests for neuro-cytotoxicity

医疗器械神经毒性评价 第2部分：神经细胞毒性试验

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Foreword

This document complies with the provisions of GB/T 1.1-2020 "Standardization Work Guidelines Part

1.Structure and Drafting Rules of Standardization Documents". Drafting. This document is Part 2 of YY/T 1670 "Evaluation of Neurotoxicity of Medical Devices". YY/T 1670 has already published the following parts.

1.Guidelines for selecting tests to evaluate potential neurotoxicity;

2.Neurotoxicity assay. Please note that some content in this document may involve patents.

The issuing organization of this document assumes no responsibility for identifying patents. This document was proposed by the National Medical Products Administration. This document is under the jurisdiction of the National Technical Committee on Standardization of Biological Evaluation of Medical Devices (SAC/TC248). This document was drafted by: China National Institutes for Food and Drug Control, Shandong Provincial Institute for Medical Device and Pharmaceutical Packaging Inspection and Testing, and Beijing Municipal Institute of Medical Device and Pharmaceutical Packaging Inspection and Testing. Medical Device Testing and Research Institute (Beijing Medical Biological Protective Equipment Testing and Research Center), Sichuan University (Sichuan Medical Device Biomaterials and Products Testing and Research Center) (Testing Center Co., Ltd.) The main drafters of this document are. Wei Lina, Liu Jia, Wang Rui, Cai Yongfu, Gai Xiaoxiao, Jia Wensi, Xu Shuang, Jia Lifang, Chen Liyuan, and Fang Haiyan. Chen Liang.

Cytotoxicity is an important safety evaluation indicator for medical devices/biomaterials. If only conventional cytotoxicity evaluation methods are used, then This does not adequately reflect the specific toxic effects of medical devices/biomaterials that come into direct or indirect contact with the nervous system on nerve cells. For scientific purposes... This document provides methods for evaluating the potential toxic risks of medical devices/biomaterials to nerve cells. Standardized testing methods for cytotoxicity provide technical support for the research and development of medical devices/biomaterials products. In vitro cell models provide an effective tool for rapid screening of neurotoxins and are also used to study the mechanisms of neurotoxicity. (Derived from rat kidney) The PC-12 (or PC12) cell line for pheochromocytoma has been widely used for the evaluation and study of neurotoxicity and its mechanism of action. According to... Based on their degree of differentiation, the PC-12 cell line can be divided into two main branches. highly differentiated and undifferentiated. Highly differentiated PC-12 cells adhere to the culture medium and grow through... Metabolic activity was measured to determine cell viability and evaluate nerve cell activity. PC-12 undifferentiated cells expressed nerve growth factor (NGF) and were affected by... The body, under the induction of NGF, can produce neuronal phenotypes (formation of neuronal processes, etc.), which can be used for evaluation of neuronal morphology. This document describes the effects of medical device/biomaterial extracts on PC-12 cell activity and NGF-induced neural cell proliferation, etc. Morphological changes are used to evaluate the potential neurotoxicity of test samples. YY/T 1670 aims to establish test methods for neurotoxicity studies of medical devices and is proposed to consist of two parts.

1.Guidelines for Testing Potential Neurotoxicity. The aim is to provide testing guidelines for evaluating the potential neurotoxicity of medical devices. Selection Guide.

2.Neurotoxicity Testing. The purpose is to provide testing methods for the neurotoxicity of medical devices. Neurotoxicity evaluation of medical devices Part

1 Scope

YY/T 1670.2 extends biological evaluation into territory the general cytotoxicity tests do not reach. It describes the test methods for evaluating the neuro-cytotoxicity of medical devices and biomaterials: the effect of a device or its extract on nerve cells specifically, rather than on the generic cell lines used in standard cytotoxicity testing. It is Part 2 of the Chinese series on neurotoxicity evaluation of medical devices, which exists because devices that contact neural tissue, from electrodes to nerve conduits to intrathecal systems, can be non-toxic by the usual measures and still damage neurons. For a manufacturer of neurostimulation electrodes, nerve repair implants or any device with a neural interface, this is the test a Chinese reviewer will look for in the biological evaluation report alongside the GB/T 16886 series.

This document describes the test methods for evaluating the neurotoxicity of medical devices/biomaterials. This document applies to the evaluation of neurotoxicity of medical devices/biomaterials that come into direct or indirect contact with the nervous system.

2 Normative references

The contents of the following documents, through normative references within the text, constitute essential provisions of this document. Dated citations are not included. For references to documents, only the version corresponding to that date applies to this document; for undated references, the latest version (including all amendments) applies. This document.

GB/T 16886.5 Biological evaluation of medical devices - Part

3 Terms and Definitions

The terms and definitions defined in GB/T 16886.5 apply to this document.

4 Experimental materials, culture media and reagents, instruments and equipment

4.1 Test Materials The main materials and requirements are as follows:

a) Cell lines. PC-12 (highly differentiated) and PC-12 (undifferentiated) cell lines are recommended for experiments. The cells should be free of mycoplasma contamination.

b) Test Samples. Test samples shall be sterile. In accordance with GB/T 16886.12, select appropriate extraction methods based on the characteristics of the test samples. Preparation of test sample extracts (refer to the extraction conditions and methods for cytotoxicity tests), evaluation of cell viability and morphology. The appropriate cell culture medium should be used as the extraction medium for each titer test.

c) Negative control. It is recommended to use materials such as high-density polyethylene that have been proven to be non-neurotoxic, and to use the same conditions as the test samples. Prepare simultaneously; if a reagent (such as 10% phosphate buffer) is used as a negative control, then use a simultaneously prepared blank control culture. Culture medium preparation.

d) Positive control. It is recommended to use materials/reagents that have been proven to have significant neurotoxicity (such as vincristine sulfate, methyl chloride). Mercury, dimethyl sulfoxide, etc., as positive controls, should be prepared simultaneously with the test samples under the same conditions or using simultaneously prepared blanks. Preparation of white control culture medium.

e) Blank control. Extraction medium without the test sample, prepared simultaneously under the same conditions as the test sample.

4.2 Culture Media and Reagents The cell culture medium and main reagents are as follows:

a) 1640 cell culture medium (containing glutamine, phenol red-free);

5 In vitro cytotoxicity tests

GB/T 16886.12 Biological evaluation of medical devices - Part