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

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Chemicals -- Testing method for skin absorption -- In vitro

化学品 皮肤吸收 体外试验方法

(English Translation)

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Foreword

This standard was drafted in accordance with GB/T 1.1-2009 given rules.

The Standards and Organisation for Economic Co-operation and Development (OECD) chemical testing methods No.428 (2004) "Skin absorption. In vitro test" (English Chinese Version) consistent with the technical content.

The standard structure and made the following editorial changes.

- Increasing the range a chapter;
- The original OECD428 the "initial consideration" and "introduction" as part of the introduction of this standard;
- The OECD428 original in the "End of program" and "analysis" as part of the standard "exposure time and sampling 4.10";
- The OECD428 original "Data and Reporting" and "conclusion" as part of the standard "5 of test data and reports";
- The original OECD428 Appendix "definition" of the present standard "2 Terms and Definitions";
- A unit of measurement unity to our legal units of measurement.

This standard is managed by the National Standardization Technical Committee chemicals dangerous (SAC/TC251) and focal points.

This standard was drafted. Chinese Center for Disease Prevention and Control of Occupational Health and Poison Control, Centers for Disease Control and Prevention, Tianjin, China Chemical Technology Development Center.

Introduction

The standard reference to the OECD chemical testing methods No.428 (2004) "Skin absorption. In vitro test" (in English). This guide in vitro skin absorption test methods provide, either in conjunction OECD skin absorption (in vivo test) [1], it can also be used alone. The measure Recommended Test Method OECD research papers on skin absorption [2] as a guidance document to assist in design of experiments based on this method is based.

OECD guidance document will help to choose the appropriate procedures in vitro, in exceptional circumstances, and to ensure that results obtained by this method Reliability fruit.

The method of detecting skin absorption and percutaneous absorption can be divided into two categories. in vitro and in vivo tests. About vivo skin absorption method has been Established and provides a different species of animal pharmacokinetic information in vivo test method in medium alone another OECD guidelines Shao [1]. In vitro method for detecting skin absorption has been used for many years. Although this method conducted formal research is still effective in vitro Absorption Undeveloped, but the OECD expert consensus in 1999 that there is sufficient data to support the process [3] In addition, the method provides More information also confirmed this point, including the important data in vivo test methods for a direct comparison of the resulting [2]. Lot monograph discusses the Perspectives and provides for the use in vitro test methods for more details [4-12]. In vitro tests can measure chemicals through the skin into the body fluid expansion Powder can also be utilized alone inactive skin to measure diffusion of this, or you can use fresh, metabolically active skin at the same time this measure Penetration and skin metabolism. The screening method to compare different chemicals in different ways to enter or transit through the skin and in the evaluation of human percutaneous absorption Collect useful model aspects of special purpose.

In vitro tests are not applicable in all situations and all types of chemicals. Initially only for qualitative evaluation of skin penetration. In some Case, reference should be further in vivo test data. OECD chemical testing methods No.428 "Skin absorption. In vitro test" (2004) (English Version) should further clarify the application of in vitro test methods, and to provide additional support to these conclusions in the report of OECD Expert Meeting for more information [3].

OECD chemical testing methods No.428 "Skin absorption. In vitro test" (2004) (in English) proposes the use of in vitro by detecting skin the general principles of the test substance transdermal absorption and transport. Vitro skin may be from a variety of mammals, including human skin. Because a permeable layer Inactive parts of the stratum corneum, the permeability of the skin in vitro after still preserved; chemicals through the skin have not been active transport mechanism to be sure. Studies have shown that certain chemicals

during percutaneous absorption, skin has ability to metabolize these chemicals [6], although it will affect the chemical nature into the blood, but this process is not actually absorbed dose limiting step.

In vitro test methods for skin absorption of chemicals

1 Scope

This standard specifies the chemical in vitro test methods for skin absorption of terms and definitions, test principle, test methods, test data and reports.

This standard does not apply to all cases detected and percutaneous absorption of all types of chemicals, only applied to the skin penetration of the initial characterization Evaluation. In some cases, reference should be further vivo data.

2 Terms and definitions

The following terms and definitions apply to this document.

Not absorbed dose unabsorbeddose After exposure, rinse down from the surface of the skin and the amount of test substance in the cover means, including exposure during evaporate from the skin surface Amount.

Absorbed dose (in vitro test) absorbeddose. invitro Within a certain time, the amount of the test substance reach the receiving liquid or circulatory system.

Absorbable dose (in vitro test) theabsorbabledose. invitro After washing, the amount left in the skin surface or skin tissue test substance.

3 Test principle

Test substance (may be a radiolabel) acts on the skin surface of the diffusion cell divided into two portions, under certain conditions, of the chemicals in the skin Acting on a certain time, then the skin with a suitable cleaning methods from the skin surface to remove the chemical. Throughout the course of the experiment, in different Acquisition time was accepted, and analyze the test substance and metabolites.

If you are using metabolic activation system, metabolites of the test substance apply the appropriate methods for analysis. At the end of the test, in an appropriate situation Under conditions, measuring the distribution of the test substance and its metabolites.

Under this standard and guidance documents [2] as described in the appropriate conditions, the use of analysis within the receptor fluid and skin test was monitored by a certain time Absorption of the test substance. Unless it can prove that the test substance is absorbed only liquid absorbed, otherwise the amount of test substance remaining in the skin should be considered to be sucked the amount received. Taking into account the

further data analysis, other components (washed down from the surface of the skin and remain in the skin) should also be analyzed package Including the distribution and recovery of all the test substance.

To illustrate the accuracy and stability of the test system, the test conclusion and related chemicals should adopt the method knot literature published on the same. This requirement should be achieved by detecting a suitable reference material (preferably with a test substance similar lipophilic), or by providing a variety of with reference to lipophilic substances (such as caffeine, benzoic acid, testosterone) empirical data sufficient to meet this requirement.

Test Method 4

4.1 Diffusion cell

Separated by skin diffusion cell made, including the supply tank and the reception tank (Figure 1 shows a typical example diffusion cell). Diffusion cell with the surrounding skin should be