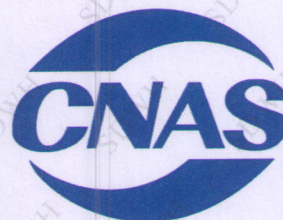




180015144061



中国认可  
国际互认  
检测  
TESTING  
CNAS L2954

# 苏州大学 卫生与环境技术研究所 最终报告

报告编号: SDWH-M201800496-1

参照 ISO 10993-5: 2009 方法进行  
无纺布单面胶的细胞毒性试验  
MTT 法  
含 10%胎牛血清的 MEM 浸提液

委托单位

上海锐泉医疗器械有限公司

制造商

上海锐泉医疗器械有限公司

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苏州大学卫生与环境技术研究所

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## 目 录

目 录.....	2
检测报告说明.....	3
试验确认与签名.....	4
1.0 摘 要.....	5
2.0 目 的.....	5
3.0 参考标准.....	5
4.0 执行规范.....	5
5.0 对照和试验样品确定.....	5
6.0 试验系统鉴别.....	6
7.0 试验系统确认.....	6
8.0 给药途径确认.....	6
9.0 试验设计.....	6
9.1 试验和对照样品制备.....	6
9.2 仪器设备.....	7
9.3 试剂.....	7
9.4 试验方法.....	7
9.5 细胞形态结果.....	7
9.6 细胞活力结果.....	8
9.7 质量检查.....	8
9.8 统计方法.....	8
9.9 评价标准.....	8
9.10 结 论.....	8
10.0 记录存储.....	8
11.0 保密协议.....	8
12.0 试验偏离声明.....	8

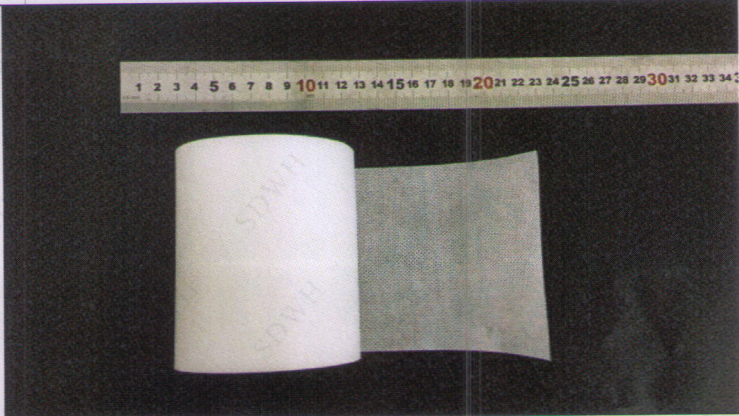


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试验确认与签名

试验样品	
接样日期:	2018-02-27
试验计划书编号:	SDWH-PROTOCOL-M201800496-1
试验计划书生效日期:	2018-03-01
试验操作开始日期:	2018-03-02
试验操作结束日期:	2018-03-07
报告完成日期:	2018-03-09

编制: 王德衡

2018.03.09  
日期

审核: 朱雨婷  
试验负责人

2018.03.09  
日期

签发: [Signature]  
授权签字人

2018-03-15  
日期

苏州大学卫生与环境技术研究所





## 1.0 摘要

试验样品浸提液与生长旺盛的 L929 细胞培养 (37℃, 5% CO<sub>2</sub>) 24h 后, 观察细胞形态, 细胞裂解情况, 采用 MTT 法测定供试品的潜在细胞毒性。结果显示 100% 样品浸提液的细胞活力为 90.5%, 对照组结果显示本次试验结果有效。

在本次试验条件下, 样品无纺布单面胶浸提液对 L929 细胞无潜在毒性影响。

## 2.0 目的

该试验目的是为了评价试验样品对 L929 哺乳动物成纤维细胞的生物学反应。该测试是根据样品浸提液而设计的。

## 3.0 参考标准

医疗器械的生物学评价-第 5 部分: 细胞毒性测试-体外法 ISO 10993-5: 2009

医疗器械的生物学评价-第 12 部分: 样品制备和参照样品 ISO 10993-12: 2012

## 4.0 执行规范

ISO/IEC 17025:2005《检测和校准实验室能力的通用要求》CNAS-CL01 检测和校准实验室能力认可准则 (中国合格评定国家认可委员会实验室认可证书 No.CNAS L2954)

检验检测机构资质认定评审准则 (中国国家认证认可监督管理委员会 资质认定 中国检验机构和实验室强制性批准 CMA 180015144061)

## 5.0 对照和试验样品确定

### 5.1 试验样品名称: 无纺布单面胶

来样原始状态: 未灭菌

CAS 编号: 未提供

型号: 未提供

规格: 未提供

批号: H20180201001

样品材料: 无纺布

包装材质: 未提供

性状: 固体

颜色: 未提供

密度: 未提供

稳定性: 未提供

溶解度: 未提供

保存条件: 室温

以上试验样品信息是由样品委托单位提供。

浸提液: 含 10% 胎牛血清的 MEM 培养液

### 5.2 阴性对照

名称: 高密度聚乙烯

制造商: 美国药典委员会

规格: 3 片装



批号: K0M357

性状: 固体

颜色: 白色

稳定性: 室温下稳定

保存条件: 室温

浸提液: 含 10%胎牛血清的 MEM 培养液

### 5.3 阳性对照样品名称: Zinc diethyldithiocarbamate

制造商: Sigma

规格: 25g

批号: MKBD516V

浓度: 1%

溶剂: 10%胎牛血清的 MEM 培养液

配制日期: 2018-03-05

性状: 固体

颜色: 白色

保存条件:  $4 \pm 2^{\circ}\text{C}$

### 5.4 空白对照样品名称: 含 10%胎牛血清的 MEM 培养液

配制日期: 2018-03-05

性状: 液体

颜色: 粉红色

保存条件:  $4 \pm 2^{\circ}\text{C}$

## 6.0 试验系统鉴别

该试验用小鼠成纤维细胞 L929,细胞系来自美国菌种保存中心。

## 7.0 试验系统确认

小鼠成纤维细胞 L929 用来检测细胞毒性试验是因为其对试验样品浸提液反应灵敏。

## 8.0 给药途径确认

试验样品通过浸提液(用一种与试验系统相容的载体浸提)与试验系统接触,被认为是最佳给药途径,也是为标准推荐的。

## 9.0 试验设计

### 9.1 试验和对照样品制备

无菌操作按下表的比例(样品:浸提液体积)用含 10%胎牛血清的 MEM 培养液浸提样品,于  $37^{\circ}\text{C}$  浸提 24 小时。浸提前后浸提液状态未发生改变。浸提液立即用于实验。浸提液 pH 值未经调整,未经过滤,离心,稀释等处理过程。

无菌操作取样		灭菌方式	惰性容器内 无菌浸提			最终浸提液	
取样方式	实际取样	Autoclave ( $121^{\circ}\text{C}$ , 30min)	取样比例	浸提液	条件	pH	是否澄清
随机取样	120cm <sup>2</sup>		6cm <sup>2</sup> : 1ml	20.0ml	$37^{\circ}\text{C}$ , 24h	7.4	澄清

同法制备空白对照、阴性对照样品和阳性对照样品。



## 9.2 仪器设备

高压灭菌器 (SDWH2204) 校正有效期 (2018-09-12) ;  
 恒温摇床 (SDWH2109) 校正有效期 (2018-11-12) ;  
 CO<sub>2</sub> 培养箱 (SDWH021) 校正有效期 (2018-08-31) ;  
 倒置显微镜 (SDWH037) 校正有效期 (2018-08-28) ;  
 钢直尺 (SDWH463) 校正有效期 (2018-09-10) ;  
 电子天平 (SDWH056) 校正有效期 (2019-01-21) ;  
 超净工作台 (SDWH454) 校正有效期 (2018-09-04) ;  
 酶联免疫检测仪 (SDWH312) 校正有效期 (2018-08-27) 。

## 9.3 试剂

MTT(3-(4, 5-二甲基噻唑-2)-2, 5-二苯基四氮唑溴盐) (SIGMA, 批号: MKBX0151V) ;  
 胎牛血清 (CORNING, 批号: 35010155) ;  
 MEM (HyClone, 批号: AC11016265) ;  
 胰酶 (GiBco, 批号: 1780400) ;  
 青霉素链霉素 (GiBco, 批号: 2046839) ;  
 异丙醇 (江苏强盛功能化学股份有限公司, 批号: 20170206) 。

## 9.4 试验方法

试验过程无菌操作:

将 L929 细胞培养在含 10%胎牛血清和抗生素(青霉素 100 U/ml,链霉素 100 µg/ml)的 MEM 培养液中, 置于 37℃, 5% CO<sub>2</sub> 培养箱中培养。用 0.25%胰酶(含 EDTA) 消化细胞制备成单细胞悬液, 细胞悬液离心 (200g, 3min), 然后将细胞重新分散于培养基中, 调整细胞密度为  $1 \times 10^5$  个/ml 的细胞悬液;

接种上述细胞悬液到 1 个 96 孔培养板中, 每孔 100 µL, 置 37℃培养箱中 (5% CO<sub>2</sub>, 37℃, >90%湿度) 培养 24 小时;

待细胞长成单层后, 吸出原来的培养液, 分别加入 100 µl 不同浓度的试验样品浸提液 (100%、75%、50%、25%)、空白对照液、阳性对照 (100%) 和阴性对照液 (100%), 37℃, 5% CO<sub>2</sub> 培养 24 小时。每组做 5 个平行样;

培养 24h 后, 取出 96 孔板先做细胞形态学观察, 然后吸出原来的培养液, 每孔加 50µl MTT (1mg/ml), 培养 2 小时, 吸弃上清, 加 100µl 99.9%纯度的异丙醇溶解结晶;

在酶标仪上以 570nm 为主吸收波长, 650nm 为参考波长测定吸光度值。

## 9.5 细胞形态结果

表 1 细胞形态学观察

组别	接种细胞前	加浸提液前	加浸提液 24h 后
空白对照	个别细胞有颗粒, 细胞无裂解, 生长状态良好。	个别细胞有颗粒, 细胞无裂解, 生长状态良好。	个别细胞有颗粒, 细胞无裂解, 生长状态良好。
阴性对照			个别细胞有颗粒, 细胞无裂解, 生长状态良好。
阳性对照			细胞裂解死亡。
100%样品浸提液			个别细胞有颗粒, 细胞无裂解, 生长状态良好。
75%样品浸提液			个别细胞有颗粒, 细胞无裂解, 生长状态良好。
50%样品浸提液			个别细胞有颗粒, 细胞无裂解, 生长状态良好。
25%样品浸提液			个别细胞有颗粒, 细胞无裂解, 生长状态良好。



## 9.6 细胞活力结果

表 2 细胞活力%

组别	Mean±SD	细胞活力%
空白对照	1.0913±0.032	100.0%
阴性对照	1.1074±0.010	101.5%
阳性对照	0.0664±0.007	6.1%
100%样品浸提液	0.9878±0.054	90.5%
75%样品浸提液	0.9954±0.048	91.2%
50%样品浸提液	1.0640±0.186	97.5%
25%样品浸提液	1.0622±0.055	97.3%

## 9.7 质量检查

阴性对照无细胞毒性影响，阳性对照造成细胞毒性影响。

在两天的试验过程中，未经处理的空白对照的光密度绝对值 OD570 表明了每个孔接种的  $1 \times 10^4$  个细胞以正常倍增时间成指数增长。

空白对照的 OD570 平均值不能小于 0.2。

检查系统的细胞接种误差，96 孔板的左侧（第 2 列）和右侧（第 11 列）作为空白对照（第 1 列和第 12 列不用作空白对照）。左右两侧空白对照的平均值不能与所有空白的平均值相差超过 15 %。

## 9.8 统计方法

均数±标准差 (Mean±SD)

细胞活力%=试验（或阳性及阴性）样品组  $\frac{OD570 - OD650}{OD570 - OD650} / \text{空白对照组} \frac{OD570 - OD650}{OD570 - OD650} \times 100\%$ 。

## 9.9 评价标准

50%的样品浸提液至少和 100%的细胞活力相同或者比 100%的细胞活力更高，否则应该重复试验。

细胞活力%越低，潜在的细胞毒性越大；

细胞活力<空白组 70%，说明样品具有潜在的细胞毒性；

100%试验样品浸提液的细胞活力%为最终结果。

## 9.10 结 论

在本次试验条件下，样品无纺布单面胶浸提液对 L929 细胞无潜在毒性影响。

## 10.0 记录存储

所有与本次试验有关的原始数据和记录都被保存在指定的 SDWH 档案文件中。

## 11.0 保密协议

签订检测委托合同即认为双方接受保密协议。

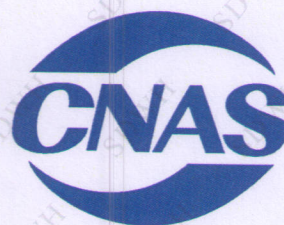
## 12.0 试验偏离声明

本次试验严格按照方案执行，未发生影响实验数据有效性的偏离。





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CNAS L2954

**Sanitation & Environment Technology Institute,  
Soochow University,  
Final Report**

Report Number: SDWH-M201800496-1

In Vitro Cytotoxicity Test of  
Non-woven tape  
using ISO 10993-5: 2009 Test Method  
MTT Method  
MEM with 10%FBS extract

Sponsor

shanghai Rui Quan medical instrument Co.,Ltd  
Manufacturer

shanghai Rui Quan medical instrument Co.,Ltd

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Sanitation & Environment Technology Institute, Soochow University

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## CONTENTS

CONTENTS.....	2
SUPPLEMENTARY EXPLANATION.....	3
STUDY VERIFICATION AND SIGNATURE.....	4
1.0 Study Summary.....	5
2.0 Purpose.....	5
3.0 Reference.....	5
4.0 Compliance.....	5
5.0 Identification of test and control articles.....	5
6.0 Identification of test system.....	6
7.0 Justification of the test system.....	6
8.0 Route of administration.....	6
9.0 Experiment design.....	6
9.1 Sample and Control Preparation.....	6
9.2 Equipment.....	7
9.3 Reagents.....	7
9.4 Test Method.....	7
9.5 Results of Cell Morphology.....	8
9.6 Results of the Cell Vitality.....	8
9.7 Quality Check.....	8
9.8 Statistical Method.....	9
9.9 Evaluation Criteria.....	9
9.10 Conclusion.....	9
10.0 Record Storage.....	9
11.0 Confidentiality Agreement.....	9
12.0 Deviation statement.....	9



### **SUPPLEMENTARY EXPLANATION**

1. Please apply for rechecking within 15 days of receiving the report if there is any objection.
2. Any erasure or without special testing seal renders the report null and void.
3. The report is only valid when signed by the persons who edited, checked and approved it.
4. The result relate only to the articles tested.
5. The report shall not be reproduced except in full without the written approval of the institute.



## STUDY VERIFICATION AND SIGNATURE

Test Article



Test Article Receipt	2018-02-27
Protocol No	SDWH-PROTOCOL-M201800496-1
Protocol Effective Date	2018-03-01
Technical Initiation Date	2018-03-02
Technical Completion Date	2018-03-07
Final Report Completion Date	2018-03-09

Edited by : Wang Deheng2018.03.09  
DateChecked by : zhu Yuting  
Study Director2018.03.09  
DateApproved by : Rong Suren  
Authorized signatory2018-03-15  
Date

Sanitation &amp; Environment Technology Institute, Soochow University





## 1.0 Study Summary

The test article extract (100, 75, 50, and 25% in growth medium) was added to L-929 cells in 96 well plates and then incubated at 37°C in 5% CO<sub>2</sub> for 24h to determine the potential cytotoxicity. The MTT method results showed that the cell viability% of the 100 % test article extract was 90.5% and the results of control groups showed the test was valid.

Under the conditions of this study, the test article Non-woven tape extract did not show potential toxicity to L-929 cells.

## 2.0 Purpose

The purpose of the test is to determine the biological reactivity of a mammalian cell culture (mouse fibroblast L-929 cells) in response to the test article.

## 3.0 Reference

Biological evaluation of Medical Devices Part 5: Tests for In Vitro Cytotoxicity (ISO 10993-5: 2009)

Biological evaluation of Medical Devices-Part 12: Sample preparation and reference materials (ISO 10993-12: 2012)

## 4.0 Compliance

ISO/IEC 17025:2005 General requirements for the competence of testing and calibration laboratories (CNAS-CL01 Accreditation Criteria for the competence of testing and calibration laboratories)

China National Accreditation Service for Conformity Assessment Laboratory Accreditation Certificate No.CNAS L2954

Accreditation Criteria for the competence of Inspection Body (Certification and Accreditation Administration of the People's Republic of China CMA 180015144061)

## 5.0 Identification of test and control articles

### 5.1 Test article name: Non-woven tape

Test article initial state: Not Sterilized

CAS Code: Not supplied by sponsor (N/S)

Model: N/S

Size: N/S

Lot/ Batch: H20180201001

Test Article Material: Non-woven

Packaging Material: N/S

Physical State: Solid

Color: N/S

Density: N/S

Stability: N/S

Solubility: N/S

Storage Condition: Room Temperature

The information about the test article was supplied by the sponsor wherever applicable.



Extracting solvent: MEM medium, with addition 10% FBS

**5.2 Negative Control Article Name: High Density Polyethylene**

Manufacturer: U.S. Pharmacopeial Convention (USP)

Size: 3 Strips

Lot/ Batch#: K0M357

Physical State: Solid

Color: White

Stability: Stable at room temperature

Storage Conditions: Room temperature

Extracting solvent: MEM medium, with addition 10% FBS

**5.3 Positive Control Article Name: Zinc diethyldithiocarbamate**

Manufacturer: Sigma

Size: 25g

Lot/ Batch#: MKBD516V

Concentration: 1%

Solvent: MEM medium, with addition 10% FBS

Date prepared: 2018-03-05

Physical State: Solid

Color: White

Storage Condition:  $4 \pm 2$  °C

**5.4 Blank Control Name: MEM medium, with addition 10% FBS**

Date prepared: 2018-03-05

Physical State: Liquid

Color: Pink

Storage Condition:  $4 \pm 2$  °C

## **6.0 Identification of test system**

L-929 mouse fibroblast cells obtained from ATCC (American Type Culture Collection), USA.

## **7.0 Justification of the test system**

Historically, mouse fibroblast L929 cells have been used for cytotoxicity studies because they demonstrate sensitivity to extractable cytotoxic articles.

## **8.0 Route of administration**

The test article was extracted and administered in vitro to mouse fibroblast L929 cells through a solvent compatible with the test system. This was the optimal route of administration available in this test system as recommended in the guidelines.

## **9.0 Experiment design**

### **9.1 Sample and Control Preparation**

Aseptic extracting the test article (test article to volume of vehicle) by MEM medium(10%FBS)



according to the table below. Sealed and incubated at 37°C for 24h. There is no change in the extraction solvent (pre- and post-extraction). Extracts were used immediately after extraction without the process of pH value adjustment, filtering, centrifugation, dilution, etc.

Aseptic Sampling		Sterilization method	Aseptic Extraction In Inert Container			Final Extract	
Sampling Manner	Actually sampling	Autoclave (121°C, 30min)	Ratio	Extracts	Condition	pH	Clear or Not
Random sampling	120cm <sup>2</sup>		6cm <sup>2</sup> : 1ml	20.0ml	37°C, 24h	7.4	Clear

The blank control (vehicle), negative and positive controls were similarly prepared.

## 9.2 Equipment

Autoclaves (SDWH2204), Calibration Expire(2018-09-12),  
 Constant temperature shaking table (SDWH2109), Calibration Expire(2018-11-12),  
 CO<sub>2</sub> Incubator (SDWH021), Calibration Expire(2018-08-31),  
 Inverted microscope (SDWH037), Calibration Expire(2018-08-28),  
 Steel Straight Scale (SDWH463), Calibration Expire(2018-09-10),  
 Electronic Balance (SDWH056), Calibration Expire(2019-01-21),  
 Clean bench (SDWH454), Calibration Expire(2018-09-04),  
 Power Wave XS Microplate Reader (SDWH312), Calibration Expire(2018-08-27).

## 9.3 Reagents

### MTT

(3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyletrazolium bromide)(SIGMA, Lot No: MKBX0151V)  
 FBS (CORNING, Lot No: 35010155)  
 MEM (HyClone, Lot No: AC11016265)  
 Trypsin (GiBco, Lot No: 1780400)  
 Penicillin, Streptomycin sulfate (GiBco, Lot No: 2046839)  
 99.9% Isopropanol (Chinasun Specialty Products Co., Ltd, Lot No: 20170206).

## 9.4 Test Method

Aseptic procedures were used for handling cell cultures.

L929 cells were cultured in MEM medium (10% FBS, Penicillin 100 U/ml, Streptomycin sulfate 100 µg/ml) at 37°C in a humidified atmosphere of 5% CO<sub>2</sub>, then digested by 0.25% trypsin containing EDTA to get single cell suspension. And obtain a 1 × 10<sup>5</sup> cells/ml suspension by centrifuging (200g, 3min) and re-dispersing in MEM medium finally.

The suspended cells were dispensed at 100µl per well in 96-well plate, and culture it in cell incubator (5% CO<sub>2</sub>, 37°C, >90% humidity). Cell morphology was evaluated to verify that the monolayer was satisfactory.

After the cells grew to form a monolayer, original culture medium was discarded. The 96-well plates were then treated with 100µl of extract of test article (100%、75%、50%、25%), control article, negative article (100%) and positive article (100%) respectively. Incubate the 96-well plate at 37°C in cell incubator of 5% CO<sub>2</sub> for 24 h. Five replicates of each test were tested.



After 24h incubation, observe the cell morphology first and then discard the culture medium. A 50 $\mu$ l aliquot of MTT (1mg/mL) was added to each well and then incubated at 37°C in a humidified atmosphere of 5% CO<sub>2</sub> for 2 hours. The liquid in each well was tipped out and 100  $\mu$ l 99.9% isopropanol was added to each well to suspend the cell layer.

Evaluate the suspension above with a dual-wavelength spectrophotometer with the measurement wavelength at 570 nm and reference wavelength at 650 nm.

### 9.5 Results of Cell Morphology

Table 1 Observation of the Cell morphology

Group	Before inoculation	Before treated with extract	24h after treatment
Blank control	Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.	Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.	Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.
Negative control			Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.
Positive control			Nearly complete or complete destruction of the cell layers.
100% Test article extract			Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.
75% Test article extract			Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.
50% Test article extract			Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.
25% Test article extract			Discrete intracytoplasmic granules, no cell lysis, no reduction of cell growth.

### 9.6 Results of the Cell Vitality

Table 2 Results of the Cell Vitality

Group	Mean $\pm$ SD	Viability%
Blank control	1.0913 $\pm$ 0.032	100.0%
Negative control	1.1074 $\pm$ 0.010	101.5%
Positive control	0.0664 $\pm$ 0.007	6.1%
100% test article extract	0.9878 $\pm$ 0.054	90.5%
75% test article extract	0.9954 $\pm$ 0.048	91.2%
50% test article extract	1.0640 $\pm$ 0.186	97.5%
25% test article extract	1.0622 $\pm$ 0.055	97.3%

### 9.7 Quality Check



No cytotoxic effect is observed for the negative controls and a cytotoxic effect is elicited by the positive controls.

The absolute value of optical density, OD570, obtained in the untreated blank indicates the  $1 \times 10^4$  cells seeded per well have grown exponentially with normal doubling time during the two days of the assay.

The mean OD570 of blanks is not less than 0.2.

Check for systematic cell seeding errors, blanks are placed both at the left side (row 2) and the right side (row 11) of the 96-well plate (row 1 and row 12 shall not be used). The left and the right mean of the blanks do not differ by more than 15 % from the mean of all blanks.

#### 9.8 Statistical Method

Mean $\pm$ standard deviation (Mean $\pm$ SD)

The Cell Viability % =  $\left[ \frac{OD570 - OD650}{OD570 - OD650} \right]$  of test (or positive and negative) article group /  $[OD570 - OD650]$  of blank control group  $\times 100\%$ .

#### 9.9 Evaluation Criteria

The 50 % extract of the test article should have at least the same or a higher viability than the 100 % extract; otherwise the test should be repeated.

The lower the Viab.% value, the higher the cytotoxic potential of the test article is.

If viability is reduced to < 70 % of the blank, it has a cytotoxic potential.

The Viab.% of the 100% extract of the test article is the final result.

#### 9.10 Conclusion

Under the conditions of this study, the test article Non-woven tape extract did not show potential toxicity to L-929 cells.

#### 10.0 Record Storage

All raw data pertaining to this study and a copy of the final report are retained in designated SDWH archive.

#### 11.0 Confidentiality Agreement

Statements of confidentiality were as agreed upon prior to study initiation.

#### 12.0 Deviation statement

There were no deviations from the approved study protocol which were judged to have any impact on the validity of the data.