403 – X-Ray and Metal Detectable Plasters

Document Number: HSE 749

Date Of Issue: 24/02/2018

Revision Number: 2

Date of Revision: 03/03/2023

Product Code	Description
403-S124-X11	Detectable Plasters 38mm x 38mm Pack of 100
403-S731-X11	Detectable Plasters 19mm x 63mm Pack of 100
403-S732-X11	Detectable Plasters 30mm x 64mm Pack of 100
403-S733-X11	Detectable Plasters 19mm x 72mm Pack of 100
403-S734-X11	Detectable Plasters 25mm x 72mm Pack of 100
403-S735-X11	Detectable Plasters 38mm x 72mm Pack of 100
403-S736-X11	Detectable Plasters 51mm x 72mm Pack of 100
403-S737-X11	Detectable Plasters Finger Pack of 50
403-S738-X11	Detectable Plasters Assorted Pack Multiple Sizes Pack of 100

Adhesive Type	Hotmalt Adhesive
Coat Weight (g/m2)	35-45
Adhesion Power (N/25mm)	20±3
Loop Track (N/25mm)	15±4
Shear (hrs)	≥20hrs

Wound Pad

Composition	Gm/sqm	1 – non adherent layer 100% PE 2 – absorption layer 75% viscose 25% PP/PE 3 - Backing: Aluminium Sheet with a Barium Sulphate ribbon 1 mm thickness and 4 mm width
Total Grammage	g/m2	220/-10%
Asorption Capacity	%	≥400
Time of Absorption	Sec	>1

Release Paper

Test	Units	Toll
Grammager	g/m2	75± 3

Wrapping Paper

A) front side wrapping paper

Test	Units	Toll
Total Weight	g/m2	45+/ -7

B) front side wrapping paper

Test	Units	Toll
Weight	g/m2	44+ -7

Sealing strength for the pouches + ≥ 1.0 N/15 mm

The validity of the certificate is subject to periodic or unexpected verification.

Effective date: February 17th, 2021 (included)
Expiry date: May 26th, 2024 (included)

Study report 2018060097 Cytotoxicity (test on extracts, DIN EN ISO 10993-5: 2009

Material and Methods

Test Material

Spun laced non-woven/PU laminate HM + Pad Pharm pore Ultra LOT: 284/11
The test material was packed, sterilized and sent by the client. The material used as negative control was polypropylene (Lot 1717/34) and as positive control medium 6 % Dimethyl Sulfoxide (DMSO) in DMEM-FCS (Dulbecco's Modification of Eagle's Minimum Essential Medium with fetal calf serum). The reagent control was cell culture medium which was extracted at the same extract conditions as the sample.

Preparation of extracts (DIN EN ISO 10993-12:2012)
A surface/volume ratio of 6 cm2 of test material per millilitre of extraction medium was used to perform the test. Before starting the analysis the cover paper was removed under sterile conditions. The material used for the negative control was polypropylene (0.2 g per millilitre of extraction medium), which was sterilized by autoclaving. The positive control medium was 6 % DMSO freshly prepared in DMEM-FCS before application. The estimated cytotoxicity of the DMSO solution is approximately 50 %.

Extraction medium: Dulbecco's Modification of Eagle's Minimum Essential Medium was used (DMEM; Fisher Scientific GmbH; Lot: 1880308). The culture medium (DMEM) was supplemented with 10 % fetal calf serum (FCS; PAN-Biotech GmbH; Lot: P122011). Extraction was performed with gentle shaking at 37 3 1 ° C for 24, 32 hours.

Preparation of cell cultures

L 929 cells (ATCC CCL 1, NCTC clone 929, connective tissue mouse, clone of strain L) were used as test cell line. The test system was chosen because this cell line has been shown to be suitable for this type of study and is recommended in the DIN EN ISO 10993-5:2009. The cells were grown in DMEM-FCS supplemented with 10 % FCS. The cells were cultured at 37 3 1 °C and 5% C02 in a humidified incubator.

24 3 2 hours before application of the extracts onto the cells, cells were harvested from standard tissue culture flasks using a trypsin/EDTA solution. The cells were resuspended in DMEM-FCS. The cell density was adjusted to 1.5 x 105 /ml, and the wells of 96 wells tissue culture plates were inoculated with 100 QI of cell suspension per weil. The plates were incubated for 24 3 2 hours in a humidified incubator in 5 %

C02 at 37 31 °C. During this time the cells formed subconfluent monolayer.

Preparation of serial dilutions of the extract

Serial dilutions of the test material extract were prepared in reagent control in order to obtain the following percentages of extract in the dilution mixture:

Extract	a	100%
	b	66%
	c	44%
	d	30%
	e	20%

Cytotoxicity testing of the test material extract was performed at all above listed levels of concentration. The extract of negative control material and the reagent control were used undiluted ("100 %") only. The positive control reagent (6 % DMSO in DMEM-FCS) was prepared in a sterile container and mixed thoroughly.

Exposure of cells to extract and control reagents.

Each dilution of extract mentioned above and all control reagents were done as four replications. A 100 Ql aliquot of the liquids were administered into each of the four wells (using the 96 wells tissue culture plates after removing the cell culture medium from the prepared wells). As a next step, the tissue culture plates were incubated in a humidified incubator in 5 % C02 at 37 3 1 ° C for at least 24 hours.

Qualitative determination of cytotoxicity

After 24 hours of incubation, the cell culture plates were examined microscopically using phase contrast microscopy at 400 x magnification.

The degree of cytotoxicity observed in each weil was numerically graded using a subjective grading system as follows:

0 (none reactivity): Discrete intracytoplasmic granules; no cell lysis; no cell growth inhibition

1 (slight reactivity): Not more than 20 % of the cells are round, loosely attached and without intracytoplasmic granules ore show changes in morphology; occasional lysed cells are present, only slight cell growth inhibition

2 (mild reactivity): Not more than 50 % of the cells are round and devoid of intracytoplasmic granules; no extensive cell lysis and empty areas between cells; not more than 50 % cell growth inhibition

3 (moderate reactivity): Not more than 70 % of cell layers contain rounded cells or are lysed; more than 50% cell growth inhibition

4 (severe reactivity): Nearly complete or complete destruction of the cell layers

Quantification of extract dilutions cytotoxicity and controls

The tetrazolium salt MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)- 2-(4-sulfophenyl)-2H-tetrazolium] (yellow) is reduced from living cells to formazan (red brown). For this purpose, electrons are transferred from the reduction equivalents NADH (nicotinamide adenine dinucleotide) and NADPH (nicotinamide adenine dinucleotide phosphate) to MTS. NADH and NADPH are formed by mitochondrial dehydrogenases of metabolically active cells. The formazan content is thus an indirect proof for the metabolic cell activity, which increases proportionally to the cell number and should be quantified here. This method is a validated assay based on the reduction of vital dye (similar to MTT [3-(4,5-dimethylthiazol-2-yl)-2,5- diphenyltetrazolium bromide]).

After microscopically examination cell culture medium was eliminated from each well. Subsequent each weil was filled with 120 Ql of MTS-solution (freshly prepared). 1 blank well (without cells) of each plate was additional filled with 120 Ql of MTS-solution. The plate was incubated at 37 3 1 °C and 5 % C02 for 40 min. The absorption wavelength was 490 nm and the reference wavelength was 630 nm. At first the average of blank (MV) was subtracted from each extinction measured at 490 nm and 630 nm. After this the deviation of absorption and reference wavelength was determined. The average of reagent control was estimated at 100 % cell growth. The results of other measurements were related to the reagent control. The relative inhibition of cell growth (% ICG) was calculated as follows:

%ICG=1OO-1OOx E(490 nm - MV blank) - (630nm - MV blank) extract

E(490 nm - MV blank) - (630nm - MV blank) reagent control

Results

Results of the macroscopic and microscopic examinations

Cells covered with reagent control prepared did not show any damage (grade 0). Also the extract of negative control material (polypropylene) did not harm the cells

(grade 0). The positive control solution (6 % DMSO dissolved in DMEM-FCS) caused, as expected, damages (degree 3-4) of the cells.

After a 24 hours incubation of cell cultures with different concentrations of the test material extract, the following results have been observed:

Grade of toxicity:

Conc. of extract	Microscopic examination (degree 0-4)
100%	0-1
66%	0-1
44%	0
30%	0
20%	0

Slight cell growth inhibition was microscopically visible with the extract concentrations of 100 % - 66 %.

Measured values of the percentage inhibition of cell growth (% ICG)

	Controls								
	RC)1	**PC)1**	**NC)1**	**100%**	**66%**	**44%**	**30%**	**20%**	**RC)1**
Measured values (490 nm blank) – (630 nm - blank)	0.389 0.370 0.370 0.359	0.109 0.111 0.109 0.108	0.398 0.391 0.385 0.378	0.354 0.337 0.332 0.334	0.367 0.341 0.354 0.331	0.370 0.355 0.353 0.353	0.353 0.405 0.371 0.343	0.380 0.376 0.379 0.377	0.382 0.437 0.420 0.399
Mean value (MV)	0.372	0.109	0.388	0.339	0.348	0.356	0.368	0.368	0.368
+ standard deviation	0.012	0.001	0.009	0.010	0.016	0.010	0.027	0.002	0.024
ICG)4 in%	**4.8**	**72.0**	**0.7**	**13.2**	**10.9**	**8.9**	**5.8**	**3.3**	**0.0**

)1 = Reagent Control (RC);)2 = Positive Control (PC, 6 % DMSO);)3 = Negative Control (NC);
)4 = inhibition of cell growth (ICG); * outlier (Nalimov outlier test); Mean valuc of all reagent controls: **0.391**
An inhibition of cell growth (ICG) of more than ( ) 30 % is considered as cytotoxic effect according to DIN EN ISO 10993-5.

Assessment of the test results

The extract of the test material caused no relevant toxicological / biological damages to subconfluent monolayer of L929 cells under the test conditions of DIN EN ISO 10993-5:2009. The test material meets the requirements of DIN EN ISO 10993-5 and is considered non-cytotoxic.

Results of negative and positive controls confirm the sensitivity and accuracy of the test system. There was a good correlation between the colorimetric results and microscopically detectable cell appearance. The test can be considered as homogeneous and valid.

Report 2018090909 Skin Irritation (DIN EN ISO 10993-10:2014)

Material and Methods

Test Material

Spunlaced non-woven HM + Pad; Pharmapore, Pharmapore IV, Cure-Aid, Cure-Aid Dressing Strips, ETO sterilized; LOT: 601/12

The test material was sterilized, packed and sent by the client. The test procedure was performed without extraction of the test material.

Animals and husbandry

Healthy, young adult albino rabbits of female sex with a body weight not less than 2 kg were used. This animal species was used since it is suitable for the test and recommended by DIN EN ISO 10993-10:2014. The rabbits were kept isolated and fed ad libitum with commercially available pellets. The animals were acclimated and permanently controlled by veterinarians according to DIN EN ISO 10993-2:2006. They were immunized against myxomatosis and RHO.

Test Procedure

The test procedure was performed without extraction of the test material because the test material has an appropriate physical state for direct application and is intended to be used directly on the skin of the patient. (DIN EN ISO 10993-10:2014, Appendix A 2.1)

The fur on the backs of three rabbits was closely clipped on both sides of the spinal column (10 x 15 cm) 19.5 hours before the test procedure started. Only animals with healthy intact skin were used. The test material was applied directly to the clipped skin of the rabbits, together with control gauze patches (25 x 25 mm). Location of skin application sites: see figure 1 of DIN EN ISO 10993-10:2014. The application sites were covered with a non-occlusive gauze patch and wrapped with an occlusive bandage for 4 hours. At the end of the contact time the dressings were removed and the residual substances were washed off with warm water. The skin was blown dry.

Test Results

The application sites were observed 1 30.1 h after removal of the gauzes and after 2432, 4832 and 7232 hours.
The skin reaction was described and scored in the following manner:

Reaction	**Numerical Grading**
Erythema and eschar formation	0
No erythema	1
Very slight erythema (barely perceptible)	2
Well-defined erythema	3
Moderated erythema	4
Severe erythema (beet-redness) to slight eschar formation	5
Edema formation	
No edema	0
Very slight edema (barely perceptible)	1
Well-defined edema (edges of area well defined by definite raising)	2
Moderated edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond exposure area)	4
Total possible score for irritation	**8**

The Primary Irritation Index (P.1.1.) was determined in the following manner:

After the 72 h grading, all erythema grades plus edema grades (24 3 2) h, (48 3 2) h and (72 3 2) h were totalled separately for each test sample and blank for each animal. The primary irritation score for an animal was calculated by dividing the sum of all the scores by 6 (two test/observation sites, three time points).

To obtain the primary irritation index for the test sample all the primary irritation scores of the individual animals were added and divided by the number of animals.

The primary irritation score of the negative control (vehicle) was subtracted from the score of the test material to obtain the primary irritation score.

The primary irritation response in rabbits is categorized as follows:

Response Category	Mean Score (P.1.1.)
Negligible	0.0 - 0.4
Slight	0.5 - 1.9
Moderate	2.0 - 4.9
Severe	5.0 - 8.0

Symptoms observed: 3 rabbits Test material in contrast to control

Symptoms observed after (Numerical Grading)				
Animal	**24h**	**48H**	**72H**	**P.I.I.**
2018-82	0	0	0	0
2018-83	0	0	0	0
2018-84	0	0	0	0
Score P.1.1.:				**0.0**

Assessment

The test material did not cause any irritation of skin after the application time of 4 hours in the course of the observation period of 72 h (P.1.1. 0.0).

Study report 2018090909 Skin Sensitization (DIN EN ISO 10993-10:2014)

Material and Methods
Test material

Spunlaced non-woven HM + Pad; Pharmapore, Pharmapore IV, Cure-Aid, Cure-Aid Dressing Strips,

ETO sterilized; LOT: 601/12
The test material was sterilized, packed and sent by the client. The test procedure was performed without extraction of the test material.

Test procedure

Animals
Healthy, young, adult, female albino guinea-pigs (strain Dunkin Hartley, Crl:(HA)BR; Charles River, Germany) were used (weight 318.8 - 364.3 g).

The test system was chosen because the guinea-pig has been shown to be suitable for this type of study and is recommended by 01 N EN ISO 10993-10:2014.

Housing and Feeding Conditions

Temperature: 2033 °C

Relative humidity: 30-70 % (other than during room cleaning)

Lighting: 12 hours light, 12 hours dark

The guinea-pigs were housed in groups of up to ten.

Feeding was done ad libitum with a commercial feeding mixture (Mühle Knull, Rostock, Germany)

Water source: tap water (drinking quality, supplemented with 1 g/vitamin C)

Food and water were given ad libitum.

The animals were kept in their cages for at least 5 days prior to test start to allow for acclimatisation to the laboratory conditions. The health of animals was controlled by veterinarians or other qualified staff members.

Number of Animals

A group of 10 animals were selected to test the test material and 5 animals were selected to test the negative control.

Induction Phase

The test procedure was performed without extraction of the test material because the test material has an appropriate physical state for direct application and is intended to be used directly on the skin of the patient. (DIN EN ISO 10993-10:2014, Appendix A 2.1)

The fur of the guinea-pigs' left flanks was closely clipped (3 x 3 cm). Only animals with healthy intact skin were used.

The test material was applied directly to the clipped skin (25 x 25 mm) and covered with a non-occlusive gauze patch, and wrapped with an occlusive bandage for 6 hours.

At the end of the contact time the wrapping was removed and residual substances washed off with warm water.
The skin was blown dry.

Five control guinea-pigs were treated with gauze patch equally.

The sensitizations were performed trice a week over a period of three weeks

Challenge Phase

14+1 days after the last application the challenge test was performed with test and control animals.

The fur of the guinea-pigs' right flanks was closely clipped (3 x 3 cm).

The test material was applied directly to the clipped skin (25 x 25 mm) of test and control animals and covered with a non-occlusive gauze patch, and wrapped with an occlusive bandage for 6 hours.

At the end of the contact time, the wrapping was removed and residual substances washed off with warm water.
The skin was blown dry

Grading of Skin Reactions

24 + 2 hours after the challenge, all animals were closely clipped at the tested areas (including 1 cm of the surrounding areas).
2 hours after that, the skin reaction was graded. The grading was repeated after 24 hours.

The skin reaction was described and scored as follows:

Reaction	Numerical Grading
No erythema	0
Scattered mild redness	1
Moderate and diffuse redness	2
Intense redness and swelling	3

Grades of 1 or larger in the test group indicate sensitization, provided that grades given for control animals are less than 1. If grades of 1 or larger are given for control animals, then the reactions of test animals which exceed the most severe control reaction are presumed to be due to sensitization.

Reliability Check

The reliability checks are performed regularly with hexyl cinnamic aldehyde (HCA -CAS No. 101-86-0) in the test laboratory (every six months).

Test conditions:

Induction phase: HCA 60% in vaseline

Challenge phase: HCA - 55% in vaseline

Results

Clinical observations

The animals did not show any visible clinical symptoms over the period of observation.

Skin reactions

Following skin reactions were observed in test animals after challenge treatment with the test material extract (table 1).

Table1: Skin reactions of test animals after treatment with the test material

Animal	Numerical Grading After	
	24 h	48 h
1	0	0
2	0	0
3	0	0
4	0	0
5	0	0
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0

Table 2 shows skin reactions of control animals after challenge treatment.

Table 2: Skin reactions of control animals

Animal	Numerical Grading After	
	24 h	48 h
K1	0	0
K2	0	0
K3	0	0
K4	0	0
K5	0	0

Reliability check

The latest reliability check was performed from 09.10.2018- 08.11.2018 with hexyl cinnamic aldehyde (HCA; CAS No. 101-86-0). Result: 80% of animals treated with positive control substance (HCA - 55% in vaseline) showed a skin reaction with numeral grading from 1 up to 2 according to

"MAGNUSSON AND KLIGMAN GRADING SCALE FOR THE EVALUATION OF CHALLENGE PATCH TEST REACTIONS"

The positive control showed the sensitization and the validity of the test system.

Assessment of results

The test material did not cause sensitization during the course of the observation period.

Trial

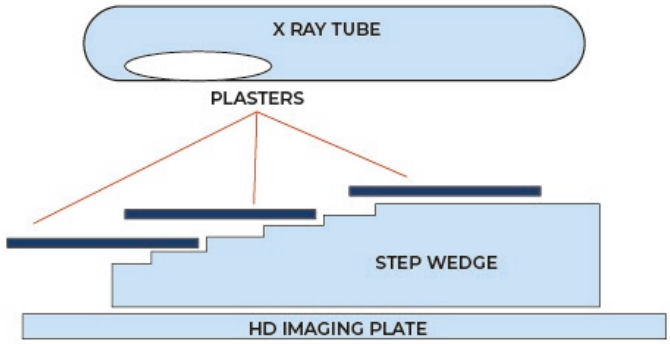
To test samples of plasters according to standard ASTM F792-08, to test the detectability of the plasters with a step wedge of different thicknesses.

Method

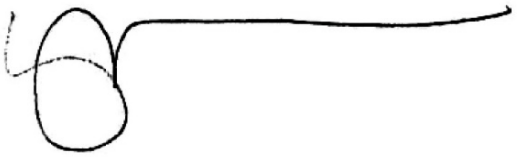
Using a Stainless-Steel step wedge with of thickness 2.35, 4.25, 6.15, 8.10 and 10.5mm, the plasters are placed on top of the step wedge furthest away from the detector plate for worst case scenario. X-rayed at 100KV, 6.5MA, 60 seconds and a FFD of 1metre, HD Imaging plate scanned at 50um

Set up

In order to create the worst possible conditions, the plasters were placed on top of the step wedged, at the remotest distance from the imaging plates, see bel



Four types of plasters were supplied, so four images were produced in the same orientation for each. Each image was identified with the thickness of the steps in the step wedge and the plaster type.



Helen Morrison
Group Managing Director