THE MODIFIED DRAIZE-95' TEST IN NORMAL INDIVIDUAL (HUMAN STUDY) TEST REQUIRED BY UNITED STATES FOOD & DRUG ADMINISTRATION FOR 510(K) CLEARANCE

GLOVE PROFILE

Name of Test Material	Powder Free Nitrile Patient Examination Gloves, Blue Coloured, Non-Sterile, Low DermatitisPotential Claim
Study Ref. No.	[TM-MDT-02]-01-2-16(29-16)
Batch/Lot No.	PA-180116-01-1-01-018
Date Test Material Received	3rd August 2016
Characteristic	Nitrile Rubber Glove
Expiry Date	3 Years
Physical Description	Solid
Quantity	300 pieces
Storage Requirement	Ambient
Condition of Use	Neat
Experimental Starting Date	Stage 1: 17th August 2016 Stage 2: 15th October 2016
Experimental Completion Date	16th December 2016

ASSESSMENT INFORMATION

Objectives:
1. To evaluate whether residual chemical additives at the level that may induce Type IV allergy in the unsensitised general user population are present in a finished Nitrile rubber containing medical device, Powder Free Nitrile Patient Examination Gloves, Blue Coloured, Non-Sterile, Low Dermatitis Potential Claim.
2. To meet requirements for the claim: This product demonstrated reduced potential for sensitising users to chemical additives. As described in Guidance for Industry and FDA Staff-Medical Glove Guidance Manual. Supporting Test Data: A negative skin sensitisation test (Modified Draized-95 Test) on a minimum of 200 non-sensitised human subjects.

Study Protocol:
Based on the "Guidance for Industry and FDA Reviewers/Staff: Premarket Notification [510(k)] Submissions for Testing for Skin Sensitisation to Chemicals in Natural Rubber Products" document (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Guid anceDocuments/ucm073793.pdf) and Medical Glove Guidance Manual (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm428191.pdf)

Study Procedure:
The inner and outer surface of the Nitrile glove are tested on the human skin. A total of 209 human subjects are patched with inner surface of Nitrile rubber glove and 102 out of the total human subjects are patched with additional outer surface of Nitrile rubber glove. The study is conducted in two stages. In the first stage, a population of 30 human subjects are tested to evaluate product for the potential to cause irritation or sensitisation. The second stage is conducted on a further number of subjects to a total of a minimum of 200 individuals after the first stage has shown that the test product does not indicate a potential for inducing severe dermal irritation and does not show sensitisation capability.

Scoring Criteria:
Patch Testing Diagnostic Criteria are based on standard scoring of the North American Contact Dermatitis Research Group (NACDRG) ("Am. J. Contact Dermatitis" 2: 122-129, 1991).

Table 1:
Scoring Criteria - The intensity of reactions were scored according to the following criteria.

Table 1a

Basic Score	Description
0	No visible reaction
0.5	Doubtful or negligible erythema reaction
1.0	Mild or just perceptible macular erythema reaction in a speckled/ follicular, patchy or confluent pattern (slight pinking)
2.0	Moderate erythema reaction in a confluent pattern (definite redness)
3.0	Strong or brisk erythema reaction that may spread beyond the test site

Table 1b

Supplemental scores	Description	Label
0.5	Edema	E
0.5	Papules	P
0.5	Vesicles	V
0.5	Bullae	B

Induction Phase

A sample of the test material, minimum size of 2cm x 2cm, is applied to each test subject in the study. The test material is patched on to the upper back area and continuously secured on the edges with a nonreactive adhesive tape, micropore* whilst ensuring the complete occlusion of the patch.

10 patches of test material are applied on each Monday, Wednesday and Saturday. The test material is removed and replaced by a new one at the same site every 48 hours for a total of 10 changes. Patches applied on Saturday are removed on Monday. Any and all skin reactions during this induction phase are recorded. Subjects that developed reaction that occurred to an initial induction test patch, are considered as a pre-sensitised individual. Reactions observed after placement of the second patch in the induction phase are generally considered as an irritation.

Note: For Subjects who develop a positive reaction (a score value of 1.5) to chemicals or show signs of irritation after patch applications, further patching on those individuals are stopped. After about 3 weeks of rest, these individuals received a challenge patch to confirm observed reaction as either pre-existing sensitivity or irritant reaction. When a local irritation caused by the occlusion material occurs, occlusion tape would be replaced with the non-irritating one, and the induction patching was further continued.
*supplied by 3M Pharmaceuticals.

01

02

Rest Period

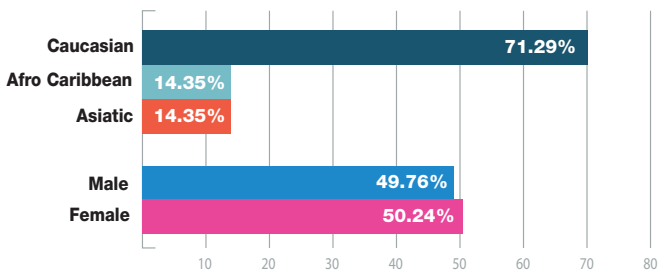
At the end of induction period, the 10th test material is removed and no further test material is applied to the test subjects for the following 3 weeks, until the challenge patches are applied.

03

Challenge Phase

Two samples of the same test material, a minimum of 2cmx2cm in size are applied consecutively to a virgin site for 48 hours each. Test site is evaluated for reaction at the time of each patch removal and again 2 to 4 days after removal of the second patch.

HUMAN SUBJECT PROFILE



Age Range: 18 to 58 years old (25.29 ± 9.13).

ASSESSMENT RESULT

Results:
All these 209 subjects had a final score of not more than 1.5 during the induction phase and the challenge phase.
Out of the 209 subjects, 102 subjects were also similarly treated with the outer surface of Nitrile rubber glove.
All these 102 subjects had a final score of not more than 1.5 during the induction phase and the challenge phase.

Interpretation of Results:
The study that was completed on 209 non-sensitised adult human subjects giving all negative results in both inner and outer surfaces, hence provides more than 95% confidence that the chemical sensitisation potential of the tested Nitrile rubber containing medical device in the user population is expected to be less than 1.5%.

Conclusion:
There was no clinical evidence of the presence of residual chemical additives at the level that may induce Type IV allergy in the unsensitised general user population in the tested material.

The skin sensitisation test ('Modified Draize-95' Test) of this medical device, Powder Free Nitrile Patient Examination Gloves, Blue Coloured, Non-Sterile, Low Dermatitis Potential Claim, tested on 209 non-sensitised human subjects are negative, hence meeting the requirements for the claim: This product demonstrated reduced potential for sensitising users to chemical additives as described in Guidance for Industry and FDA Staff – Medical Glove Guidance Manual.

Conducted by:
Kossan International Sdn Bhd

REFERENCES:
1) "Guidance for Industry and FDA Reviewers/Staff: Premarket Notification [510(k)] Submissions for Testing for Skin Sensitisation to Chemicals in Natural Rubber Products" on the World Wide Web at: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073793.pdf
2) "Medical Glove Guidance Manual" on the World Wide Web at: http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm428191.pdf

THE MODIFIED DRAIZE-95' TEST IN NORMAL INDIVIDUAL (HUMAN STUDY) TEST REQUIRED BY UNITED STATES FOOD & DRUG ADMINISTRATION FOR 510(K) CLEARANCE

GLOVE PROFILE

Name of Test Material	Powder Free Nitrile Patient Examination Gloves, White Coloured, Non-Sterile, Low Dermatitis Potential Claim
Study Ref. No.	[TM-MDT-02]-01-1-16(27-16)
Batch/Lot No.	PB-130716-12-1-03-001
Date Test Material Received	3rd August 2016
Characteristic	Nitrile Rubber Glove
Expiry Date	3 Years
Physical Description	Solid
Quantity	300 pieces
Storage Requirement	Ambient
Condition of Use	Neat
Experimental Starting Date	Stage 1: 17th August 2016 Stage 2: 15th October 2016
Experimental Completion Date	16th December 2016

ASSESSMENT INFORMATION

Objectives:
1. To evaluate whether residual chemical additives at the level that may induce Type IV allergy in the unsensitised general user population are present in a finished Nitrile rubber containing medical device, Powder Free Nitrile Patient Examination Gloves, White Coloured, Non-Sterile, Low Dermatitis Potential Claim.
2. To meet requirements for the claim: This product demonstrated reduced potential for sensitising users to chemical additives. As described in Guidance for Industry and FDA Staff-Medical Glove Guidance Manual. Supporting Test Data: A negative skin sensitisation test (Modified Draized-95 Test) on a minimum of 200 non-sensitised human subjects.

Study Protocol:
Based on the "Guidance for Industry and FDA Reviewers/Staff: Premarket Notification [510(k)] Submissions for Testing for Skin Sensitisation to Chemicals in Natural Rubber Products" document (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Guid anceDocuments/ucm073793.pdf) and Medical Glove Guidance Manual (http://www.fda.gov /MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm428191.pdf).

Study Procedure:
The inner and outer surface of the Nitrile glove are tested on the human skin. A total of 209 human subjects are patched with inner surface of Nitrile rubber glove and 107 of the total human subjects are patched with additional outer surface of Nitrile rubber glove. The study is conducted in two stages. In the first stage, a population of 30 human subjects are tested to evaluate product for the potential to cause irritation or sensitisation. The second stage is conducted on a further number of subjects to a total of a minimum of 200 individuals after the first stage has shown that the test product does not indicate a potential for inducing severe dermal irritation and does not show sensitisation capability.

Scoring Criteria:
Patch Testing Diagnostic Criteria are based on standard scoring of the North American Contact Dermatitis Research Group (NACDRG) ("Am. J. Contact Dermatitis" 2: 122-129, 1991).

Table 1:
Scoring Criteria - The intensity of reactions were scored according to the following criteria.

Table 1a

Basic Score	Description
0	No visible reaction
0.5	Doubtful or negligible erythema reaction
1.0	Mild or just perceptible macular erythema reaction in a speckled/ follicular, patchy or confluent pattern (slight pinking)
2.0	Moderate erythema reaction in a confluent pattern (definite redness)
3.0	Strong or brisk erythema reaction that may spread beyond the test site

Table 1b

Supplemental scores	Description	Label
0.5	Edema	E
0.5	Papules	P
0.5	Vesicles	V
0.5	Bullae	B

Induction Phase

A sample of the test material, minimum size of 2cm x 2cm, is applied to each test subject in the study. The test material is patched on to the upper back area and continuously secured on the edges with a nonreactive adhesive tape, micropore* whilst ensuring the complete occlusion of the patch.

10 patches of test material are applied on each Monday, Wednesday and Saturday. The test material is removed and replaced by a new one at the same site every 48 hours for a total of 10 changes. Patches applied on Saturday are removed on Monday. Any and all skin reactions during this induction phase are recorded. Subjects that developed reaction that occurred to an initial induction test patch, are considered as a pre-sensitised individual. Reactions observed after placement of the second patch in the induction phase are generally considered as an irritation.

Note: For Subjects who develop a positive reaction (a score value of 1.5) to chemicals or show signs of irritation after patch applications, further patching on those individuals are stopped. After about 3 weeks of rest, these individuals received a challenge patch to confirm observed reaction as either pre-existing sensitivity or irritant reaction. When a local irritation caused by the occlusion material occurs, occlusion tape would be replaced with the non-irritating one, and the induction patching was further continued.
*supplied by 3M Pharmaceuticals.

01

02

Rest Period

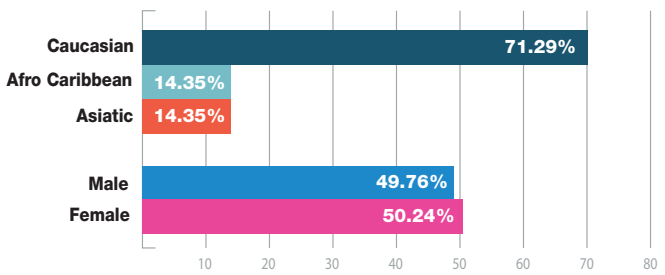
At the end of the induction period, the 10th test material is removed and no further test material is applied to the test subjects for the following 3 weeks, until the challenge patches are applied.

03

Challenge Phase

Two samples of the same test material, a minimum of 2cmx2cm in size are applied consecutively to a virgin site for 48 hours each. Test site is evaluated for reaction at the time of each patch removal and again 2 to 4 days after removal of the second patch.

HUMAN SUBJECT PROFILE



Age Range: 18 to 58 years old (25.29 ± 9.13).

ASSESSMENT RESULT

Results:
All these 209 subjects had a final score of not more than 1.5 during the induction phase and the challenge phase.
Out of the 209 subjects, 107 subjects were also similarly treated with the outer surface of Nitrile rubber glove.
All these 107 subjects had a final score of not more than 1.5 during the induction phase and the challenge phase.

Interpretation of Results:
The study that was completed on 209 non-sensitised adult human subjects giving all negative results in both inner and outer surfaces, hence provides more than 95% confidence that the chemical sensitisation potential of the tested Nitrile rubber containing medical device in the user population is expected to be less than 1.5%.

Conclusion:
There was no clinical evidence of the presence of residual chemical additives at the level that may induce Type IV allergy in the unsensitised general user population in the tested material.

The skin sensitisation test ('Modified Draize-95' Test) of this medical device, Powder Free Nitrile Patient Examination Gloves, White Coloured, Non-Sterile, Low Dermatitis Potential Claim, tested on 209 non-sensitised human subjects are negative, hence meeting the requirements for the claim: This product demonstrated reduced potential for sensitising users to chemical additives as described in Guidance for Industry and FDA Staff – Medical Glove Guidance Manual.

Conducted by:
Kossan International Sdn Bhd

REFERENCES:
1) "Guidance for Industry and FDA Reviewers/Staff: Premarket Notification [510(k)] Submissions for Testing for Skin Sensitisation to Chemicals in Natural Rubber Products" on the World Wide Web at: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073793.pdf
2) "Medical Glove Guidance Manual" on the World Wide Web at: http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm428191.pdf

THE MODIFIED DRAIZE-95' TEST IN NORMAL INDIVIDUAL (HUMAN STUDY) TEST REQUIRED BY UNITED STATES FOOD & DRUG ADMINISTRATION FOR 510(K) CLEARANCE

GLOVE PROFILE

Name of Test Material	Powder Free Nitrile Patient Examination Gloves, Black Coloured, Non-Sterile, Low Dermatitis Potential Claim
Study Ref. No.	[TM-MDT-02]-03-3-18(27-18)
Batch/Lot No.	PB11031815103032
Date Test Material Received	4th August 2018
Characteristic	Nitrile Glove
Expiry Date	3 Years
Physical Description	Solid
Quantity	300 pieces
Storage Requirement	Ambient
Condition of Use	Neat
Experimental Starting Date	Stage 1: 8th October 2018 Stage 2: 24th November 2018
Experimental Completion Date	Stage 1: 2nd Desember 2018 Stage 2: 16th February 2019

ASSESSMENT INFORMATION

Objectives:

1 To evaluate whether residual chemical additives at the level that may induce Type IV allergy in the unsensitised general user population are present in a finished Nitrile rubber containing medical device, Powder Free Nitrile Patient Examination Gloves, Black Coloured, Non-Sterile, Low Dermatitis Potential Claim.

2 To meet requirements for the claim: This product demonstrated reduced potential for sensitising users to chemical additives as described in Guidance for Industry and FDA Staff-Medical Glove Guidance Manual. Supporting Test Data: A negative skin sensitisation test (Modified Draized-95 Test) on a minimum of 200 non-sensitised human subjects.

Study Protocol:

1 This study protocol is based on the "Guidance for Industry and FDA Reviewers/Staff: Premarket Notification [510(k)] Submissions for Testing for Skin Sensitisation to Chemicals in Natural Rubber Products" document (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073792.htm#e_2_4).

2 Medical Glove Guidance Manual (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm150053.htm) with some modification.

Study Procedure:

The inner and outer surface of the Nitrile glove was tested on the human skin. A total of 210 human subjects were patched with inner and outer surface of Nitrile rubber glove. The study was conducted in two stages. In the first stage, a population of 30 human subjects are tested to evaluate product for the potential to cause irritation or sensitisation. The second stage was conducted on a further number of subjects to a total of a minimum of 210 individuals after the first stage has shown that the test product does not indicate a potential for inducing severe dermal irritation and does not show sensitisation capability.

Scoring Criteria:

Patch Testing Diagnostic Criteria are based on standard scoring of the North American Contact Dermatitis Research Group (NACDRG) ("Am. J. Contact Dermatitis" 2: 122-129, 1991).

Table 1:
Scoring Criteria - The intensity of reactions were scored according to the following criteria.

Table 1a

Basic Score	Description
0	No visible reaction
0.5	Doubtful or negligible erythema reaction
1.0	Mild or just perceptible macular erythema reaction in a speckled/ follicular, patchy or confluent pattern (slight pinking)
2.0	Moderate erythema reaction in a confluent pattern (definite redness)
3.0	Strong or brisk erythema reaction that may spread beyond the test site

Table 1b

Supplemental scores	Description	Label
0.5	Edema	E
0.5	Papules	P
0.5	Vesicles	V
0.5	Bullae	B

Induction Phase

Samples of the test material, both inner and outer surface with minimum size of 2cm by 2cm each, was applied to each test subject in the study. The test material is patched on to the upper back area and continuously secured on the edges with a nonreactive adhesive tape, micropore* whilst ensuring the complete occlusion of the patch.

10 patches of test material are applied on each Monday, Wednesday and Saturday. The test material is removed and replaced by a new one at the same site every 48 hours for a total of 10 changes. Patches applied on Saturday are removed on Monday. Any and all skin reactions during this induction phase are recorded. Subjects that developed reaction that occurred to an initial induction test patch, were considered as a pre-sensitised individual. Reactions observed after placement of the second patch in the induction phase are generally considered as an irritation.

Note: For Subjects who develop a positive reaction (a score value of 1.5) to chemicals or show signs of irritation after patch applications, further patching on those individuals are stopped. After about 3 weeks of rest, these individuals received a challenge patch to confirm observed reaction as either pre-existing sensitivity or irritant reaction. When a local irritation caused by the occlusion material occurs, occlusion tape would be replaced with the non-irritating one, and the induction patching was further continued. *supplied by 3M Pharmaceuticals.

01

02

Rest Period

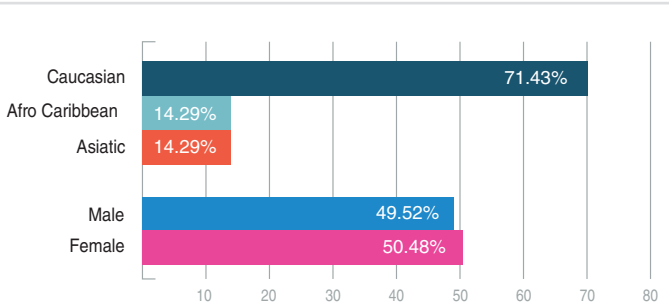
At the end of the three weeks induction period, the 10th test material was removed and no further test material was applied to the test subjects for the next 2 to 3 weeks, until the challenge patches are applied.

03

Challenge Phase

Two samples of the same test material, both the inner and outer surface with minimum of 2cm by 2cm in size were applied consecutively to a virgin site for 48 hours each. Test site is evaluated for reaction at the time of each patch removal and again 2 to 4 days after removal of the second patch.

HUMAN SUBJECT PROFILE



Age Range: 18 to 54 years old (25.72 ± 10.15).

ASSESSMENT RESULT

Results:

All these 210 subjects had a final score of not more than 1.5 during the induction phase and the challenge phase. Out of the 210 subjects, 210 and 209 subjects were treated with the inner surface and outer surface of nitrile rubber glove. All these 210 subjects had a final score of not more than 1.5 during the induction phase and the challenge phase.

Interpretation of Results:

The study that was completed on 210 non-sensitised adult human subjects giving all negative results in both inner and outer surfaces, hence provides more than 95% confidence that the chemical sensitisation potential of the tested Nitrile rubber containing medical device in the user population is expected to be less than 1.5%.

Conclusion:

There was no clinical evidence of the presence of residual chemical additives at the level that may induce Type IV allergy in the unsensitised general user population in the tested material.

The skin sensitisation test ('Modified Draize-95' Test) of this medical device, Powder Free Nitrile Patient Examination Gloves, Black Coloured, Non-Sterile, Low Dermatitis Potential Claim, tested on 210 non-sensitised human subjects with outer surface are negative, hence meeting the requirements for the claim: This product demonstrated reduced potential for sensitising users to chemical additives as described in Guidance for Industry and FDA Staff – Medical Glove Guidance Manual.

Conducted by:
Kossan International Sdn Bhd

REFERENCES:

1) "Guidance for Industry and FDA Reviewers/Staff: Premarket Notification [510(k)] Submissions for Testing for Skin Sensitisation to Chemicals in Natural Rubber Products" on the World Wide Web at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073792.htm#e_2_4

2) "Medical Glove Guidance Manual" on the World Wide Web at: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm150053.htm