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54 Method for treatment of natural rubber products.

57 The present invention relates to a method of reducing allergenicity of natural rubber latex products caused by allergens by reducing extractable protein levels found for said products, said method comprising the steps of:
subjecting said products to a wash in a strong alkaline solution to deteriorate the allergens, and a system for reducing allergenicity of natural rubber latex products caused by allergens by reducing extractable protein levels found for said products, and a product, such as a glove or condom, manufactured from natural rubber latex.

NL C 1035901

Dit octrooi is verleend ongeacht het bijgevoegde resultaat van het onderzoek naar de stand van de techniek en schriftelijke opinie. Het octrooischrift komt overeen met de oorspronkelijk ingediende stukken.

METHOD FOR TREATMENT OF NATURAL RUBBER PRODUCTSTECHNICAL FIELD OF THE INVENTION

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Natural Rubber Latex (herein also referred to as NRL) is being used for many products in for instance the health care industry, such as surgical gloves, and for manufacturing prophylactics, such as condoms.

10

Due to the stretchability, the natural feeling touch, its barrier properties including puncture resistance and even some self seallability after a puncture, Natural Rubber Latex is the preferred material for examination and surgical gloves. The latex sap harvested from the Hevea Brasiliensis tree contains proteins, which are functional for the stability of the latex suspension used in production of such products, for instance by dipping and/or molding. However, such proteins give rise to allergic reactions to sensitive people coming into physical contact with products made of this natural material.

15
20BACKGROUND OF THE INVENTION

This allergic sensitivity of specific persons to the material has become a major problem in the health care industry and solutions are needed to prevent health care institutes from switching to inferior synthetic alternatives.

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Some solutions have been proposed which denature the allergens. These methods mostly use added stabilizers to keep the rubber particles of the NRL from clogging. This changes the surface properties of the suspended rubber particles, resulting in different mechanical properties of

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the material. Other methods include washing finished latex products in aqueous solutions to remove surface proteins. None of the existing methods is able to completely prevent allergens to leach from latex products when they are
5 immersed in water: all methods show detectable amounts of leachable allergens.

This invention thus relates to products made of natural rubber latex (NRL) that come into contact with humans and especially to NRL that exhibits no detectable amount of
10 leachable allergens (and therefore or at least strongly reduced allergenicity potential) without the loss of physical properties or the introduction of new components altering the NRL formulation.

Solutions have been found in denaturing the allergens
15 in the natural rubber latex suspension using proteases, strong oxidatives and bases. One of the major drawbacks of denaturing the proteins and allergens in the latex suspension is that the stabilizing function of these proteins is lost with it as well. This problem can be solved
20 by adding stabilizers, but these will be present in the product after drying affecting the physical and mechanical properties of the NRL product. This invention therefore focuses on treatment of the NRL product after its production process.

25 The use of proteases in the latex suspension (JP9071604, JP2003020301, JP2001081107, JP2000109596, US20020091232) results in a lowered allergen content. However, a problem with these prior art solutions is, that these do not provide a sufficient solution to the problem of
30 preventing allergic reactions in sensitized people that come into physical contact with NRL. Another disadvantage is that proteases themselves are known to be a source of allergic reactions, so care must be taken to completely remove the

proteases from the final product and care should be taken while working with these proteases.

The oxidative washes (US20020103333, US5910567) generally use a strong chlorine or hypochlorite wash, which
5 is able to reduce the leaching of allergens from NRL upon contact with water. However, in case the oxidator concentration is too strong, the NRL is affected by this wash, resulting in diminished gripping, elastomeric and tactile properties. In general the product becomes stiff,
10 exhibiting hysteresis and requiring a heavy load to stretch. In case of a glove, the result is a poor fit and fatigue during use. These problems can be countered by using an additive to the NRL formulation that opposes these effects (US2002103333), but the material and its mechanical
15 properties are still different from regular NRL. No cases have been reported where the NRL itself is not affected in a negative way by an oxidative wash (by choosing mild oxidation conditions) and wherein no detectable amounts of leachable allergens are found to remain after such a known
20 treatment. The leachable allergen levels are in these prior art documents lowered, but still remain to be detectable.

The use of chemical proteolysis (DE4406584) by increasing the pH in the latex suspension is another option to remove the allergenicity. Experiments using this
25 treatment resulted in products with inferior mechanical properties and poor processability into NRL products. Drying of the product took longer and the product could easily be torn apart by stretching.

Notwithstanding the fact, that many possible solutions
30 have hitherto been presented, no satisfactory solution has been made available in the relevant technical field to more substantially reduce the allergen levels, preferable to practically undetectable levels (at least: undetectable with

currently available and commonly employed testing methods), while maintaining the desired properties of the NRL products.

5 SUMMARY OF THE INVENTION

The present invention is directed at decreasing the problems of the prior art method. More in particular, a solution is presented with which it is possible to reduce
10 the extractable amount of allergens to very low and even undetectable levels, according to the most sensitive analyses methods. Thus, according to the invention it has become possible to achieve results which have never been reached before, at least not without affecting the physical
15 properties of the Natural Rubber Latex matrix.

According to the present invention, as a solution to the problems of the prior art mentioned above, chemical proteolysis is applied to the NRL product after the production process. Due to the fact that no formulation
20 changes are introduced of the NRL suspension, the processability is being maintained while the products physical and mechanical properties are not being altered. This method is capable of removing extractable protein of the NRL product to undetectable levels, by just adding or
25 altering one washing step in the production process to remove the protein by chemical proteolysis.

According to the present invention the conditions considered necessary are applied to not only wash away the proteins but actually destroy the allergens by breaking the
30 peptide bonds of the proteins by chemical proteolysis.

The presented method is mainly based on chemical proteolysis of the proteins at the surface of a product made of Natural Rubber Latex. This proteolysis occurs by washing

the product in a strong alkaline solution (pH>10) at elevated temperatures. Higher temperatures and pH will speed up the proteolysis allowing shorter contact times. In these conditions peptide bonds will be subject to nucleophilic attacks by nucleophiles like OH⁻ (stronger nucleophiles may also be applied), breaking the peptide bond of the proteins through a nucleophilic substitution reaction. The amide group of the protein bond will act as the leaving group and the remaining carboxyl group will be deprotonized due to the high pH, leaving a stabilized carboxylate group which cannot be subject to a nucleophilic attack again.

The needed level of proteolysis is achieved by washing the NRL product using an alkaline solution at elevated temperatures. Washing using alkaline solution at room temperature, or washing using elevated temperatures and a neutral pH, does not reduce extractable protein levels more than 99%, even at long contact times (e.g. 1 day). Washing at 118°C and pH 14, for example during 1 hour, reduces extractable protein levels to undetectable levels.

It is acknowledged that some proposed procedures apply the use of an alkaline wash to remove proteins (JP9071604, JP2003020301, US20020103333). The focus of this wash is actually only to remove or modify the structure of the protein, and not to destroy the primary structure of the proteins. The conditions used for these washing steps are considered too mild to be considered an embodiment of chemically proteolysing the peptide bonds of the proteins. Moreover, in all these prior art disclosures, no decrease to undetectable amounts of leachable allergens is known to have been reported.

When looking at the actual allergen concentration of a NRL product, washing at pH 14 and 118°C for 1 hour removes all allergens to levels which are below the current

detection limits of the QuattroMed FitKit allergens testing kit (<0,15 µg/g for the four main allergens of NRL: <0,050 µg/g for Hevb1, <0.050 µg/g for Hevb3, <0.025 µg/g for Hevb5 and <0.025 µg/g for Hevb6.02). It is noted that washing at
5 room temperature (18-20°C) enables a reduction of the allergen concentration from 30 µg/g to 1 µg/g.

Thus according to the invention as defined in the appended claims, a new washing procedure has been developed for natural rubber latex products. A washing process (on an
10 aqueous basis) according to the present invention was tested on medical gloves. At testing, for both powdered and non-powdered gloves, an elimination in allergen leaching from the gloves after the treatment was noticeably detected. More accurately it is noted, that the quantities of the four
15 mayor NRL allergens were all below the detection limit of the FITkit method, as performed by and/or in accordance with guidelines from the company Quattromed in Estland.

The washing process has been investigated with respect to the material properties of the resulting NRL products,
20 and appears not to affect the mechanical properties, and is considered to be technically and economically feasible on a large scale production level.

The table below shows results using commonly used gloves from arbitrary producers.

Sample	Total protein leaching (ug/g), measured with a total protein essay ¹	Leaching of 4 allergens (ug/g), determined by Quattromed's FITkit measuring method
glove ex dipping machine	52 (+/- 2.0)	Total: 7.81 (Heb b1: undetectable, Hev b3: 0.07, Hev b5: 2.97, Hev b 6.02: 4.77)
glove chlorinated	4.5 (+/- 1.0)	Results not determined
glove ex dipping machine washed using the present new method	0.0 (+/- 1.0)	Total: undetectable (detection limit: 0.15 ug/g) All 4 allergens: undetectable
glove Chlorinated washed using the present new method	0.0 (+/- 1.0)	Total: undetectable (detection limit: 0.15 ug/g) All 4 allergens: undetectable

1. Measurement performed after 1 hour of extraction in PBS, pH=7.25, room temperature.

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It was found that, for both types of gloves, the current new washing process reduced the allergen leaching to zero, or at least a level undetectable with current and presently common testing methods, as determined by a total protein essay (detection limit approx. 1 ug/g), and by the FITkit method (detection limit of sum of 4 allergens: 0.15 ug/g).

The gloves treated in accordance with the new method of the present invention were further also tested to determine the Stress-strain curves of these treated gloves. This did not show any changes in mechanical properties of the gloves, which could have resulted from the new method according to

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the present invention. It is anticipated that subsequent storage will probably not affect the mechanical properties either, since in another test gloves (no brand) were treated and stored for 6 months. These gloves did not either exhibit
5 any significant changes in the tested stress-strain curve, which could have occurred during storage.

In summary, the obtained results are unique and very promising. Moreover, the method is considered to be applicable and affordable in practice. The new method of the
10 present invention can be upscaled and made suitable for the current large scale production practice without undue burden. Several different options are considered to be applicable for the new method of the invention: the method can be used as an additional step, or replace existing steps
15 (e.g. the chlorination). Further, the new method is anticipated to result in beneficial economic effects, which may positively affect cost price, and may lead to lower prices, if the method can be used to replace a more expensive step in the production.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Below a number of not-limiting examples of embodiments of the invention are described.

Example 1

In a first embodiment NRL products are washed in a strong alkaline suspension. The products have been
30 previously manufactured by dipping a mold into a NRL suspension. After manufacture, the product is washed in a strong alkaline solution. The alkaline solution had a pH of 10. The temperature of the solution is elevated to

approximately 30 degrees. The product is washed in the solution for 10 minutes and already a considerable improvement is then detectable.

5 Example 2

10 In a second embodiment NRL products are washed in a strong alkaline suspension. The products have been previously manufactured by molding a NRL suspension, where the suspension is injected or otherwise introduced into a mold. After manufacture, the product is washed in a strong alkaline solution. The alkaline solution has a pH of 10. The temperature of the solution is elevated, before or even during washing, to approximately 30 degrees. The product is
15 washed in the solution for 10 minutes and already a considerable improvement is detectable.

Example 3

20 In another embodiment of the invention, the method is the same as either of examples 1 and 2, with as a difference that the time of washing is increased to 1 hour, where a further increase in the effectiveness was detectable.

25 Example 4

30 In this exemplary embodiment the washing time is increased one day, and all other features remain unchanged relative to example 3. Again a further increase in the effectiveness is made detectable.

Example 5

In this embodiment of the invention, the method is the same as any one of the examples 1, 2, 3 and 4, with as a difference that the strength of the alkaline solution is increased to a pH of 14, where yet a further increase in the effectiveness is detectable.

Example 6

In the embodiment of this example, all features of examples 1-5 are unaltered, except that the temperature is raised to 50°C.

Example 7

In the embodiment of this example, all features of examples 1-5 is unaltered, except that the temperature is raised to 70°C.

Example 8

In the embodiment of this example, all features of examples 1-5 are unaltered, except that the temperature is raised to 90°C.

Example 9

In the embodiment of this example, all features of examples 1-5 are unaltered, except that the temperature is raised to 110°C.

Example 10

In the embodiment of this example, all features of examples 1-5 are unaltered, except that the temperature is raised to 118°C.

5 Example 11

In this embodiment the features of any one of the examples 6-10 are the same, with the exception that a pressure vessel, such as an autoclave, is used to contain
10 the strong alkaline solution (pH=10 or 14, with one of NaOH and KOH having a concentration of at least 0,01M). In the vessel pressure is increased to keep the solution in fluid phase and prevent evaporation.

15 Example 12

The features are in this example the same as in the previous example, except the concentration of NaOH and/or KOH could also be taken as high as 1M.

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Example 13

In addition to or instead of NaOH or KOH other nucleophilic substances can be used, such as H₂O, OH, CH₃-
25 CH₂-O-, I- and CN-.

Example 14

The features in this example are the same as in any one
30 of the preceding examples. Additionally, in a step surfactants in a solution are provided and the product is washed or submerged in this solution. Such a surfactant may comprise or be SDS (sodium dodecyl sulfate).

Example 15

5 In addition to the steps in any one of the preceding examples, a protease treatment is employed, where a solution comprising enzymes is provided for the products to be washed or submerged in.

Example 16

10 In addition to the steps in any one of the preceding examples, the products are subjected to an oxidative treatment, wherein for instance a chlorine solution is provided for the products to be washed or at least submerged
15 in the solution.

Example 17

20 As a consequence of the extra-ordinary results of the method according to the present invention, it has again become possible to use a talcum or similar type powdering for the products. In the past, powdering the products, such as surgical gloves, with a talcum powdering has become less and less usual, since the powders used were found to provide
25 a basis for allergens to attach to. To date powdered gloves are still being produced and sold, but less and less so, precisely because of the attachment of allergens to the powders used. Now that no or at least far less allergens remain on the products after subjecting the products to the
30 method according to the present invention, powdering may yet again become desirable in view of the improved ease of handling. For instance, a powdered glove is far easier arranged on a user's hand than a product without powdering.

As a consequence it is believed that powdering can provide a further improved result of the method in as far as the resulting product is concerned.

5 After the preceding disclosure of the present invention, many additional and alternative embodiments will have become apparent to the skilled person, which are all considered to lie within the grasp of the skilled person on the basis of his common general knowledge and within the
10 scope of protection for the present invention as defined in the appended claims, unless such further embodiments depart substantially in spirit or definition from these appended claims. For instance the skilled person could and would contemplate other temperatures, specifically higher
15 temperatures than those specifically mentioned above. Also the step of powdering is not essential. However, a powdered product with hardly any or practically undetectable amounts of leachable allergens will provide a strong indication of an embodiment of the invention as a consequence of the
20 otherwise (without a method according to the invention) generally very high allergen content of such products and the present day common practice - prior to the present invention - of refraining, by many producers and users from powdering the products and using such powdered products.
25 Also, many examples have been provided, and it is emphasized here that all combinations of distinctly presented embodiments are also within the scope of the invention.

Conclusies

1. Een werkwijze voor het verminderen van de allergene eigenschappen van natuurlijke rubber latex
5 omvattende producten, welke worden veroorzaakt door allergenen, door de extraheerbare niveaus aan proteïne te verminderen, welke in deze producten worden aangetroffen, waarbij de werkwijze de stappen omvat van: het onderwerpen van de producten aan een spoeling in een sterk alkalijne
10 oplossing om de allergenen te verminderen.
2. De werkwijze volgens conclusie 1, waarbij de sterke alkalijne oplossing een pH-waarde van 10 of meer heeft.
15
3. De werkwijze volgens conclusie 2, waarbij de sterk alkalijne oplossing een pH-waade heeft van 14 .
4. De werkwijze volgens conclusie 1, 2 of 3,
20 waarbij de sterk alkalijne oplossing en oplossing van NaOH of KOH is in een concentratie van bij voorkeur 0,01M of hoger, met meer voorkeur een concentratie van 1M.
5. De werkwijze volgens een van de voorgaande
25 conclusies, waarbij het gehalte aan extraheerbare proteïne van het product bij kamertemperatuur (18°C) is verlaagd tot lagere concentraties dan 10 mg/g.
6. De werkwijze volgens een willekeurige van de
30 voorgaande conclusies, waarbij de stap van het onderwerpen van het product aan de sterk alkalijne oplossing omvat: Het verhogen van de temperatuur van de sterk alkalijne oplossing tot boven de kamertemperatuur om een benodigde contacttijd te reduceren van het product met de alkalijne oplossing en

om lagere allergeenconcentraties te verkrijgen, dan die welke mogelijk zijn bij kamertemperatuur.

5 7. De werkwijze volgens conclusie 6, waarbij de temperatuur van de sterk alkalijne oplossing tot 90°C wordt verhoogd, bij voorkeur tot 100°C wordt verhoogd, en met meer voorkeur tot 110°C wordt verhoogd, en met de meeste voorkeur tot bij benadering tot 118°C wordt verhoogd.

10 8. De werkwijze volgens conclusie 7, verder omvattende het onder druk brengen van de sterk alkalijne oplossing om de sterk alkalijne oplossing in een vloeibare fase te houden en verdamping daarvan te voorkomen.

15 9. De werkwijze volgens een willekeurige van de voorgaande conclusies, waarbij de sterk alkalijne oplossing ten minste 1 nucleofiel omvat uit de groep, die tenminste omvat: H₂O, OH, CH₃-CH₂-O, I⁻ en CN⁻.

20 10. De werkwijze volgens een willekeurige van de voorgaande conclusies, waarbij de stap van het onderwerpen van de producten aan een spoeling in een sterk alkalijne oplossing wordt gehandhaafd gedurende tenminste 5
25 minuten, met meer voorkeur ten minste een uur.

 11. De werkwijze volgens een willekeurige van de voorgaande conclusies, waarbij aan de alkalijne oplossing een toevoeging is toegevoegd van surfactanten om de
30 bevochtigbaarheid te bevorderen en de nucleofiele substitutiereactie te verbeteren.

 12. De werkwijze volgens een willekeurige van de

voorgaande conclusies, welke een stap vormt in een proces bij het vervaardigen van het product, waarbij de vervaardiging van het product ten minste een stap omvat uit de groep, die omvat: het vormgeven van het product uit een
5 natuurlijk rubber omvattende suspensie, het dippen van een mal in een natuurlijke rubber latex omvattende suspensie, het vulkaniseren van het natuurlijke rubber latex omvattende product.

10 13. De werkwijze volgens een van de voorgaande conclusies, verder omvattende als aanvullende stap een protease behandeling voor het verminderen van de allergene eigenschappen van het product.

15 14. De werkwijze volgens een willekeurige van de voorgaande conclusies, verder omvattende als aanvullende stap een oxidatieve behandeling om de allergene eigenschappen van het product te verminderen.

20 15. De werkwijze volgens een willekeurige van de voorgaande conclusies, verder omvattende het bepoederen van het product, bijvoorbeeld met talkpoeder.

25 16. Systeem voor het ten uitvoer brengen van de werkwijze volgens een willekeurige van de voorgaande conclusies voor het verminderen van de allergene eigenschappen van natuurlijk rubber latex omvattende
30 producten, welke worden veroorzaakt door allergenen, door extraheerbare proteïne niveaus te verlagen, welke worden aangetroffen op de producten, welk systeem omvat: een vat, omvattende een sterk alkalijne oplossing voor het verminderen van de allergenen.

17. Een product, zoals een handschoen of een
condoom, welke is vervaardigd uit natuurlijk rubber latex en
is onderworpen aan een werkwijze, zoals die gedefinieerd is
5 in een willekeurige van de voorgaande conclusies 1-14.

18. Het product volgens conclusie 17, verder
omvattende een bepoedering, bijvoorbeeld met talkpoeder.

SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE	KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE
	W/2GE09/ML/23
Nederlands aanvraag nr.	Indieningsdatum
1035901	05-09-2008
	Ingeroepen voorrangsdatum
Aanvrager (Naam)	
Budev B.V.	
Datum van het verzoek voor een onderzoek van internationaal type	Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr.
03-02-2009	SN 51559
I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)	
Volgens de internationale classificatie (IPC)	
C08C1/04	C08L7/00
B29C71/00	C08J5/02
II. ONDERZOCHE GEBIEDEN VAN DE TECHNIEK	
Onderzochte minimumdocumentatie	
Classificatiesysteem	Classificatiesymbolen
IPC	B29C
	C08C
	C08J
	C08F
Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen	
III. ☐	GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES (opmerkingen op aanvullingsblad)
IV. ☐	GEBREK AAN EENHEID VAN UITVINDING (opmerkingen op aanvullingsblad)

**ONDERZOEKSRAPPORT BETREFFENDE HET
RESULTAAT VAN HET ONDERZOEK NAAR DE STAND
VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE**

Nummer van het verzoek om een onderzoek naar
de stand van de techniek

NL 1035901

A. CLASSIFICATIE VAN HET ONDERWERP

INV. C08C1/04 C08L7/00 B29C71/00 C08J5/02

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimum documentatie (classificatie gevolgd door classificatiesymbolen)

B29C C08C C08J C08F

Onderzochte andere documentatie dan de minimum documentatie, voor dergelijke documenten, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en, waar uitvoerbaar, gebruikte trefwoorden)

EPO-Internal, WPI Data, COMPENDEX

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	US 5 910 567 A (TANAKA YASUYUKI [JP] ET AL) 8 juni 1999 (1999-06-08)	1-7, 9-14,16, 17 8
Y	kolom 2, regels 61-67 kolom 3, regels 8-41 kolom 6, regel 52 - kolom 7, regel 43 kolom 9, regels 20-24 voorbeelden 2-5; tabel 1 ----- -/--	

☒ Verdere documenten worden vermeld in het vervolg van vak C.

☒ Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

A niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft

D in de octrooiaanvraag vermeld

E eerdere octrooi(aanvraag), gepubliceerd op of na de indieningsdatum, waarin dezelfde uitvinding wordt beschreven

L om andere redenen vermelde literatuur

O niet-schriftelijke stand van de techniek

P tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur *G* lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

T na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvraag, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding

X de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur

Y de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid

5 Juni 2009

Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type

Naam en adres van de instantie

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De bevoegde ambtenaar

Denis, Cécile

**ONDERZOEKSRAPPORT BETREFFENDE HET
RESULTAAT VAN HET ONDERZOEK NAAR DE STAND
VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE**

Nummer van het verzoek om een onderzoek naar
de stand van de techniek

NL 1035901

C.(Vervolg). VAN BELANG GEACHTE DOCUMENTEN

Categorie *	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	GB 2 366 509 A (DEPROTIN INC [SG]) 13 maart 2002 (2002-03-13)	1-5,9, 10,12, 15-18
Y	bladzijde 2, regels 18-34 bladzijde 3, regel 27 - bladzijde 4, regel 2 bladzijde 4, regel 29 - bladzijde 5, regel 10 bladzijde 6, regels 9-11 -----	8
X	US 6 107 455 A (ROSHOLM PETER [MY] ET AL) 22 augustus 2000 (2000-08-22)	1,2,5, 9-13,16, 17
Y	kolom 1, regels 42-60 kolom 3, regels 37-55 voorbeeld 2 voorbeeld comp.ex.1 -----	8

**ONDERZOEKSRAPPORT BETREFFENDE HET
RESULTAAT VAN HET ONDERZOEK NAAR DE STAND
VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE**

Informatie over leden van dezelfde octrooifamilie

Nummer van het verzoek om een onderzoek naar
de stand van de techniek

NL 1035901

In het rapport genoemd octrooigeschrift	Datum van publicatie	Overeenkomend(e) geschrift(en)	Datum van publicatie
US 5910567	A	08-06-1999	AT 280193 T 15-11-2004
			AU 697663 B2 15-10-1998
			AU 4954096 A 02-10-1996
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OCTROOICENTRUM NEDERLAND

WRITTEN OPINION

File No. SN51559	Filing date (day/month/year) 05.09.2008	Priority date (day/month/year)	Application No. NL1035901
International Patent Classification (IPC) INV. C08C1/04 C08L7/00 B29C71/00 C08J5/02			
Applicant Budev B.V. te St. Michielsgestel			

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the application
- ☐ Box No. VIII Certain observations on the application

Examiner Denis, Cécile

WRITTEN OPINION

Application number

NL1035901

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the application as filed.
 - ☐ filed together with the application in electronic form.
 - ☐ furnished subsequently for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes: Claims	8
	No: Claims	1-7,9-18
Inventive step	Yes: Claims	
	No: Claims	1-18
Industrial applicability	Yes: Claims	1-18
	No: Claims	

2. Citations and explanations

see separate sheet

Reference is made to the following documents:

D1: US-A-5 910 567 (TANAKA YASUYUKI [JP] ET AL) 8 juni 1999 (1999-06-08)

D2: GB-A-2 366 509 (DEPROTIN INC [SG]) 13 maart 2002 (2002-03-13)

D3: US-A-6 107 455 (ROSHOLM PETER [MY] ET AL) 22 augustus 2000 (2000-08-22)

1. The present application does not meet the criteria of patentability, because the subject-matter of claims 1 to 7 and 9 to 18 is not new.

Document D1 discloses a method for producing a formed product of deproteinized natural rubber latex capable of reducing a content of an allergen in a natural rubber latex material (column 3, lines 8-41). The method comprises a step of cleaning removal carried out after vulcanisation and forming with an aqueous alkali solution (NaOH or ammonia) at a temperature of 20 °C to 100 °C for several minutes to 24 hours (column 6, line 52 to column 7, line 43). This cleaning can be combined with a cleaning using an aqueous solution with free chlorine (column 7, line 45 to column 8, line 15). The cleaning treatment can be carried out at 40 °C for 24 hours (example 2, table 1). The cleaning time can be reduced to 0,5 hour and the level of remaining allergen reduced when the temperature of the cleaning treatment is increased to 100 °C (example 4, table 1). D1 differs from claims 8, 15 and 18 in that the cleaning does not involve different pressure conditions and the natural rubber products after the cleaning treatment are not powdered.

The subject-matter of claims 1 to 7, 9 to 14, 16 and 17 of the present application is therefore not novel in view of D1.

Document D2 describes a method for removing proteins from dipped latex rubber goods comprising (1) removing any corn starch powder which has previously been applied to the goods by treating the goods with hot water to dissolve the powder, (2) treating the goods with an aqueous solution comprising an alkali metal hydroxide to remove the proteins; and (3) treating the goods with one or more surface active agents in aqueous solution to remove the remaining proteins (page 2, lines 18-34 and page 3, line 33 to page 4, line 2). The treatment with an aqueous solution of KOH is carried out at room temperature for 10 to 30 minutes. After the cleaning treatment, the natural rubber products may further be

powdered. D2 differs from claims 6 to 8, 11, 13 and 14 in that the washing treatment is not carried out at high temperatures, under pressure or in presence of surfactants. D2 does not disclose either the combination with an oxidative treatment.

The subject-matter of claims 1 to 5, 9, 10, 12 and 15 to 18 of the present application is therefore not novel in view of D2.

Document D3 relates to a method for lowering the extractable protein content of an article made of natural rubber latex comprising the step of washing the article with a solution comprising a soluble silicate at a pH of 10,5 to 12 (column 1, lines 42-60) is carried out at a temperature of 30 °C to 60 °C for 5 to 30 minutes (column 3, lines 36-56). The solution may also contain a protease and/or surfactants to further degrade the allergen protein (column 2, lines 43-64). D3 differs from claims 3, 4, 6 to 8, 14, 15 and 18 in that the washing treatment is not carried out at high temperature, under pressure or in presence of surfactants. Moreover, the pH of the aqueous solution remains below 14. D2 does not disclose either the combination with an oxidative treatment or the powdering of the treated articles.

The subject-matter of claims 1, 2, 5, 9 to 13, 16 and 17 of the present application is therefore not novel in view of D2.

2. The present application does not meet the criteria of patentability, because the subject-matter of claim 8 does not involve an inventive step.

Document D2 is considered to represent the closest prior art.

Claim 8 of the present application differs from D2 in that the cleaning treatment for removing allergen proteins is not carried out under pressure.

There is no evidence in the present application of a special technical effect directly linked to that distinguishing feature.

The objective problem to be solved by the present application may therefore be considered as to provide an alternative process for reducing the level of allergen proteins present in natural rubber formed articles.

Increasing the pressure during the treatment is a feature that is merely one of several straightforward possibilities (eg. increase of the temperature) from which the skilled person would select without the exercise of inventive skill, in order to solve the problem posed.

The subject-matter of claim 8 is therefore not inventive.