1	Transmittal of New Application	Transmittal.pdf	132502 cb1af5e20cc2b96e733fa40d6e5d76b7a64063dc	no	2
Warnings:					
Information:					
2	Preliminary Amendment	Preliminary_Amendment.pdf	85776 4d4aa4040d35de6da5917e9360f65fe403cb7928	no	5
Warnings:					
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3	Documents submitted with 371 Applications	Specification.pdf	414632 e78ddc5c32c3a087fcec081888e0cfb9e4ee3388	no	11
Warnings:					
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4	Transmittal Letter	IDS.pdf	81989 9ce5d386341501f6cddcb558245695debbdd6b29	no	2
Warnings:					
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5	Foreign Reference	Ref1.pdf	354204 05bc1592cf271434b2096597afed05b93079aa4a	no	10
Warnings:					
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6	Foreign Reference	Ref2.pdf	402052 edbad226ba9f754ce9b6d5b1cfc47043b00169ad	no	9
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7	Foreign Reference	Ref3.pdf	1438814 ff04cefb0b5041be3c3a192d7973140e617406ae	no	37
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8	Foreign Reference	Ref4.pdf	887061 473f6e5e1537e6c758ed07d4aa068568c64c7c2e	no	22
Warnings:					
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Warnings:					
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11	Documents submitted with 371 Applications	Search_Report.pdf	147985 c736ba587273fe2f7f198e61ed57d93728e269c6	no	5
Warnings:					
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12	Fee Worksheet (PTO-875)	fee-info.pdf	36370 f244ecd7b13e28d97f2e2c584c33bc1fb3e1e415	no	2
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(71) Applicant *(for all designated States except US)*: **DSM IP ASSETS B.V.** [NL/NL]; Het Overloon 1, NL-6411 TE Heerlen (NL).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **SIMMELINK, Joseph, Arnold, Paul, Maria** [NL/NL]; Kerkstraat 5, NL-6267 EA Cadier en Keer (NL). **VAZ, Claudia, Maria** [PT/NL]; Bellefroidlunet 41E, NL-6221 KS Maastricht (NL).

(74) Agent: **HANSEN, J., R.**; DSM Intellectual Property, P.O. Box 9, NL-6160 MA Geleen (NL).

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(54) Title: COLORED SUTURE

(57) Abstract: Suture containing filaments of ultra-high molecular weight polyethylene (UHMwPE), characterized in that the suture contains a multi-filament yarn that is obtained by a process comprising the steps of: a) Providing a mixture containing UHMwPE, a spinning solvent and a pigment b) Spinning a multi-filament yarn from the mixture by the gel spinning process.

COLORED SUTURE

The invention relates to a colored suture. The coloring of sutures is for example used to make the suture better contrast with the blood or tissue in the operating area. In complicated surgical operations, for example in arthroscopic surgery, when different suture ends are used in a small area, sutures of different color are used to assist surgeons in differing between the suture ends. It is also possible for this reason to combine filaments of different colors in a suture in a certain pattern, to aid surgeons in identifying the travel direction of the suture during surgery, particularly during arthroscopic operations.

Next to coloring is also suture strength an important consideration in selecting filaments for producing a suture. Very strong filaments, at present available for the production of sutures, are filaments of ultra-high molecular weight polyethylene (UHMwPE), produced according to the gel spinning process.

A problem of such filaments is that they are difficult to color. Due to the a-polar character of the UHMwPE a colorant like a dye or a colored coating material adheres poorly to the surface of the filament. If adhesion is insufficient the filaments may loose part or all of the colorant because of the handling during production of the sutures, or may loose part of the colorant in place in the human or animal body, which is undesired because of negative effects on the health. Attempts have been made to enhance the adhesion of colorants to the filaments by giving the filaments a pre-treatment, for example a plasma treatment. Such pre-treatments in general however have an adverse effect on the mechanical properties of the filaments, like for instance the tensile strength and often don't improve adhesion enough to make the filaments suitable to be used in sutures.

In another attempt filaments of UHMwPE were dyed using super critical carbon dioxide as a solvent for the dye, as disclosed in EP-A-0 873 445. In this case the dye penetrated in the body of the filament, so that adhesion problems did no longer play a role. However such a dye shows a tendency to leach out, which is unfavorable for application of the filaments in sutures. Also in US-5,613,987 it was proposed to use a dye to color the UHMwPE filaments. Here the same problems occur.

Polyolefinic filaments, of which polypropylene filaments are the best example, are often colored by the incorporation of a pigment in the polymer composition of the filaments during extrusion of the filaments. In Prog. Polym. Sci. 27 (2002) 853-913 the process for pigmentation of polypropylene filaments is described.

CONFIRMATION COPY

The pigments are in a first step uniformly dispersed in a so-called carrier polymer to obtain a concentrated pre-mixture. In order to obtain a sufficient dispersion of the pigment the wetting of the pigment particles must be enhanced by the use of a low viscous carrier polymer and dispersants. A low viscous carrier polymer has a negative influence on mechanical properties of the UHMwPE filaments. Furthermore such filaments have a very low diameter compared to the diameter of polypropylene filaments, so that un-dispersed or re-agglomerated clumps of pigment particles will have a detrimental effect on the tensile strength of the filaments. Therefore it is disadvised in US 5,613,987 to use pigments in UHMwPE filaments. Also the use of dispersants in filaments that are used in sutures is disadvantages, because such filaments must be biocompatible and dispersants have a negative effect on that.

One solution proposed to overcome the problems of the coloring of filaments of UHMwPE is to combine the filaments in a suture with filaments of a different polymer, preferably nylon, as disclosed in US-7,029,490. Such sutures however have a complicated structure and the nylon filaments only contribute to the strength of the suture at a lower level compared to the filaments of UHMwPE.

Object of the invention is to provide a colored suture, which suture does not show the problems described above.

Surprisingly such a suture is obtained if the suture contains a multi-filament yarn that is obtained by a process comprising the steps of:

a) Providing a mixture containing UHMwPE , a spinning solvent and a pigment
b) Spinning a multi-filament yarn from the mixture by the gel spinning process.

The preparation of filaments of ultra high molecular weight polyethylene (UHMWPE) filaments, prepared by a gel spinning process, is for example described in EP 0205960 A, EP 0213208 A1, US 4413110, GB 2042414 A, EP 0200547 B1, EP 0472114 B1, WO 01/73173 A1, and Advanced Fiber Spinning Technology, Ed. T. Nakajima, Woodhead Publ. Ltd (1994), ISBN 1-855-73182-7, and references cited therein. Gel spinning is understood to include at least the steps of spinning filaments from a solution of ultra-high molecular weight polyethylene in a spin solvent; cooling the filament obtained to form a gel filament; removing at least partly the spin solvent from the gel filament; and drawing the filament in at least one drawing step before, during or after removing spin solvent. Suitable spin solvents include for example paraffin's, mineral oil, kerosene or decalin. Spin solvent can be removed by evaporation, by extraction, or by a combination of evaporation and extraction routes. Such filaments are commercially available as Spectra® or Dyneema® grades.

Good results are obtained if the UHMWPE has an intrinsic viscosity (IV, as determined according to method PTC-179 (Hercules Inc. Rev. Apr. 29, 1982) at 135°C in decalin, with dissolution time of 16 hours, with anti-oxidant DBPC in an amount of 2 g/l solution, and the viscosity at different concentrations extrapolated to zero concentration) of above 5 dl/g. Particularly suitable is UHMWPE with IV of between about 8 and 40 dl/g, more preferably between 10 and 30, even more preferably between 12 and 28, most preferably between 15 and 25 dl/g. These ranges represent an optimum in polymer processability and filament properties. Intrinsic viscosity is a measure for molar mass (also called molecular weight) that can more easily be determined than actual molar mass parameters like M_n and M_w. There are several empirical relations between IV and M_w, but such relation is highly dependent on molar mass distribution. Based on the equation $M_w = 5.37 \times 10^4 [IV]^{1.37}$ (see EP 0504954 A1) an IV of 8 dl/g would be equivalent to Mw of about 930 kg/mol.

Preferably, the UHMWPE is a linear polyethylene with less than one branch per 100 carbon atoms, and preferably less than one side chain per 300 carbon atoms, a branch usually containing at least 10 carbon atoms. The linear polyethylene may further contain up to 5 mol% of one or more comonomers, such as alkenes like propylene, butene, pentene, 4-methylpentene or octene.

In a preferred embodiment, the UHMWPE contains a small amount of relatively small groups as side chains, preferably a C1-C4 alkyl group. It is found that a filament from UHMWPE with a certain amount of such groups show reduced creep behaviour. Too large a side chain, or too high an amount of side chains, however, negatively affects the processing and especially the drawing behaviour of the filaments. For this reason, the UHMWPE preferably contains methyl or ethyl side chains, more preferably methyl side chains. The UHMWPE therefore contains preferably at least 0.2, more preferably at least, still more preferably at least 0.3, still more preferably at least 0.4, most preferably at least 0.5 methyl or ethyl side chains. The amount of side chains is preferably at most 20, more preferably at most 10 per 1000 carbon atoms.

The UHMwPE can be a single polymer grade, but also a mixture of two or more different grades, e.g. differing in IV or molar mass distribution, and/or number of side chains. Preferably the polymeric part of the filaments is a single grade UHMwPE.

The number of filaments in the multi-filament yarn may be between 10 and 1000. Preferably the number of filaments in the multi-filament yarn is more than 20, more preferably more than 30.

The mixture containing the UHMwPE, the spinning solvent and the pigment may be provided at different stages in the gel spinning process. It is for example possible to produce in a first step a dry mixture of UHMwPE powder and the pigment, to produce in a second step a slurry of that mixture in a spinning solvent, to dissolve the UHMwPE in the spinning solvent in a third step to obtain a slurry of the pigment in a solution of UHMwPE in the spinning solvent and to spin the multi-filament yarn from that solution. It is also possible to produce a solution of UHMwPE in the spinning solvent first and to add the pigment to that solution.

The UHMwPE filaments preferably contain less than 800 ppm of residual amounts of spin solvent, more preferably less than 500, even more preferably less than 250, most preferably less than 100 ppm, such as less than 80 ppm, or less than 60 ppm. Filaments and suture with low residual amount of spin solvent is highly advantageous in being more suitable for implantation.

Suitable pigments include organic and inorganic pigments. Examples of organic pigments include azo-pigments and phtalo-pigments. Good results are obtained with C.I. Vat brown I and C.I. Solvent Yellow 18. Examples of inorganic pigments include pigments containing titanium dioxide, iron oxides and chromium oxides. Good results are obtained with aluminium-chromium-cobalt oxide, since a suture with good mechanical properties and a low degree of leaching out is obtained.

The amount of pigment used may be between 0.1 – 7 wt.% of the final filament, as used for the production of the suture. Preferably the final filament contains at least 0.3 wt.%, more preferably at least 0.5 wt.% even more preferably at least 0.7 wt.% of pigment. Preferably the final filament contains at most 5.0 wt.%, more preferably at most 3 wt.% of pigment, even more preferably at least 2.5 wt.%, most preferably at most 2 wt.%. This is in view of obtaining a bright colour and good mechanical properties.

The UHMwPE filaments in the suture according to the invention consist preferably of UHMwPE, the pigment and less than 1000 ppm of further constituents, preferably less than 500 ppm of further constituents, more preferably less than 200 ppm of further constituents, most preferably less than 100 ppm of further constituents, such as less than 80 ppm, or less than 60 ppm.

A suitable size for the suture according to the invention may be in the full USP range for sutures (e.g. 12-0 to 10). A USP value of 10 corresponds with a maximum diameter of 1.3 mm. In one preferred embodiment the suture member has a titer of between 25 and 500 dtex. In that case the suture is very suitable for

cardiovascular operations. In another preferred embodiment the suture has a titer of between 500 and 3000 dtex. In that case the suture is very suitable for use in orthopaedic applications. In yet another preferred embodiment the suture has a titer of between 3000 and 9000 dtex. In that case the suture is very suitable to be used in heavy orthopaedic applications.

The suture may in addition to the ultra high molecular polyolefin filaments comprise further components, for example compounds that provide some functional effect, like anti-microbial or anti-inflammatory action, or that further improve knotting performance. The amount of such other components is generally limited to at most 20 mass% (relative to total cable mass), preferably at most 10, more preferably at most 5 mass%.

The suture according to the invention comprises preferably at least 50 mass% of the ultra high molecular weight polyolefin filaments. The ultra high molecular weight polyolefin filaments contribute most to the strength properties of the member. Furthermore the filaments enhance the sliding properties of the suture through tissue. Therefore more preferably the suture comprises at least 60 mass% of the ultra high molecular weight polyolefin filaments, more preferably at least 70, 80 or at least 90 mass%. The suture may further comprise other fibres, e.g. other biocompatible materials like polymers, to provide some other additional properties to the suture, including improved knot slip behaviour or visual contrast. Such other fibres may be present in the form of one or more strands in the suture. However, preferably each strand has the same composition, so that each strand comprises the same amount of the polyolefin filaments and of the other filaments. This ensures that the suture has a homogeneous structure.

Suitable examples of other fibrous materials include filaments or staple fibres made from non-absorbable polymers like other polyolefin's, fluoro-polymers, or semi-aromatic polyesters like polyethylene terephthalate, absorbable polymers like aliphatic polyesters based on e.g. lactides.

Most preferably the suture consists of the polyolefin filaments.

The invention also relates to the use of the suture according to the invention in surgical method.

The invention is further explained in the examples, without being limited to the examples.

Methods

Intrinsic viscosity.

The Intrinsic Viscosity (IV) is determined according to method PTC-179 (Hercules Inc. Rev. Apr. 29, 1982) at 135°C in decalin, the dissolution time being 16 hours, with DBPC as anti-oxidant in an amount of 2 g/l solution, by extrapolating the viscosity as measured at different concentrations to zero concentration;

Tensile properties.

Tensile properties: tenacity, tensile modulus (or modulus) and elongation at break (or eab) are defined and determined on multifilament yarns with a procedure in accordance with ASTM D885M, using a nominal gauge length of the fibre of 500 mm, a crosshead speed of 50%/min and Instron 2714 clamps, of type Fibre Grip D5618C. On the basis of the measured stress-strain curve the modulus is determined as the gradient between 0.3 and 1% strain. For calculation of the modulus and strength, the tensile forces measured are divided by the titre, as determined by weighing 10 metres of fibre; values in GPa are calculated assuming a density of 0.97 g/cm^3;

Leaching tests

According to the requirements of ISO 10993-12:2002(E) an extraction was performed with samples of multi-filament yarn in both polar (distilled water) and non-polar (cottonseed oil) solvents. The extraction conditions were 37 °C for 24 and 72 hours.

After dilution with acetonitrile, the different phases were analyzed on the presence of pigment using Liquid Chromatography-Mass Spectrometry (LC-MS) and Gas Chromatography-Mass Spectrometry (GC-MS). In case no leaching I was observed means that leaching was lower than 10 ppb.

Cytotoxicity.

Cytotoxicity tests were performed according to ISO 10993-5, 1999: Biological Evaluation of Medical Devices – Part 5: Tests for in vitro cytotoxicity. The biological reactivity of a mammalian monolayer, L929 mouse fibroblast cell culture, in response to the test item extracts (samples containing up to 2.0 wt.% pigment) was determined. Extracts were prepared at 37°C (± 1) for 24 hours in a humidified atmosphere containing 5±1% CO_2. Positive (natural rubber) and negative (silicone)

control articles were prepared to verify the proper functioning of the test system. The maintenance medium of the cell cultures was replaced by the extracts of the tests item or control article in triplicate and the cultures incubated for 48 hours, at 37°C (± 1). Biological reactivity was rated on the following scale:

- grade 0 (no reactivity)
- grade 1 (slight reactivity)
- grade 2 (mild reactivity)
- grade 3 (moderate reactivity)
- grade 4 (severe reactivity)

Examples 1 – 4.

Slurries containing decalin, 6 mass % of powder of UHMwPE having an IV of 14 and 0.5, 1, 1.5 respectively 2 wt. % of aluminum-chromium-cobalt oxide pigment (of the cations is 32.5 % Co, 32% Al and 35.5 Cr) were prepared in a mixer.

The slurries were fed to a twin screw extruder having a diameter of 25 mm, being equipped with a gear-pump at a temperature setting of 180°C. In the extruder the UHMwPE was dissolved in the decalin and the so obtained mixture of the UHMwPE dissolved in the decalin and the pigment was extruded through a spin plate having 24 spin holes into a nitrogen atmosphere with a rate of 1.0 g/min per hole. The so obtained solution filaments were cooled in a water bath kept at about 35°C and with a water flow rate of about 5 cm/s perpendicular to the filaments entering the bath, and taken-up at such rate that a draw ratio of 15 was applied to the as-spun filaments in the air-gap of 15 mm. The filaments subsequently entered an oven at 130°C. The filaments were further stretched, during which process the decalin evaporated from the filaments. After the stretching process the filaments were kept taut in an oxygen free environment for 24 hours at 100 °C.

Mechanical properties, leaching out and cytotoxicity were determined on the so obtained multi-filament yarns.

The mechanical properties are reported in table 1. Favourable mechanical properties were obtained.

No compounds related to pigment, or other unknown compounds, where found. The pigment < 10 µg/kg (< 10 ppb).

From these results it can be concluded that the bio-availability of pigment due to leaching from sutures according to the invention containing the multi-filament yarn is negligible.

All the extracts of the colored samples when submitted to the cytotoxicity test exhibited no reactivity (grade 0) by the cell cultures. Severe reactivity (grade 4) was observed for the positive control article. The negative control article showed no signs of reactivity (grade 0). Therefore it can be concluded that sutures according to the invention containing the multi-filament yarn are non-cytotoxic.

The yarns furthermore show a homogeneous and bright colour.

Comparative test A.

Multi-filament yarn was produced according to examples 1-4, however no pigment was used.

The multi-filament yarn was dyed with D&C blue No 6 (delivered by Sigma Aldrich of the USA) by placing the multi-filament yarn for 7 hours at 120°C in a solution of the dye in super-critical carbon dioxide.

The resulting yarns presented a non-homogeneous color distribution pattern.

Mechanical properties and leaching out were determined.

Mechanical properties are reported in table 1. A serious decline in mechanical properties was observed (tenacity decreased about 40%).

Considerable leaching out took place in coconut oil as was already clear from the disappearing color of the multi-filament yarn.

From these results it is clear that sutures containing the multi-filament yarn according to comparative test A are not suitable for use in surgery.

Comparative test B.

Multi-filament yarn was produced according to examples 1-4, however no pigment was used.

The multi-filament yarn was dip-coated with a polyurethane coating containing an azo-dye (Sudan Red D, delivered by Sigma Aldrich).

Test data of the multi-filament yarn were measured and reported in table I. It is clear that considerable leaching out took place and that the cyto-toxicity of the filaments is insufficient. Therefore sutures containing the multi-filament yarn according to comparative test B are not suitable for use in surgery.

Table. 1.

Example/ Xomp. exp.	Tenacity [cN/dTex]	Modulus [cN/dTex]	Eab [%]	leaching [-]	cytotox. [-]	colouring [-]
I	37	1439	2.8	No	0	homogeneous
II	37	1377	2.9	No	0	Homogeneous
III	40	1501	3.0	No	0	Homogeneous
IV	37	1414	2.9	No	0	Homogeneous
A	21	-	-	Yes	-	Inhomogeneous
B	37	1381	2.8	Yes	-	Inhomogeneous

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CLAIMS

1. Suture containing filaments of ultra-high molecular weight polyethylene (UHMwPE), characterized in that the suture contains a multi-filament yarn that is obtained by a process comprising the steps of:
   a) Providing a mixture containing UHMwPE , a spinning solvent and a pigment
   b) Spinning a multi-filament yarn from the mixture by the gel spinning process.
2. Suture according to claim 1, characterized in that the UHMwPE has an intrinsic viscosity (IV) of at least 5 dl/g.
3. Suture according to claim 1 or claim 2, characterized in that the amount of pigment used is between 0.1 and 7.0 wt. % in the final filament as used for the production of the suture.
4. Suture according to claim 3, characterized in that the amount of pigment used is lower than 5.0 wt. %.
5. Suture according to claim 4, characterized in that the amount of pigment used is lower than 2.0 wt. %.
6. Suture according to any one of claims 1 – 6, characterized in that the pigment used is an inorganic pigment.
7. Suture according to claim 6, characterized that the pigment contains chromium oxide.
8. Suture according to claim 7, characterized in that the pigment contains aluminum-chromium-cobalt oxide.
9. Suture according to any one of the claims 1 to 8, characterized in the filaments contain less than 800 ppm of residual amounts of spin solvent, preferably less than 500 ppm of residual amounts of spin solvent, more preferably less than 250 ppm of residual amounts of spin solvent, most preferably less than 100 ppm of residual amounts of spin solvent, such as less than 80 ppm of residual amounts of spin solvent, or less than 60 ppm of residual amounts of spin solvent.
10. Use of the suture according to any one of claims 1-9 in a surgical method.

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Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécificée à la page suivante.

Patentanmeldung Nr. | **Patent application No.** | **Demande de brevet n°**

07010217.3 / EP07010217

The organization code and number of your priority application, to be used for filing abroad under the Paris Convention, is EP07010217

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le President de l'Office européen des brevets
p.o.

R.C. van Dijk

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DSM IP Assets B.V.
Het Overloon 1
6411 TE Heerlen/NL

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(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
Si aucun titre n'est indiqué se referer à la description.)

Colored suture

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The invention relates to a colored suture. The coloring of sutures is for example used to make the suture better contrast with the blood or tissue in the operating area. In complicated surgical operations, for example in arthroscopic surgery, when different suture ends are used in a small area, sutures of different color are used to assist surgeons in differing between the suture ends. It is also possible for this reason to combine filaments of different colors in a suture in a certain pattern, to aid surgeons in identifying the travel direction of the suture during surgery, particularly during arthroscopic operations.

Next to coloring is also suture strength an important consideration in selecting filaments for producing a suture. Very strong filaments, at present available for the production of sutures, are filaments of ultra-high molecular weight polyethylene (UHMwPE), produced according to the gel spinning process.

A problem of such filaments is that they are difficult to color. Due to the a-polar character of the UHMwPE a colorant like a dye or a colored coating material adheres poorly to the surface of the filament. If adhesion is insufficient the filaments may loose part or all of the colorant because of the handling during production of the sutures, or may loose part of the colorant in place in the human or animal body, which is undesired because of negative effects on the health. Attempts have been made to enhance the adhesion of colorants to the filaments by giving the filaments a pre-treatment, for example a plasma treatment. Such pre-treatments in general however have an adverse effect on the mechanical properties of the filaments, like for instance the tensile strength and often don't improve adhesion enough to make the filaments suitable to be used in sutures.

In another attempt filaments of UHMwPE were dyed using super critical carbon dioxide as a solvent for the dye, as disclosed in EP-A-0 873 445. In this case the dye penetrated in the body of the filament, so that adhesion problems did no longer play a role. However such a dye shows a tendency to leach out, which is unfavorable for application of the filaments in sutures. Also in US-5,613,987 it was proposed to use a dye to color the UHMwPE filaments. Here the same problems occur.

Polyolefinic filaments, of which polypropylene filaments are the best example, are often colored by the incorporation of a pigment in the polymer composition of the filaments during extrusion of the filaments. In Prog. Polym. Sci. 27 (2002) 853-913 the process for pigmentation of polypropylene filaments is described.

The pigments are in a first step uniformly dispersed in a so-called carrier polymer to obtain a concentrated pre-mixture. In order to obtain a sufficient dispersion of the pigment the wetting of the pigment particles must be enhanced by the use of a low viscous carrier polymer and dispersants. A low viscous carrier polymer has a negative influence on mechanical properties of the UHMwPE filaments. Furthermore such filaments have a very low diameter compared to the diameter of polypropylene filaments, so that un-dispersed or re-agglomerated clumps of pigment particles will have a detrimental effect on the tensile strength of the filaments. Therefore it is disadvised in US 5,613,987 to use pigments in UHMwPE filaments. Also the use of dispersants in filaments that are used in sutures is disadvantages, because such filaments must be biocompatible and dispersants have a negative effect on that.

One solution proposed to overcome the problems of the coloring of filaments of UHMwPE is to combine the filaments in a suture with filaments of a different polymer, preferably nylon, as disclosed in US-7,029,490. Such sutures however have a complicated structure and the nylon filaments only contribute to the strength of the suture at a lower level compared to the filaments of UHMwPE.

Object of the invention is to provide a colored suture, which suture does not show the problems described above.

Surprisingly such a suture is obtained if the suture contains a multi-filament yarn that is obtained by a process comprising the steps of:

a) Providing a mixture containing UHMwPE , a spinning solvent and a pigment
b) Spinning a multi-filament yarn from the mixture by the gel spinning process.

The preparation of filaments of ultra high molecular weight polyethylene (UHMWPE) filaments, prepared by a gel spinning process, is for example described in EP 0205960 A, EP 0213208 A1, US 4413110, GB 2042414 A, EP 0200547 B1, EP 0472114 B1, WO 01/73173 A1, and Advanced Fiber Spinning Technology, Ed. T. Nakajima, Woodhead Publ. Ltd (1994), ISBN 1-855-73182-7, and references cited therein. Gel spinning is understood to include at least the steps of spinning filaments from a solution of ultra-high molecular weight polyethylene in a spin solvent; cooling the filament obtained to form a gel filament; removing at least partly the spin solvent from the gel filament; and drawing the filament in at least one drawing step before, during or after removing spin solvent. Suitable spin solvents include for example paraffin's, mineral oil, kerosene or decalin. Spin solvent can be removed by evaporation, by extraction, or by a combination of evaporation and extraction routes. Such filaments are commercially available as Spectra® or Dyneema® grades.

Good results are obtained if the UHMWPE has an intrinsic viscosity (IV, as determined according to method PTC-179 (Hercules Inc. Rev. Apr. 29, 1982) at 135°C in decalin, with dissolution time of 16 hours, with anti-oxidant DBPC in an amount of 2 g/l solution, and the viscosity at different concentrations extrapolated to zero concentration) of above 5 dl/g. Particularly suitable is UHMWPE with IV of between about 8 and 40 dl/g, more preferably between 10 and 30, even more preferably between 12 and 28, most preferably between 15 and 25 dl/g. These ranges represent an optimum in polymer processability and filament properties. Intrinsic viscosity is a measure for molar mass (also called molecular weight) that can more easily be determined than actual molar mass parameters like M_n and M_w. There are several empirical relations between IV and M_w, but such relation is highly dependent on molar mass distribution. Based on the equation $M_w = 5.37 \times 10^4 [IV]^{1.37}$ (see EP 0504954 A1) an IV of 8 dl/g would be equivalent to Mw of about 930 kg/mol.

Preferably, the UHMWPE is a linear polyethylene with less than one branch per 100 carbon atoms, and preferably less than one side chain per 300 carbon atoms, a branch usually containing at least 10 carbon atoms. The linear polyethylene may further contain up to 5 mol% of one or more comonomers, such as alkenes like propylene, butene, pentene, 4-methylpentene or octene.

In a preferred embodiment, the UHMWPE contains a small amount of relatively small groups as side chains, preferably a C1-C4 alkyl group. It is found that a filament from UHMWPE with a certain amount of such groups show reduced creep behaviour. Too large a side chain, or too high an amount of side chains, however, negatively affects the processing and especially the drawing behaviour of the filaments. For this reason, the UHMWPE preferably contains methyl or ethyl side chains, more preferably methyl side chains. The UHMWPE therefore contains preferably at least 0.2, more preferably at least, still more preferably at least 0.3, still more preferably at least 0.4, most preferably at least 0.5 methyl or ethyl side chains. The amount of side chains is preferably at most 20, more preferably at most 10 per 1000 carbon atoms.

The UHMwPE can be a single polymer grade, but also a mixture of two or more different grades, e.g. differing in IV or molar mass distribution, and/or number of side chains. Preferably the polymeric part of the filaments is a single grade UHMwPE.

The number of filaments in the multi-filament yarn may be between 10 and 1000. Preferably the number of filaments in the multi-filament yarn is more than 20, more preferably more than 30.

The mixture containing the UHMwPE, the spinning solvent and the pigment may be provided at different stages in the gel spinning process. It is for example possible to produce in a first step a dry mixture of UHMwPE powder and the pigment, to produce in a second step a slurry of that mixture in a spinning solvent, to dissolve the UHMwPE in the spinning solvent in a third step to obtain a slurry of the pigment in a solution of UHMwPE in the spinning solvent and to spin the multi-filament yarn from that solution. It is also possible to produce a solution of UHMwPE in the spinning solvent first and to add the pigment to that solution.

The UHMwPE filaments preferably contain less than 800 ppm of residual amounts of spin solvent, more preferably less than 500, even more preferably less than 250, most preferably less than 100 ppm.
Suitable pigments include organic and inorganic pigments. Examples of organic pigments include azo-pigments and phtalo-pigments. Good results are obtained with C.I. Vat brown I and C.I. Solvent Yellow 18. Examples of inorganic pigments include pigments containing titanium dioxide, iron oxides and chromium oxides. Good results are obtained with aluminium-chromium-cobalt oxide, since a suture with good mechanical properties and a low degree of leaching out is obtained.

The amount of pigment used may be between 0.1 – 7 wt.% of the final filament, as used for the production of the suture. Preferably the final filament contains at least 0.3 wt.%, more preferably at least 0.5 wt.% even more preferably at least 0.7 wt.% of pigment. Preferably the final filament contains at most 5.0 wt.%, more preferably at most 3 wt.% of pigment, even more preferably at least 2.5 wt.%, most preferably at most 2 wt.%. This is in view of obtaining a bright colour and good mechanical properties.

The UHMwPE filaments in the suture according to the invention consist preferably of UHMwPE, the pigment and less than 1000 ppm of further constituents, preferably less than 500 ppm of further constituents, more preferably less than 200 ppm of further constituents, most preferably less than 100 ppm of further constituents.

A suitable size for the suture according to the invention may be in the full USP range for sutures (e.g. 12-0 to 10). A USP value of 10 corresponds with a maximum diameter of 1.3 mm. In one preferred embodiment the suture member has a

titer of between 25 and 500 dtex. In that case the suture is very suitable for cardiovascular operations. In another preferred embodiment the suture has a titer of between 500 and 3000 dtex. In that case the suture is very suitable for use in orthopaedic applications. In yet another preferred embodiment the suture has a titer of between 3000 and 9000 dtex. In that case the suture is very suitable to be used in heavy orthopaedic applications.

The suture may in addition to the ultra high molecular polyolefin filaments comprise further components, for example compounds that provide some functional effect, like anti-microbial or anti-inflammatory action, or that further improve knotting performance. The amount of such other components is generally limited to at most 20 mass% (relative to total cable mass), preferably at most 10, more preferably at most 5 mass%.

The suture according to the invention comprises preferably at least 50 mass% of the ultra high molecular weight polyolefin filaments. The ultra high molecular weight polyolefin filaments contribute most to the strength properties of the member. Furthermore the filaments enhance the sliding properties of the suture through tissue. Therefore more preferably the suture comprises at least 60 mass% of the ultra high molecular weight polyolefin filaments, more preferably at least 70, 80 or at least 90 mass%. The suture may further comprise other fibres, e.g. other biocompatible materials like polymers, to provide some other additional properties to the suture, including improved knot slip behaviour or visual contrast. Such other fibres may be present in the form of one or more strands in the suture. However, preferably each strand has the same composition, so that each strand comprises the same amount of the polyolefin filaments and of the other filaments. This ensures that the suture has a homogeneous structure.

Suitable examples of other fibrous materials include filaments or staple fibres made from non-absorbable polymers like other polyolefin's, fluoro-polymers, or semi-aromatic polyesters like polyethylene terephthalate, absorbable polymers like aliphatic polyesters based on e.g. lactides.

Most preferably the suture consists of the polyolefin filaments.
The invention also relates to the use of the suture according to the invention in surgical method.

The invention is further explained in the examples, without being limited to the examples.

Methods

Intrinsic viscosity.

The Intrinsic Viscosity (IV) is determined according to method PTC-179 (Hercules Inc. Rev. Apr. 29, 1982) at 135°C in decalin, the dissolution time being 16 hours, with DBPC as anti-oxidant in an amount of 2 g/l solution, by extrapolating the viscosity as measured at different concentrations to zero concentration;

Tensile properties.

Tensile properties: tenacity, tensile modulus (or modulus) and elongation at break (or eab) are defined and determined on multifilament yarns with a procedure in accordance with ASTM D885M, using a nominal gauge length of the fibre of 500 mm, a crosshead speed of 50%/min and Instron 2714 clamps, of type Fibre Grip D5618C. On the basis of the measured stress-strain curve the modulus is determined as the gradient between 0.3 and 1% strain. For calculation of the modulus and strength, the tensile forces measured are divided by the titre, as determined by weighing 10 metres of fibre; values in GPa are calculated assuming a density of 0.97 g/cm^3;

Leaching tests

According to the requirements of ISO 10993-12:2002(E) an extraction was performed with samples of multi-filament yarn in both polar (distilled water) and non-polar (cottonseed oil) solvents. The extraction conditions were 37 °C for 24 and 72 hours.

After dilution with acetonitrile, the different phases were analyzed on the presence of pigment using Liquid Chromatography-Mass Spectrometry (LC-MS) and Gas Chromatography-Mass Spectrometry (GC-MS). In case no leaching I was observed means that leaching was lower than 10 ppb.

Cytotoxicity.

Cytotoxicity tests were performed according to ISO 10993-5, 1999: Biological Evaluation of Medical Devices – Part 5: Tests for in vitro cytotoxicity. The biological reactivity of a mammalian monolayer, L929 mouse fibroblast cell culture, in response to the test item extracts (samples containing up to 2.0 wt.% pigment) was determined. Extracts were prepared at 37°C (± 1) for 24 hours in a humidified

atmosphere containing 5±1% CO_2. Positive (natural rubber) and negative (silicone) control articles were prepared to verify the proper functioning of the test system. The maintenance medium of the cell cultures was replaced by the extracts of the tests item or control article in triplicate and the cultures incubated for 48 hours, at 37°C (± 1). Biological reactivity was rated on the following scale:

- grade 0 (no reactivity)
- grade 1 (slight reactivity)
- grade 2 (mild reactivity)
- grade 3 (moderate reactivity)
- grade 4 (severe reactivity)

Examples 1 – 4.

Slurries containing decalin, 6 mass % of powder of UHMwPE having an IV of 14 and 0.5, 1, 1.5 respectively 2 wt. % of aluminum-chromium-cobalt oxide pigment (of the cations is 32.5 % Co, 32% Al and 35.5 Cr) were prepared in a mixer.

The slurries were fed to a twin screw extruder having a diameter of 25 mm, being equipped with a gear-pump at a temperature setting of 180°C. In the extruder the UHMwPE was dissolved in the decalin and the so obtained mixture of the UHMwPE dissolved in the decalin and the pigment was extruded through a spin plate having 24 spin holes into a nitrogen atmosphere with a rate of 1.0 g/min per hole. The so obtained solution filaments were cooled in a water bath kept at about 35°C and with a water flow rate of about 5 cm/s perpendicular to the filaments entering the bath, and taken-up at such rate that a draw ratio of 15 was applied to the as-spun filaments in the air-gap of 15 mm. The filaments subsequently entered an oven at 130°C. The filaments were further stretched, during which process the decalin evaporated from the filaments. After the stretching process the filaments were kept taut in an oxygen free environment for 24 hours at 100 °C.

Mechanical properties, leaching out and cytotoxicity were determined on the so obtained multi-filament yarns.

The mechanical properties are reported in table 1. Favourable mechanical properties were obtained.

No compounds related to pigment, or other unknown compounds, where found. The pigment < 10 µg/kg (< 10 ppb).

From these results it can be concluded that the bio-availability of pigment due to leaching from sutures according to the invention containing the multi-filament yarn is negligible.

All the extracts of the colored samples when submitted to the cytotoxicity test exhibited no reactivity (grade 0) by the cell cultures. Severe reactivity (grade 4) was observed for the positive control article. The negative control article showed no signs of reactivity (grade 0). Therefore it can be concluded that sutures according to the invention containing the multi-filament yarn are non-cytotoxic.

The yarns furthermore show a homogeneous and bright colour.

Comparative test A.

Multi-filament yarn was produced according to examples 1-4, however no pigment was used.

The multi-filament yarn was dyed with D&C blue No 6 (delivered by Sigma Aldrich of the USA) by placing the multi-filament yarn for 7 hours at 120°C in a solution of the dye in super-critical carbon dioxide.

The resulting yarns presented a non-homogeneous color distribution pattern.

Mechanical properties and leaching out were determined.

Mechanical properties are reported in table 1. A serious decline in mechanical properties was observed (tenacity decreased about 40%).

Considerable leaching out took place in coconut oil as was already clear from the disappearing color of the multi-filament yarn.

From these results it is clear that sutures containing the multi-filament yarn according to comparative test A are not suitable for use in surgery.

Comparative test B.

Multi-filament yarn was produced according to examples 1-4, however no pigment was used.

The multi-filament yarn was dip-coated with a polyurethane coating containing an azo-dye (Sudan Red D, delivered by Sigma Aldrich).

Test data of the multi-filament yarn were measured and reported in table I. It is clear that considerable leaching out took place and that the cyto-toxicity of the filaments is insufficient. Therefore sutures containing the multi-filament yarn according to comparative test B are not suitable for use in surgery.

Table. 1.

Example/ Xomp. exp.	Tenacity [cN/dTex]	Modulus [cN/dTex]	Eab [%]	leaching [-]	cytotox. [-]	colouring [-]
I	37	1439	2.8	No	0	homogeneous
II	37	1377	2.9	No	0	Homogeneous
III	40	1501	3.0	No	0	Homogeneous
IV	37	1414	2.9	No	0	Homogeneous
A	21	-	-	Yes	-	Inhomogeneous
B	37	1381	2.8	Yes	-	Inhomogeneous

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EPO -DG 1
30. 05. 2007
118

CLAIMS

1. Suture containing filaments of ultra-high molecular weight polyethylene (UHMwPE), characterized in that the suture contains a multi-filament yarn that is obtained by a process comprising the steps of:
   a) Providing a mixture containing UHMwPE , a spinning solvent and a pigment
   b) Spinning a multi-filament yarn from the mixture by the gel spinning process.
2. Suture according to claim 1, characterized in that the UHMwPE has an intrinsic viscosity (IV) of at least 5 dl/g.
3. Suture according to claim 1 or claim 2, characterized in that the amount of pigment used is between 0.1 and 7.0 wt. % in the final filament as used for the production of the suture.
4. Suture according to claim 3, characterized in that the amount of pigment used is lower than 5.0 wt. %.
5. Suture according to claim 4 characterized in that the amount of pigment used is lower than 2.0 wt. %.
6. Suture according to any one of claims 1 – 6, characterized in that the pigment used is an inorganic pigment.
7. Suture according to claim 6, characterized that the pigment contains chromium oxide.
8. Suture according to claim 7, characterized in that the pigment contains aluminum-chromium-cobalt oxide.
9. Use of the suture according to any one of claims 1-8 in a surgical method.

ABSTRACT

Suture containing filaments of ultra-high molecular weight polyethylene (UHMwPE), characterized in that the suture contains a multi-filament yarn that is obtained by a process comprising the steps of:

a) Providing a mixture containing UHMwPE , a spinning solvent and a pigment
b) Spinning a multi-filament yarn from the mixture by the gel spinning process.

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30. 05. 2007

118

PATENT APPLICATION FEE DETERMINATION RECORD
Effective September 30,2007

Application or Docket Number
12/599869

CLAIMS AS FILED - PART I

	(Column 1)	(Column 2)	SMALL ENTITY TYPE ☐		OR	OTHER THAN SMALL ENTITY	
U.S. NATIONAL STAGE FEES			RATE	FEE		RATE	FEE
BASIC FEE	SMALL ENT. = $155	LARGE ENT. = $ 310	BASIC FEE		OR	BASIC FEE	330
EXAMINATION FEE	Satisfies PCT Article 33(1)-(4) = $ 50 / $ 100	All other situations = $ 100 / $ 200	EXAM. FEE			EXAM. FEE	220
SEARCH FEE	U.S. is ISA = $ 50 / $ 100 ALL other countries = $ 205 / $ 410	ALL other situations = $ 255 / $ 510	SEARCH FEE			SEARCH FEE	430
FEE FOR EXTRA SPEC. PGS.	11 minus 100 =	/ 50 =	X$130			X$260	
TOTAL CHARGEABLE CLAIMS	10 minus 20 =	*	X $ 25 =		OR	X $ 50 =	
INDEPENDENT CLAIMS	1 minus 3 =	*	X $ 105 =		OR	X $ 210=	
MULTIPLE DEPENDENT CLAIM PRESENT ☐			$185		OR	$370	
			TOTAL		OR	TOTAL	980

* If the difference in column 1 is less than zero, enter "0" in column 2

CLAIMS AS AMENDED - PART II

AMENDMENT A

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM ☐				

SMALL ENTITY RATE	ADDI-TIONAL FEE	OR	OTHER THAN SMALL ENTITY RATE	ADDI-TIONAL FEE
X $ 25 =		OR	X $ 50 =	
X$105		OR	X$210	
$185		OR	$370	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

AMENDMENT B

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
Total	*	Minus	**	=
Independent	*	Minus	***	=
FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM ☐				

SMALL ENTITY RATE	ADDI-TIONAL FEE	OR	OTHER THAN SMALL ENTITY RATE	ADDI-TIONAL FEE
X $ 25 =		OR	X $ 50 =	
X$105		OR	X$210	
$185		OR	$370	
TOTAL ADDIT. FEE		OR	TOTAL ADDIT. FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than '20', enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than '3', enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

MULTIPLE DEPENDENT CLAIM FEE CALCULATION SHEET (FOR USE WITH FORM PTO-875)	SERIAL NO. 09/599869	FILING DATE
	APPLICANT(S)	

CLAIMS

	AS FILED		AFTER 1st AMENDMENT		AFTER 2nd AMENDMENT	
	IND.	DEP.	IND.	DEP.	IND.	DEP.
1	1		1			
2		1		1		
3		8				
4						
5		3				
6		0		6		
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9		0				
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TOTAL IND.			1			
TOTAL DEP.			9			
TOTAL CLAIMS			10			

	AS FILED		AFTER 1st AMENDMENT		AFTER 2nd AMENDMENT	
	IND.	DEP.	IND.	DEP.	IND.	DEP.
51						
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100						
TOTAL IND.						
TOTAL DEP.						
TOTAL CLAIMS						

HONEYWELL Ex. 1030, Page 158 of 426
HONEYWELL INTERNATIONAL INC. v. DSM IP ASSETS B.V.
IPR2024-00493

PTO/SB/06 (07-06)
Approved for use through 1/31/2007. OMB 0651-0032
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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
12/599,869	01/14/2010	

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY ☐ RATE ($)	SMALL ENTITY ☐ FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =		OR	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =			X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT	11/12/2009	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE ($)	SMALL ENTITY ADDITIONAL FEE ($)	OR	OTHER THAN SMALL ENTITY RATE ($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 10	Minus	** 20	= 0	X $ =		OR	X $52=	0
	Independent (37 CFR 1.16(h))	* 1	Minus	***3	= 0	X $ =		OR	X $220=	0
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)	OR	RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =		OR	X $ =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =		OR	X $ =	
	☐ Application Size Fee (37 CFR 1.16(s))									
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

Legal Instrument Examiner:
/MYRTLE B. LEIGH/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

RULE 63 (37 C.F.R. 1.63)
INVENTORS DECLARATION FOR PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

As a below named inventor, I hereby declare that my residence, mailing address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

COLORED SUTURE

the specification of which (**check** applicable **box(s)**):

☐ is attached hereto
☐ was filed on as U.S. Application Serial No.
☒ was filed as PCT International application No. PCT/EP2008/004135 on 23.05.2008
and (if applicable to U.S. or PCT application) was amended on

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose to the Patent Office all information known to me to be material to patentability as defined in 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 35 U.S.C. 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed or, if no priority is claimed, before the filing date of this application:

Priority Foreign Application(s):

Application Number	Country	Day/Month/Year Filed
07010217.3	Europe	23.05.2007

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

Application Number	Date/Month/Year Filed

I hereby claim the benefit under 35 U.S.C. 120/365 of all prior United States and PCT international applications listed above or below:

Prior U.S./PCT Application(s): Application Serial No.	Day/Month/Year Filed	Status: patented pending, abandoned
PCT/EP2008/004135	23.05.2008	Pending

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon. And on behalf of the owner(s) hereof, I hereby appoint Nixon & Vanderhye P.C., telephone number 703-816-4000 (to whom all communications are to be directed) and the attorneys of: **Customer Number 23117**, individually and collectively owner's/owners' attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent. I also authorize Nixon & Vanderhye to add or delete attorneys from that Customer Number, and to act and rely solely on instructions directly communicated from the person, assignee, attorney, firm, or other organization sending instructions to Nixon & Vanderhye on behalf of the owner(s).

1. Inventor's Signature: Date: 10 - 11 - 09
Inventor: Joseph Arnold Paul Maria | J A P M | SIMMELINK | The Netherlands
(first) | MI | (last) | (citizenship)
Residence: (city) CADIER EN KEER (state/country) The Netherlands
Post Office Address: Kerkstraat 5
(Zip Code) 6267EA

2. Inventor's Signature: Date: 10 - 11 - 2009
Inventor: Claudia | C. | VAZ | Portugal
(first) | MI | (last) | (citizenship)
Residence: (city) MAASTRICHT (state/country) The Netherlands
Post Office Address: Bellefroidlunet 41E
(Zip Code) 6221KS

3. Inventor's Signature: Date:
Inventor: | | | Greek
(first) | MI | (citizenship)
Residence: (city) (state/country)
Post Office Address:
(Zip Code)

4. Inventor's Signature: Date:
Inventor: | | |
(first) | MI | (last)
Residence: (city) (state/country)
Post Office Address:
(Zip Code)

Electronic Acknowledgement Receipt

EFS ID:	6810403
Application Number:	12599869
International Application Number:	
Confirmation Number:	3921
Title of Invention:	COLORED SUTURE
First Named Inventor/Applicant Name:	Joseph Arnold Paul Maria SIMMELINK
Customer Number:	23117
Filer:	Bryan H. Davidson/Valerie Williams
Filer Authorized By:	Bryan H. Davidson
Attorney Docket Number:	BHD-4662-1326
Receipt Date:	14-JAN-2010
Filing Date:	
Time Stamp:	13:58:43
Application Type:	U.S. National Stage under 35 USC 371

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Oath or Declaration filed	01-14-2010_Declaration.pdf	324409 471c79a9ec41d6bc7532446527d33ee6e69e0af	no	1

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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
12/599,869	Joseph Arnold Paul Maria J.A.P.M Simmelink	BHD-4662-1326

23117
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

INTERNATIONAL APPLICATION NO.	
PCT/EP08/04135	
I.A. FILING DATE	PRIORITY DATE
05/23/2008	05/23/2007

CONFIRMATION NO. 3921
371 ACCEPTANCE LETTER

OC000000041650257

Date Mailed: 05/19/2010

NOTICE OF ACCEPTANCE OF APPLICATION UNDER 35 U.S.C 371 AND 37 CFR 1.495

The applicant is hereby advised that the United States Patent and Trademark Office in its capacity as a Designated / Elected Office (37 CFR 1.495), has determined that the above identified international application has met the requirements of 35 U.S.C. 371, and is ACCEPTED for national patentability examination in the United States Patent and Trademark Office.

The United States Application Number assigned to the application is shown above and the relevant dates are:

01/14/2010	01/14/2010
DATE OF RECEIPT OF 35 U.S.C. 371(c)(1), (c)(2) and (c)(4) REQUIREMENTS	DATE OF COMPLETION OF ALL 35 U.S.C. 371 REQUIREMENTS

A Filing Receipt (PTO-103X) will be issued for the present application in due course. **THE DATE APPEARING ON THE FILING RECEIPT AS THE " FILING DATE" IS THE DATE ON WHICH THE LAST OF THE 35 U.S.C. 371 (c)(1), (c)(2) and (c)(4) REQUIREMENTS HAS BEEN RECEIVED IN THE OFFICE. THIS DATE IS SHOWN ABOVE.** *The filing date of the above identified application is the international filing date of the international application (Article 11(3) and 35 U.S.C. 363).* Once the Filing Receipt has been received, send all correspondence to the Group Art Unit designated thereon.

The following items have been received:

- Copy of the International Application filed on 11/12/2009
- Copy of the International Search Report filed on 11/12/2009
- Preliminary Amendments filed on 11/12/2009
- Information Disclosure Statements filed on 11/12/2009
- Oath or Declaration filed on 01/14/2010
- U.S. Basic National Fees filed on 11/12/2009
- Priority Documents filed on 11/12/2009
- Specification filed on 11/12/2009
- Claims filed on 11/12/2009
- Abstracts filed on 11/12/2009

FORM PCT/DO/EO/903 (371 Acceptance Notice)

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

PAULETTE R KIDWELL

Telephone: (571) 272-0398

FORM PCT/DO/EO/903 (371 Acceptance Notice)

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
12/599,869	01/14/2010		1110	BHD-4662-1326	10	1

CONFIRMATION NO. 3921

23117
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

FILING RECEIPT

OC000000041650256

Date Mailed: 05/19/2010

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please submit a written request for a Filing Receipt Correction. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

Applicant(s)

Joseph Arnold Paul Maria J.A.P.M Simmelink, Cadier En Keer, NETHERLANDS;
Claudia C. Vaz, Maastricht, NETHERLANDS;

Power of Attorney: The patent practitioners associated with Customer Number 23117

Domestic Priority data as claimed by applicant

This application is a 371 of PCT/EP08/04135 05/23/2008

Foreign Applications

EUROPEAN PATENT OFFICE (EPO) 07010217.3 05/23/2007

If Required, Foreign Filing License Granted: 05/16/2010

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 12/599,869**

Projected Publication Date: 08/26/2010

Non-Publication Request: No

Early Publication Request: No

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HONEYWELL INTERNATIONAL INC. v. DSM IP ASSETS B.V.
IPR2024-00493