(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 February 2015 (05.02.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/014540 A1

(51) International Patent Classification:
C09J 4/06 (2006.01) *C08F 283/06* (2006.01)
C08L 71/02 (2006.01) *C08F 222/32* (2006.01)

(21) International Application Number:
PCT/EP2014/063130

(22) International Filing Date:
23 June 2014 (23.06.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
1313688.2 31 July 2013 (31.07.2013) GB

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2015/014540 A1

(54) Title: IMPROVED CYANOACRYLATE COMPOSITIONS

(57) Abstract: A cyanoacrylate composition, comprising: (a) at least one 2-cyanoacrylate ester; and (b) at least one monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer. The composition can be applied to a variety of materials and is particularly suitable as a biomedical adhesive. The invention also provides a method of closing a wound comprising, applying to the wound the above 2-cyanoacrylate ester composition.

Improved Cyanoacrylate Compositions

Field of the Invention

The present invention relates to compositions of cyanoacrylate monomer with improved properties.

Background to the Invention

Cyanoacrylate adhesive compositions are well known, and widely used as quick setting, instant adhesives with a wide variety of uses. See H.V. Coover, D.W. Dreifus and J.T. O'Connor, "Cyanoacrylate Adhesives" in Handbook of Adhesives, 27, 463-77, I. Skeist, ed. , Van Nostrand Reinhold, New York, 3rd ed. (1990). See also G.H. Millet "Cyanoacrylate Adhesives" in Structural Adhesives: Chemistry and Technology, S.R. Hartshorn, ed., Plenun Press, New York, p. 249-307 (1986).

Nonetheless, various techniques have been used to improve further the fixture times of cyanoacrylate adhesive compositions for certain applications where it is important to be able to secure one substrate to another quickly, while allowing the bond strength to develop over time. In addition, substrates constructed of certain materials have proven in the past difficult to bond, irrespective of the application to which the adhesive and the substrate are to be placed.

To combat these issues, technologies based on calixarene and oxacalixarene compounds have been developed. Generally, the addition of such materials to cyanoacrylate compositions allow for accelerated fixturing of substrates to-be-bonded together. See US4556700, US4622414, US4636539, US4695615, US4718966, and US4855461.

In addition to calixarene compounds, technologies based on the addition of silacrown compounds to cyanoacrylate adhesive compositions to accelerate fixturing have also been developed. For instance, US4906317 is directed to cyanoacrylate adhesive compositions which include silacrown compounds as additives to give substantially reduced fixture and cure times on de-activating substrates such as wood. The silacrown compounds are preferably employed at levels from about 0.1wt% to about 5wt% based on the total weight of the composition.

Henkel KGaA developed technology based on the addition to cyanoacrylate compositions of cyclodextrins to accelerate fixturing. In US5312864 (Wenz), the acceleration of the setting

properties of a cyanoacrylate adhesive composition by adding thereto a hydroxyl group derivative of an α-, β-, γ-cyclodextrin which is at least partly soluble in the cyanoacrylate is described. Other approaches have also been investigated, such as in US4837260 (Sato), in which the use of crown ethers in cyanoacrylate adhesive compositions is reported to reduce fixture and cure times.

In WO200411147, a range of esters are employed as additives in cyanoacrylate compositions, to overcome problems with cure speed. The inclusion of these accelerators in the cyanoacrylate compositions provided, improved fixture speeds particularly on substrates constructed of certain woods and ceramics, and combinations thereof, without sacrificing shelf life.

US6294629 discloses an alternative way of accelerating the cure of cyanoacrylate adhesive compositions. In US6294629, a cyanoacrylate adhesive composition is provided with a first accelerator component selected from calixarenes and oxacalixarenes, silacrowns, cyclodextrins, crown ethers, and combinations thereof; and a second accelerator component selected from poly (ethyleneglycol) di (meth) acrylates, ethoxylated hydric compounds, and combinations thereof. In US6475331, a cyanoacrylate adhesive composition is described, based on a cyanoacrylate component; and an accelerator component consisting essentially of (i) calixarenes, oxacalixarenes, or a combination thereof, and (ii) at least one crown ether, where the composition exhibits a fixturing speed of less than 20 seconds for bonding two substrates, at least one of which is constructed of a material selected from steel, epoxy glass or balsawood.

Cyanoacrylate adhesive compositions are extensively used in different fields due to their excellent long term bond strength and applicability to a large range of substrates. These adhesive compositions are widely used as instantaneous adhesives in industry, domestically and increasingly in medicine.

In the surgical arena, the use of biomedical adhesives rather than suturing or stapling tissues, has several highly attractive features, such as reduced scarring. In order to be effective the adhesive must be fast acting, and assure complete wound closure and adhesive efficiency for the time required. Tissue adhesives must be biocompatible and degrade within approximately the same time interval as the healing process, while providing and maintaining a union robust enough to withstand physiological pressures for the duration of the healing process.

Cyanoacrylate adhesive compositions are widely used as medical adhesives, for example in plastic surgery, in protecting surface injuries including abrasions, lacerations, sores, burns, in

adhering the cornea during cataract surgery (Alio et al., Ophthalmic Surgery and Lasers, 1996, 27, 270) and in various gynecological applications.

See US5328687; US3527841; US3722599; US3995641; and US3940362, for examples of α-cyanoacrylates that are useful as surgical adhesives. All of the foregoing references are hereby incorporated by reference herein.

Some monomeric α-cyanoacrylates are extremely reactive, polymerizing rapidly in the presence of even minute amounts of an initiator, including moisture present in the air or on surfaces such as animal tissue. Polymerization of monomers of α-cyanoacrylates can occur upon contact with anions, free radicals, zwitterions or ion pairs. Once polymerization has been initiated, the cure rate can be very rapid, depending on the choice of monomer. Therefore, in order to obtain a monomeric α-cyanoacrylate composition with a suitable shelf-life, polymerization inhibitors such as anionic and free radical stabilizers are often added to the compositions. However, addition of certain stabilizers may result in substantial retardation of the cure rate of the composition. Moreover, some commonly used stabilizers are known to be toxic, mutagenic or carcinogenic, depending on the composition and/or amount used.

In US20070078207, several compositions are described comprising one or more polymerizable cyanoacrylate monomers and at least two stabilizer additives. Examples of stabilizers employed include: free radical stabilizers (such as hydroquinone) and anionic stabilizers.

In medical adhesives, the cyanoacrylate monomers used are determined by the toxicity and occurrence of the degradation products. This in turn is controlled by the rate of degradation. Modifying the cyanoacrylate monomer has resulted in the formation of several commercial products, such as Indermil and Histoacryl (wherein the monomer is n-butyl cyanoacrylate); Dermabond and Omnex (wherein the monomer is 2-octyl cyanoacrylate); and PeriAcryl (wherein the composition comprises a mixture of n-butyl cyanoacrylate and 2-octylcyanoacrylate monomers). Each of these compositions has sought to overcome issues with the use of cyanoacrylate adhesive compositions in a clinical setting.

There are several properties of alkyl cyanoacrylates which are undesirable in a clinical setting and have limited their use. For example (i) cyanoacrylates act as an organic solvent inside the body; (ii) once polymerized, polycyanoacrylates tend to form rigid glassy structures, which can cause pain and discomfort to the patient; and (iii) controlling the adhesion rate can be problematic.

While earlier compositions seek to address these issues through the addition of additives, it would be desirable to have alternative compositions to choose from.

Short chain cyanoacrylates such as n-butylcyanoacrylate, when polymerized form glassy structures and the brittleness of the polymerized material can lead to undesired flaking at the wound site before the wound is necessarily healed.

Cyanoacrylates designed to be more flexible such as 2-octylcyanoacrylate were subsequently developed as alternative products.

However, longer chain cyanoacrylates, such as 2-octylcyanoarylate, have slower curing rates than shorter chain cyanoacrylate derivatives. To overcome these disadvantages activators or accelerators have been included in formulations to improve the cure speed.

One of the approaches to overcoming brittleness of polymerized cyanoacrylates is the addition of plasticizers.

US5350789 discloses 2-cyanoacrylate-based tissue adhesives employing biocompatible oxalate polymers as reactive plasticizers and thickening agents. The adhesives are capable of being formulated to allow modulus of elasticity matching of the adhesive and the substrate.

WO9731598 discloses biomedical monomer compositions, comprising monomers which when polymerized will form a biomedically acceptable polymer, plasticizers, such as tributyl citrate or tributyl-*O*-acetyl citrate (TBAC); and an acidic stabilizing agent. No evidence of increased flexibility and/or reduced brittleness or flakiness is provided.

WO200072761 discloses blends of commercially available cyanoacrylate adhesives and biodegradable polymers or copolymers, composed of different degradable monomers. In this case, the biodegradable polymers, such as lactide-epsilon-caprolactone copolymers, were added as thickeners of the cyanoacrylate monomer and plasticizers of the resultant polycyanoacrylates. US6977278 and US2776232 refer to overcoming the problems of brittleness by employing mixtures of monomeric α-cyanoacrylates and plasticizers in their compositions. In US6977278 the plasticizer component is present in the amount from about 15wt% to about 40wt% based on the total weight of the composition. In US2776232 no data supporting increased flexibility in the polymer or the polymeric bond is provided and it is thought that any increase in flexibility achieved will not be maintained over time.

WO2009155594 employs pluronic polymers to overcome problems with cure speed and viscosity, in cyanoacrylate compositions. In addition, methods for preparing sterilized cyanoacrylate adhesive compositions are described.

To overcome common problems associated with cyanoacrylates, in particular those used in the closure of topical wounds, two additives, namely, an accelerator and a plasticizer, are required. This increases formulation, manufacturing and packaging complexity and can also potentially increase costs.

Notwithstanding the state of the art, it would be desirable to provide alternative technologies to improve fixture speed and flexibility of cyanoacrylates. It would be particularly desirable if a single additive could be employed to enhance the cure speed and flexibility of cyanoacrylate adhesives.

Summary of the Invention

In one aspect, the present invention provides a cyanoacrylate composition, comprising:

(a) at least one 2-cyanoacrylate ester; and

(b) at least one monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer.

The present invention addresses the need for alternative compositions with enhanced flexibility, for use in, for example, biomedical adhesives. The present invention also addresses the need for improving curing times of cyanoacrylates, which is particularly problematic for longer chain cyanoacrylate ester derivatives, for example, 2-octylcyanoacrylate.

In the above composition the cyanoacrylate ester of component (a) is in the uncured or monomeric form, and this is mixed with the polymeric component (b).

It will be appreciated that the present invention in particular relates to a sterilized form of the composition, and in particular a composition suitable for application to a wound in a living body. Advantageously, the adhesives of the present invention are fast acting, while providing and maintaining a wound closure robust enough to withstand physiological conditions, including pressures which may otherwise cause the wound to open, for the time required.

The cyanoacrylate composition of the present invention may comprise a 2-cyanoacrylate ester, which can be selected from C_{4-30} alkyl 2-cyanoacrylates, desirably the 2-cyanoacrylate ester is 2-octyl 2-cyanoacrylate.

Suitably, the 2-cyanoacrylate ester is present in an amount of from about 60 wt% to about 99.9 wt%, preferably in an amount of from about 80 wt% to about 98 wt%, based on the total weight of the cyanoacrylate composition.

In one aspect of the present invention, the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is a monoalkyl ether.

In other embodiments, the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is a random copolymer.

Suitably, the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is at least one poly(ethyleneglycol-ran-propylene glycol) C_{1-20} alkyl monoether.

Preferably, the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is at least one poly(ethyleneglycol-ran-propylene glycol) C_{2-10} alkyl monoether.

Suitably the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is poly(ethyleneglycol-ran-propylene glycol) monobutyl ether.

Desirably monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is poly(ethyleneglycol-ran-propylene glycol) monobutyl ether and is present in an amount of about 5 wt% based on the total weight of the composition.

Desirably, the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer has a weight average molecular weight (M_w) in the range of from about 250 g/mol to about 2500 g/mol, preferably in the range of from about 500 g/mol to about 1500 g/mol. The weight average molecular weight (M_w) is determined by gel permeation chromatography using a polystyrene standard.

The monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer can be present in an amount of from about 0.1 wt% to about 20 wt%, preferably in an amount of from about 2 wt% to about 10 wt%, based on the total weight of the cyanoacrylate composition.

Advantageously, the present invention provides an alternative technology to improve fixture speed and flexibility of cyanoacrylates. Furthermore, the present invention provides a solution to a long standing problem by providing compositions in which hydroxyl-terminated ethylene glycol-

propylene glycol copolymers are employed as a single additive to simultaneously enhance the cure speed and flexibility of cyanoacrylate adhesives.

The cyanoacrylate composition may also comprise one or more additives each selected independently from the group consisting of free radical stabilizers, anionic stabilizers, plasticizers, thickeners, dyes, thixotropic agents, toughening agents, and accelerators.

The cyanoacrylate composition may also be produced, in such a manner that said composition is sterile. For example the composition may be irradiated for example exposed to sufficient radiation, such as by gamma irradiation, to make it sufficiently sterile for application to a wound on a living body.

Another aspect of the present invention relates to the polymerized product of the cyanoacrylate composition.

The polymerized product of the cyanoacrylate composition can have a mean flexibility in the range of from about 20 mm to about 50 mm as determined in accordance with ASTM 3787-07.

The polymerized product of the cyanoacrylate composition will preferably have a mean flexibility in the range of from about 30 mm to about 50 mm as determined in accordance with ASTM 3787-07.

In one aspect the present invention provides a method of preparing an optionally sterile cyanoacrylate composition comprising:

i) providing at least one 2-cyanoacrylate ester;

ii) combining therewith, for example with mixing, at least one monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer and optionally one or more additives; and

iii) optionally sterilizing the mixture.

Another aspect of the present invention relates to the use of a monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer to simultaneously increase the polymerization rate of 2-cyanoacrylate esters and the flexibility of the polymerized products thereof.

Advantageously, the present invention provides a single, dual acting additive for the simultaneous improvement of flexibility and cure times of cyanoacrylate adhesive compositions, thereby reducing manufacturing cost and simplifying the production process.

The present invention provides a single, dual acting additive for the simultaneous improvement of flexibility and cure times of cyanoacrylate adhesive compositions, thereby addressing formulation shortfalls of the current state of the art.

The invention also relates to a pack comprising a container and a composition of the invention within the container. Desirably the container/composition is sterilized. The pack is desirably hermetically sealed to maintain a sterile environment within the container. Optionally the container is a dispensing pack. For example it may be a squeezable dispensing container. The pack may further comprise an external pack, for example a plastic or foil wrap to protect the container.

The invention further relates to a method of closing a wound comprising applying to the wound a composition of the invention. The composition of the invention cures to close the wound.
The invention extends to a composition of the invention as described herein.

It will be appreciated by those skilled in the art that embodiments of the present invention may further comprise one or more additives each selected independently from the group consisting of free radical stabilizers, anionic stabilizers, plasticizers, thickeners, dyes, thixotropic agents, toughening agents, and accelerators.

Detailed Description

Example 1:

15 commercially available PEG related polymers were added to 2-octylcyanoacrylate. Polymer casts were made by curing ~5g samples in a plastic mould using 20-50 μL of 3,5-dimethyl pyrazine as an initiator. The resulting polymer discs were manually examined for their flexibility. Those which could be bent over double without breaking, were deemed flexible. The results are shown below. Entry 1 is a control experiment wherein the composition comprises 100% 2-octylcyanoacrylate. Subsequent entries are distinguished by the weight percentage of additive, the type of additive included in the composition and the comparative flexibility observed for each composition. Entry 2 is a comparative sample comprising the plasticizer tributyl-*O*-acetyl citrate in an amount of 5wt% based on the total weight of the 2-octylcyanoacrylate composition.

Table 1

Entry	Formulation	Additive	Comparative (Manual) Flexibility
1[a]	CA1	None	Very brittle/complete shattering
2[a]	CA2	5wt% TBAC	Flexible no cracking
3[a]	CA3	1wt% fumarate	Very brittle/complete shattering
4[a]	CA4	3wt% fumarate	Moderately flexible but cracking occurs
5[a]	CA5	3wt% Dimethyl PEG 600	Very brittle/complete shattering
6[a]	CA6	5wt% fumarate	Shattered at first bend
7[a]	CA7	5wt% PEG 400	Shattered at second bend
8	CA8	5wt% PEG-r-PPG monobutyl ether	Very flexible
9[a]	CA9	5wt% PEG dioleate	Only partially soluble in monomer
10[a]	CA10	5wt% PEG mono-oleate	Insoluble in monomer
11[a]	CA11	5wt% diethylene glycol diadipate	Flexible but cracked
12[a]	CA12	PEG monotridecyl ether	Insoluble in monomer
13[a]	CA13	2wt% PEG dioleate	Very flexible
14[a]	CA14	5wt% PEG monododecyl ether (Polidocanol)	Very flexible
15[a]	CA15	5wt% PEG bis ethyl hexanoate	Very flexible

[a] Comparative example

As can be seen 4 additives (Table 1, formulations CA8, CA13-CA15) gave flexibilities, which appeared to be as good as or better than the comparative sample (CA2) containing an industry standard plasticizer (tributyl-*O*-acetyl citrate (TBAC)). Of these formulation CA13, comprising PEG dioleate was discounted because of a tendency to polymerize the cyanoacrylate on standing.

As can be seen from Table 1, monoether polymers are significantly more effective plasticizers than diether polymers, particularly when one compares the results of formulation CA5 with CA8 and/or CA14. In addition, monoether polymers enhance flexibility significantly in comparison to bis-hydroxyl terminating polymers, see for example, Table 1 CA7 versus CA8 and/or CA14.

Example 2:

Track free time (TFT) measurement is a common way to compare the cure speed of various cyanoacrylate formulations. Latex rubber sheeting was used as a substrate to determine which if any of the 4 additive-containing flexible formulations selected above (Table 1; formulations CA8, CA14-CA15) also showed improved cure speed.

The TFT test was carried out wiping the latex sheet with IPA. 5 min was allowed for excess IPA to evaporate. 3 μL of formulation was spread over a ~1cm diameter area and the time taken from the point where the spreading was complete to the point where the polymer was tack free (dry to the touch) was recorded as the TFT. The cyanoacrylate containing non-accelerating plasticizer tributyl-*O*-acetyl citrate (TBAC) was used as a control (formulation CA2).

TFT of flexible formulations on latex rubber

Table 2

Entry	Formulation	Additive	Tack Free Time (Latex)	Stability @ 82 °C
1	CA2	5wt%TBAC	30-50 sec	45 days
2	CA8	5wt% PEG-r-PPG monobutyl ether	15-20 sec	35 days
3	CA14	5wt% PEG monododecyl ether (Polido-canol)	35-40 sec	27 days
4	CA15	5wt% PEG bis ethyl hexanoate	50 sec	Not measured

As can be seen the best track free time result was for CA8 which was subsequently subjected to additional advanced testing.

Example 3:

Further testing was carried out on the formulation on CA8 (5wt% poly(ethyleneglycol-*ran*-propylene glycol) monobutyl ether (CAS 9038-95-3, Avg MW 970) in 2-octylcyanoacrylate) relative to the control (5wt% TBAC in 2-octylcyanoacrylate). Results obtained with CA8 were superior to that of the control experiment, in every test bar the nylon bond strength, although even this result is above the level required for effective skin adhesion. Particularly noticeable is the effect on flexibility (29% increase), tensile strength on porcine (57% increase) and cure speed (56% reduction in mean TFT on human skin, 47% reduction in TFT on Latex, 92% reduction in fixture time on ABS).

Table 3

Entry	Test	CA2 (5wt% TBAC control)	CA8 5wt% poly(ethyleneglycol-ran-propylene glycol) monobutyl ether
1	Mean TFT on Human skin (sec)	57	25
2	Mean TFT on Latex (sec)	30	16
3	Mean TFT on porcine skin (sec)	30-75	30-45
4	Mean tensile strength on porcine skin (g) (ASTM F2458-05)	572	901
5	Mean flexibility (displacement, mm ASTM D3787-07(2011))	34.69	44.70
6	Bond Strength on Nylon 6,6; N/mm^2 (STM#700)	2.05	1.21
7	Fixture Time on ABS/sec (STM#701)	120	10
8	Viscosity @ 25°C, MPas (STM#740)	6.37	7.23

List of abbreviations: TBAC (tributyl-O-acetyl citrate); PEG (poly ethylene glycol); PPG (poly propylene glycol); TFT (Track free time); IPA (isopropyl alcohol); ABS (Acrylonitrile butadiene styrene) ASTM (American Society for Testing and Materials)

ASTM D3787 - 07(2011) Standard Test Method for Bursting Strength of Textiles-Constant-Rate-of-Traverse (CRT) Ball Burst Test.

ASTM D3787 - 07(2011)

An ASTM designation number identifies a unique version of an ASTM standard.

D3787 - 07(2011)

D = miscellaneous materials;

3787 = assigned sequential number

07 = year of original adoption (or, in the case of revision, the year of last revision)

(2011) = year of last re-approval

The words “comprises/comprising” and the words “having/including” when used herein with reference to the present invention are used to specify the presence of stated features, integers, steps or components but do not preclude the presence or addition of one or more other features, integers, steps, components or groups thereof.

It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination.

Claims

1. A cyanoacrylate composition, comprising:
   a) at least one 2-cyanoacrylate ester; and
   b) at least one monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer.

2. The cyanoacrylate composition of claim 1, wherein the 2-cyanoacrylate ester is selected from C_{4-30} alkyl 2-cyanoacrylates, for example 2-octyl 2-cyanoacrylate.

3. The cyanoacrylate composition according to any preceding claim, wherein the 2-cyanoacrylate ester is present in an amount of about 60 wt% to about 99.9 wt%, preferably in an amount of about 80 wt% to about 98 wt%, based on the total weight of the cyanoacrylate composition.

4. The cyanoacrylate composition according to any preceding claim, wherein the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is a monoalkyl ether.

5. The cyanoacrylate composition according to any preceding claim, wherein the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is a random copolymer.

6. The cyanoacrylate composition according to any preceding claim, wherein the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is at least one poly(ethyleneglycol-ran-propylene glycol) C_{2-10} alkyl monoethers.

7. The cyanoacrylate composition according to any preceding claim, wherein the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer has a weight average molecular weight (M_w) in the range from about 250 g/mol to about 4500 g/mol, preferably from about 500 g/mol to about 1500 g/mol.

8. The cyanoacrylate composition according to any preceding claim, wherein the monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer is present in an amount from about 0.1 wt% to about 20 wt%, preferably in an

amount from about 2 wt% to about 10 wt%, based on the total weight of the cyanoacrylate composition.

9. The cyanoacrylate composition according to any preceding claim, wherein said composition is sterile.

10. The polymerized product of a cyanoacrylate composition according to any one of claims 1 to 9, optionally wherein said product has a mean flexibility in the range from about 20 mm to about 50 mm as determined in accordance with ASTM 3787-07.

11. A method of preparing a cyanoacrylate composition according to any one of claims 1 to 9, said method comprising:

a) providing at least one 2- cyanoacrylate ester;

b) combining therewith, at least one monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer and optionally one or more additives; and

c) optionally sterilizing the mixture.

12. Use of a monoether of a hydroxyl-terminated ethylene glycol-propylene glycol copolymer to simultaneously increase the polymerization rate of 2-cyanoacrylate esters and the flexibility of the polymerized products thereof.

13. A pack comprising:

a. a container; and

b. a composition of any of Claims 1 to 9 within the container.

14. A pack according to Claim 13 wherein the container/composition is sterilized, optionally wherein the pack is hermetically sealed to maintain a sterile environment within the container.

15. A method of closing a wound comprising applying to the wound a composition of any of Claims 1 to 9.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/063130

A. CLASSIFICATION OF SUBJECT MATTER
INV. C09J4/06 C08L71/02 C08F283/06 C08F222/32
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C09J C08F C08L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 170 585 A (KIMURA KAORU [JP] ET AL) 9 October 1979 (1979-10-09) example 8 table 1 column 4, line 20 - column 5, line 16	1-8, 10-12
Y	EP 2 303 342 A2 (ADHEZION BIOMEDICAL LLC [US]) 6 April 2011 (2011-04-06) examples 1-14 tables 1-3 claims 1-40	1-15
Y	EP 2 303 343 A2 (ADHEZION BIOMEDICAL LLC [US]) 6 April 2011 (2011-04-06) examples 1-23 claims 1-33 page 28, line 1 - page 29, line 11	1-15

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
12 December 2014	18/12/2014

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