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(54) Title: OPHTHALMIC AND OTORHINOLARYNGOLOGICAL DEVICE MATERIALS

(57) Abstract: Disclosed are soft, high refractive index, acrylic device materials. The materials comprise di-block or tri-block macromers containing hydrophilic side-chains. The materials have improved glistening resistance.

OPHTHALMIC AND OTORHINOLARYNGOLOGICAL DEVICE MATERIALS

Field of the Invention

This invention is directed to improved ophthalmic and otorhinolaryngological device materials. In particular, this invention relates to soft, high refractive index acrylic device materials that have improved glistening resistance and mechanical properties.

Background of the Invention

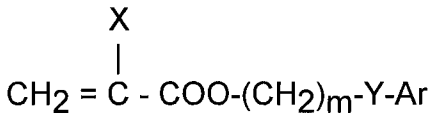
With the recent advances in small-incision cataract surgery, increased emphasis has been placed on developing soft, foldable materials suitable for use in artificial lenses. In general, these materials fall into one of three categories: hydrogels, silicones, and acrylics.

In general, hydrogel materials have a relatively low refractive index, making them less desirable than other materials because of the thicker lens optic necessary to achieve a given refractive power. Conventional silicone materials generally have a higher refractive index than hydrogels, but tend to unfold explosively after being placed in the eye in a folded position. Explosive unfolding can potentially damage the corneal endothelium and/or rupture the natural lens capsule. Acrylic materials are desirable because they typically have a high refractive index and unfold more slowly or controllably than conventional silicone materials.

U.S. Patent No. 5,290,892 discloses high refractive index, acrylic materials suitable for use as an intraocular lens ("IOL") material. These acrylic materials contain, as principal components, two aryl acrylic monomers. The IOLs made of these acrylic materials can be rolled or folded for insertion through small incisions.

U.S. Patent No. 5,331,073 also discloses soft acrylic IOL materials. These materials contain as principal components, two acrylic monomers which are defined by the properties of their respective homopolymers. The first monomer is defined as one in which its homopolymer has a refractive index of at least about 1.50. The second monomer is defined as one in which its homopolymer has a glass transition temperature less than about 22 °C. These IOL materials also contain a cross-linking component. Additionally, these materials may optionally contain a fourth constituent, different from the first three constituents, which is derived from a hydrophilic monomer. These materials preferably have a total of less than about 15% by weight of a hydrophilic component.

U.S. Patent No. 5,693,095 discloses foldable, high refractive index ophthalmic lens materials containing at least about 90 wt.% of only two principal components: one aryl acrylic hydrophobic monomer and one hydrophilic monomer. The aryl acrylic hydrophobic monomer has the formula



wherein: X is H or CH_3 ;
m is 0-6;
Y is nothing, O, S, or NR, wherein R is H, CH_3, C_nH_{2n+1} (n=1-10), iso-OC_3H_7, C_6H_5, or $CH_2C_6H_5$; and
Ar is any aromatic ring which can be unsubstituted or substituted with CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, OCH_3, C_6H_{11}, Cl, Br, C_6H_5, or $CH_2C_6H_5$.

The lens materials described in the '095 Patent preferably have a glass-transition temperature ("T_g") between about –20 and +25 °C.

Flexible intraocular lenses may be folded and inserted through a small incision. In general, a softer material may be deformed to a greater extent so that it can be inserted through an increasingly smaller incision. Soft acrylic or

methacrylic materials typically do not have an appropriate combination of strength, flexibility and non-tacky surface properties to permit IOLs to be inserted through an incision as small as that required for silicone IOLs.

Polyethylene glycol (PEG) dimethacrylates are known to improve glistening resistance of hydrophobic acrylic formulations. See, for example, U.S. Patent Nos. 5,693,095; 6,528,602; 6,653,422; and 6,353,069. Both the concentration and molecular weight of PEG dimethacrylates have an impact on glistening performance. Generally, use of higher molecular weight PEG dimethacrylates (1000 MW) yield copolymers with improved glistening performance at low PEG concentrations (10 – 15 wt%), as compared to lower molecular weight PEG dimethacrylates (<1000 MW). However, low PEG dimethacrylate concentrations are desirable to maintain a high refractive index copolymer. Addition of PEG dimethacrylates also tends to decrease the modulus and tensile strength of the resulting copolymer. Also, higher molecular weight PEG dimethacrylates are generally not miscible with hydrophobic acrylic monomers.

Summary of the Invention

Improved soft, foldable acrylic device materials which are particularly suited for use as IOLs, but which are also useful as other ophthalmic or otorhinolaryngological devices, such as contact lenses, keratoprostheses, corneal rings or inlays, otological ventilation tubes and nasal implants, have been discovered. These polymeric materials comprise di-block or tri-block macromers containing hydrophilic side-chains.

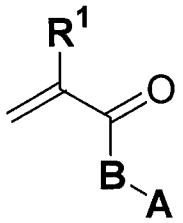
The subject macromers allow synthesis of glistening resistant, low equilibrium water content, high refractive index IOLs. The use of di-block or tri-block macromer containing hydrophilic side-chains allows incorporation of higher molecular weight hydrophilic ingredients into hydrophobic copolymer formulations. Higher molecular weight hydrophilic ingredients are more efficient glistening resistance ingredients than comparable weight fractions of

lower molecular weight hydrophilic polymers. This resulting hydrophilic ingredient concentration reduction results in reduced equilibrium water content, higher refractive index, and a smaller mass intraocular lens that can be inserted through a smaller incision.

Detailed Description of the Invention

Unless indicated otherwise, all component amounts are presented on a % (w/w) basis ("wt.%").

The device materials of the present invention are copolymers comprising a) a monofunctional acrylate or methacrylate monomer [1], b) a difunctional acrylate or methacrylate cross-linker [2], and c) a di-block or tri-block macromer [3] (which may be a macromer of formula [3a], [3b], [3c], [3d], or [3e]). The device materials may contain more than one monomer [1], more than one monomer [2], and more than one macromer [3]. Unless indicated otherwise, references to each ingredient are intended to encompass multiple monomers or macromers of the same formula and references to amounts are intended to refer to the total amount of all monomers of each formula.



[1]

wherein

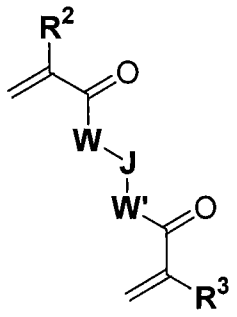
B = $-O(CH_2)_n-$, $-(OCH_2CH_2)_n-$, $-NH(CH_2)_n-$, or $-NCH_3(CH_2)_n-$;

R^1 = H, CH_3, CH_2CH_3, or CH_2OH;

n = 0 - 12;

A = C_6H_5 or $O(CH_2)_mC_6H_5$, where the C_6H_5 group is optionally substituted with $-(CH_2)_nH$, $-O(CH_2)_nH$, $-CH(CH_3)_2$, $-C_6H_5$, $-OC_6H_5$, $-CH_2C_6H_5$, F, Cl, Br, or I; and

m = 0 – 18;



[2]

wherein

R^2, R^3 independently = H, CH_3, CH_2CH_3, or CH_2OH;

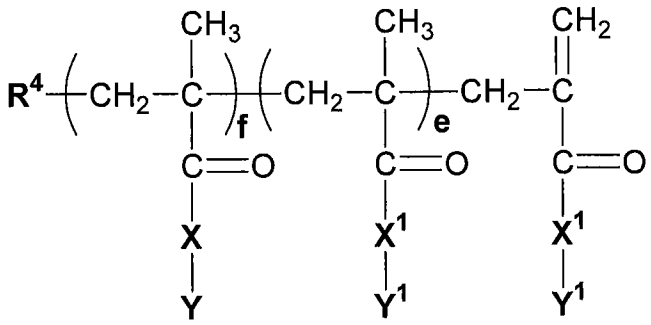
W, W' independently = $O(CH_2)_d$, $NH(CH_2)_d$, $NCH_3(CH_2)_d$, $O(CH_2)_dC_6H_4$, $O(CH_2CH_2O)_dCH_2$, $O(CH_2CH_2CH_2O)_dCH_2$, $O(CH_2CH_2CH_2CH_2O)_dCH_2$, or nothing;

J = $(CH_2)_a$, $O(CH_2CH_2O)_b$, O, or nothing, provided that if W and W' = nothing, then J ≠ nothing;

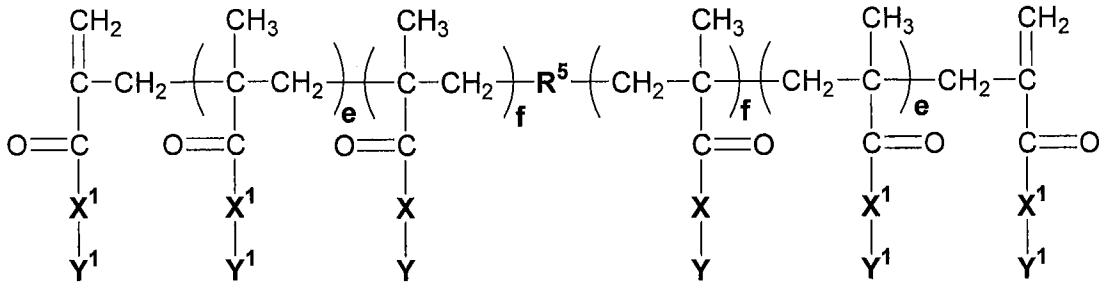
d = 0 - 12;

a = 1 – 12;

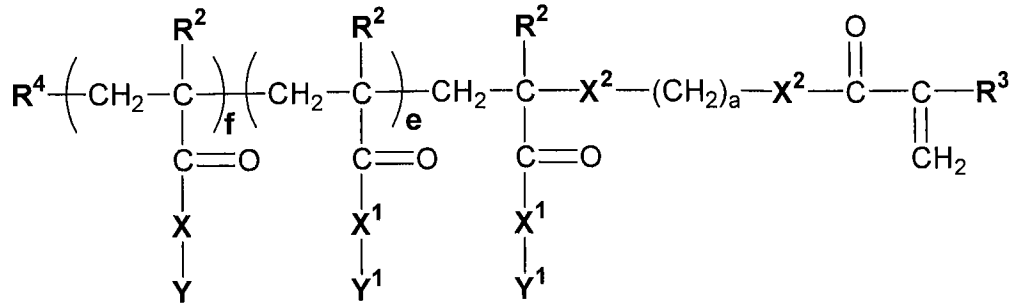
b = 1 – 24;



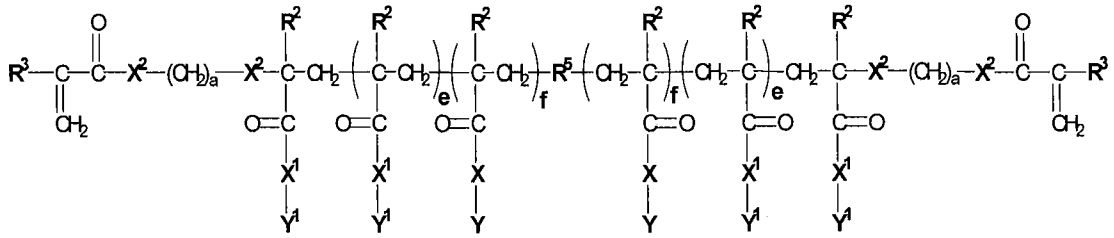
[3a]



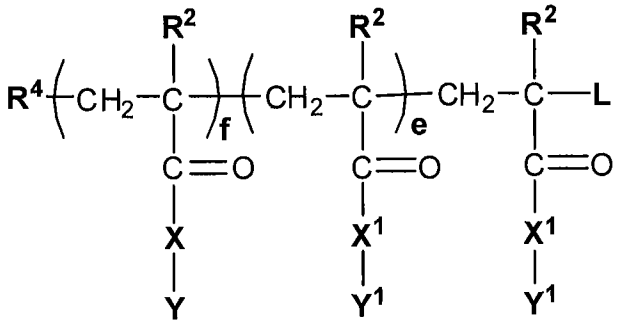
[3b]



[3c]



[3d]



[3e]

wherein for formulas [3a], [3b], [3c], [3d], and [3e] (collectively, "formula [3]")

e, f independently = 1 – 100;

X, X^1, X^2 independently = O, NH-, $N(CH_3)$-, $N(CH_2CH_3)$-, or $N(C_6H_5)$-;

Y, Y^1 independently = -H, $-(CH_2)_pH$, $-(CH_2)_pOH$, $-CHC(CH_3)_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $CH_2CH_2N(C_6H_5)_2$, $-CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2OC_6H_5$, $(CH_2CH_2O)_qCH_3$, $(CH_2CH(CH_3)O)_qCH_3$, $(CH_2CH_2CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qH$, $(CH_2CH(CH_3)O)_qH$, $(CH_2CH_2CH_2CH_2O)_qH$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, $(CH_2)_tOC_6H_5$, or $CH_2CH_2N(-C(O)CH_2CH_2CH_2-)$,

provided that $Y \neq Y^1$,

and further provided that at least one of Y and Y^1 = $CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $CH_2CH_2N(C_6H_5)_2$, $-CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2OC_6H_5$, $(CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qH$, $(CH_2CH_2O)_qC_6H_5$, or $CH_2CH_2N(-C(O)CH_2CH_2CH_2-)$; and the other of Y and Y^1 = -H, $-(CH_2)_pH$, , $-CHC(CH_3)_2$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, or $(CH_2)_tOC_6H_5$;

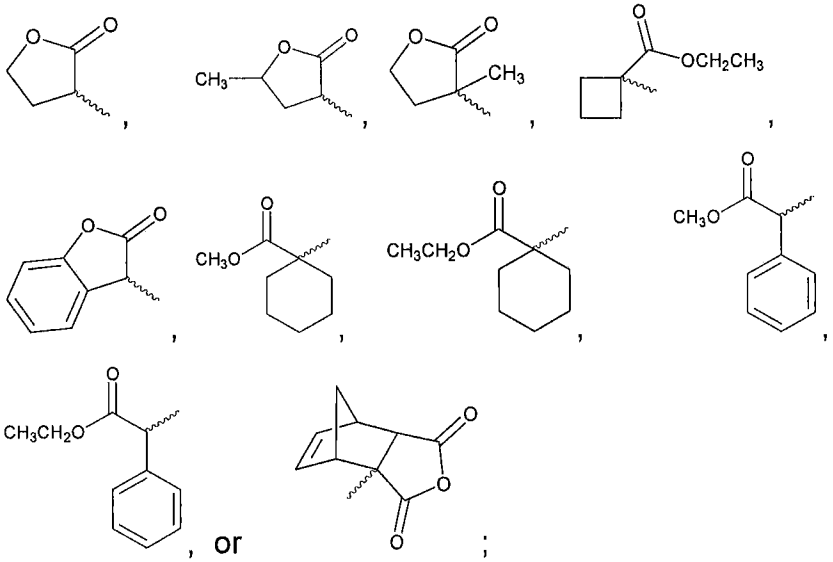
p = 1 – 18;

q = 1 – 230;

t = 0 – 6;

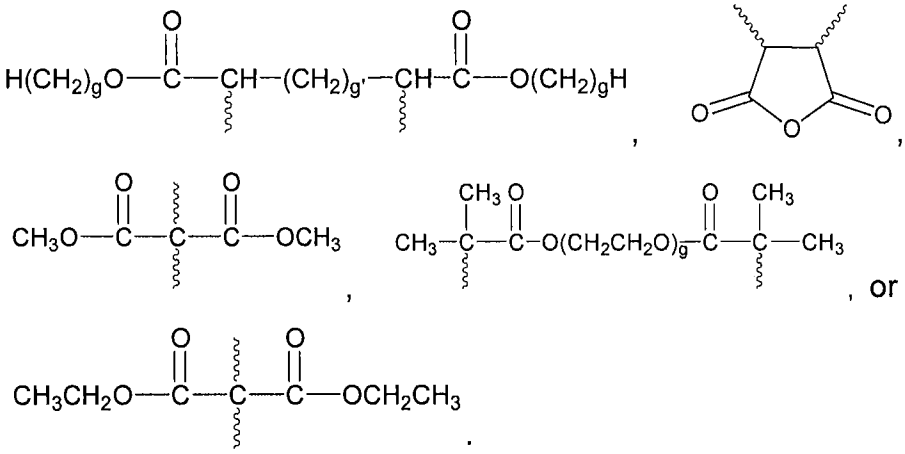
R^4 = $CH_3OC(O)CH(CH_3)$-, $CH_3OC(O)C(CH_3)_2$-, $HOCH_2CH_2OC(O)C(CH_3)_2$-, $(CH_2=C(R^3)CO_2CH_2CH_2OC(O)C(CH_3)_2$-, $CH_3CH_2OC(O)CH(CH_3)$-, $CH_3CH_2OC(O)C(CH_3)_2$-, $CH_3OC(O)CH(CH_2CH_3)$-, $CH_3CH_2OC(O)CH(CH_2CH_3)$-, $CH_2=CHCH_2OC(O)C(CH_3)_2$-, $CH_3CH_2OC(O)CH(CH_2CH_2CH_3)$-,

$CH_3OC(O)CH(CH_2CH_2CH_2CH_3)$-, $[CH_3OC(O)]_2CH$-,
$[CH_3CH_2OC(O)]_2CH$-, $[CH_3CH_2OC(O)]_2C(CH_3)$-,
$CH_3CH_2OC(O)CH(CH_2CH_2CH_2CH_3)$-, $(CH_3)_3COC(O)C(CH_3)_2$-,
$CH_3CH_2OC(O)CH_2CH_3(CH_2CH_2CH_2CH_3)$-,
$CH_3CH_2OC(O)CH(CH_2CH_2CH_2CH_2CH_3)$-,
$CH_3CH_2OC(O)CH(CH_2CH_2CH_2CH_2CH_2CH_3)$-,



, or ;

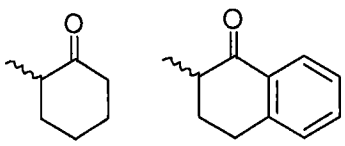
R^5 =



, or ;

g, g' independently = 1 – 12; and

L = H, Cl, Br, $-CH_2C(O)CH_3$, $CH_2C(O)C(CH_3)_3$, $-CH_2C(O)C_6H_5$, -



$CH_2C(O)C_6H_4OH$, $-CH_2C(O)C_6H_4OCH_3$, , or $CH_2CH=CH_2$.

Preferred monomers of formula [1] are those wherein:

B = $-O(CH_2)_n-$ or $-(OCH_2CH_2)_n-$;

R^1 = -H or $-CH_3$;

n = 1 - 5;

A = $-C_6H_5$, $O(CH_2)_mC_6H_5$; and

m = 0 – 4.

Preferred monomers of formula [2] are those wherein:

R^2, R^3 independently = H or CH_3;

W, W' independently = $O(CH_2)_d$, $O(CH_2)_dC_6H_4$, or nothing;

J = $O(CH_2CH_2O)_b$ or nothing, provided that if W and W' = nothing, then J ≠ nothing;

d = 0 - 6; and

b = 1 – 10.

Preferred macromers of formula [3] are those wherein:

e, f independently = 5 - 75;

X, X^1, X^2 independently = O or $N(CH_3)-$;

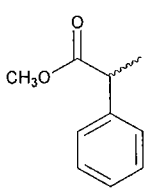
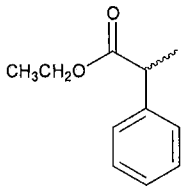
Y, Y^1 independently = $-(CH_2)_pH$, $(CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qH$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, or $(CH_2)_tOC_6H_5$;

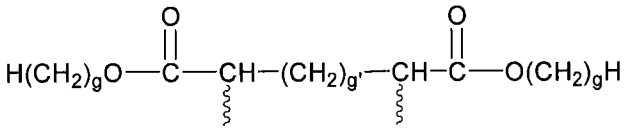
p = 1 - 12;

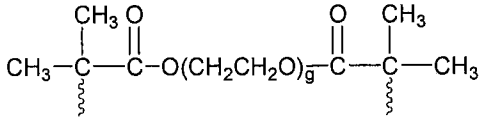
q = 2 - 60;

t = 1 - 5;

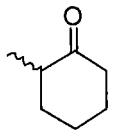
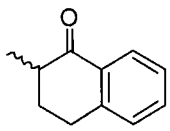
R^4 = $CH_3OC(O)CH(CH_3)-$, $CH_3OC(O)C(CH_3)_2-$, $HOCH_2CH_2OC(O)C(CH_3)_2-$, $(CH_2=C(R^3)CO_2CH_2CH_2OC(O)C(CH_3)_2-$, $CH_3CH_2OC(O)CH(CH_3)-$, $CH_3CH_2OC(O)C(CH_3)_2-$, $CH_3OC(O)CH(CH_2CH_3)-$, $CH_3CH_2OC(O)CH(CH_2CH_3)-$, $(CH_3)_3COC(O)C(CH_3)_2-$,


, or 
;

R^5 =  or


;

g, g' independently = 1 – 12; and

L = H, Cl, Br, $-CH_2C(O)CH_3$, $CH_2C(O)C(CH_3)_3$, $-CH_2C(O)C_6H_5$, $CH_2C(O)C_6H_4OH$, $-CH_2C(O)C_6H_4OCH_3$, , , or $CH_2CH=CH_2$.

Most preferred macromers of formulas [3] are those wherein:

e, f independently = 5 - 60;

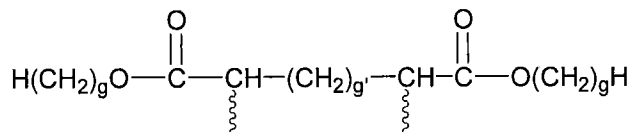
X, X^1, X^2 = O;

Y, Y^1 independently = $-(CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, or $(CH_2)_tOC_6H_5$;

q = 2 - 40;

t = 1-2;

R^4 = $CH_3OC(O)CH(CH_3)-$, $CH_3OC(O)C(CH_3)_2-$, $HOCH_2CH_2OC(O)C(CH_3)_2-$, $(CH_2=C(R^3)CO_2CH_2CH_2OC(O)C(CH_3)_2-$, or $CH_3OC(O)CH(CH_2CH_3)-$;

R^5 = 
;

g, g' independently = 1-6; and

L = H, $-CH_2C(O)C_6H_5$, $-CH_2C(O)C_6H_4OH$, $-CH_2C(O)C_6H_4OCH_3$, or $CH_2CH=CH_2$.

Monomers of formula [1] are known and can be made by known methods. See, for example, U.S. Patent Nos. 5,331,073 and 5,290,892. Many monomers of formula [1] are commercially available from a variety of sources. Preferred monomers of formula [1] include benzyl methacrylate; 2-phenylethyl methacrylate; 3-phenylpropyl methacrylate; 4-phenylbutyl methacrylate; 5-phenylpentyl methacrylate; 2-phenoxyethyl methacrylate; 2-(2-phenoxyethoxy)ethyl methacrylate; 2-benzyloxyethyl methacrylate; 2-(2-(benzyloxy)ethoxy)ethyl methacrylate; and 3-benzyloxypropyl methacrylate; and their corresponding acrylates.

Monomers of formula [2] are known and can be made by known methods. Many are commercially available. Preferred monomers of formula [2] include ethylene glycol dimethacrylate; diethylene glycol dimethacrylate; triethylene glycol dimethacrylate; 1,6-hexanediol dimethacrylate; 1,4-butanediol dimethacrylate; 1,4-benzenedimethanol dimethacrylate; and their corresponding acrylates. Most preferred is 1,4-butanediol diacrylate.

Macromers of formula [3] can be made by known methods, including controlled radical polymerization methods. For example, macromers of structure [3a] and [3b] may be prepared by atom transfer radical polymerization (ATRP). The methacrylate monomer is combined with copper(I) halide, amine ligand and solvent and polymerization is initiated with an activated alkyl halide. Once the desired conversion has been achieved, a second methacrylate monomer is added and the polymerization continued until the desired molecular weight is obtained. Alternatively, the polymerization of the first monomer is stopped by exposure to air and the polymer mixture is purified to remove residual monomer. The polymer is then recombined with copper(I) halide, amine ligand and solvent, and the second methacrylate monomer is added. In both cases, once the target copolymer molecular weight has been obtained, a radical scavenger or catalytic chain transfer reagent is added to produce a methacrylic polymer with unsaturated

end groups. See for example Norman, J. et al. *Macromolecules* **2002**, *35*, 8954-8961, or Bon, S. A. F. et al. *J. Polym. Sci., Polym. Chem.* **2000**, *38*, 2678.

Macromers of formula [3c] and [3d] may also be prepared by atom transfer radical polymerization (ATRP). In these cases, once the desired copolymer molecular weight has been obtained, the polymer is purified and reacted with a hydroxyl-functional primary amine to yield, for example, a hydroxyl terminated acrylic or methacrylic polymer. This product is then reacted with for example, methacryloyl chloride or isocyanatoethyl methacrylate to produce an unsaturated polymer chain end that is suitable for copolymerization with other acrylate or methacrylate monomers. See, generally, U.S. Patent Nos. 5,852,129, 5,763,548, and 5,789,487, and also Neugebauer, et al., "Densely-grafted and double-grafted PEO brushes via ATRP. A route to soft elastomers," *Macromolecules* **2003**, *36*, 6746-6755; Ishizu, et al., "Aggregation behaviors of AB-type brush-block-brush amphiphilic copolymers in aqueous media," *Journal of Materials Science* **2004**, *39*, 4295-4300; Kurjata, et al., "Synthesis of poly[dimethylsiloxane-block-oligo(ethylene glycol) methyl ether methacrylate]: an amphiphilic copolymer with a comb-like block," *Polymer* **2004**, *45*, 6111-6121; and Wang, et al., "Facile Atom Transfer Radical Polymerization of Methoxy-Capped Oligo(ethylene glycol) Methacrylate in Aqueous Media at Ambient Temperature," *Macromolecules* **2000**, *33*, 6640 – 6647.

Macromers of structure [3e] may also be prepared by atom transfer radical polymerization (ATRP). The methacrylate monomer is combined with copper(I) halide, amine ligand and solvent and polymerization is initiated with an activated alkyl halide. Once the desired conversion has been achieved, a second methacrylate monomer is added and the polymerization continued until the desired molecular weight is obtained. Alternatively, the polymerization of the first monomer is stopped by exposure to air and the polymer mixture is purified to remove residual monomer. The polymer is then

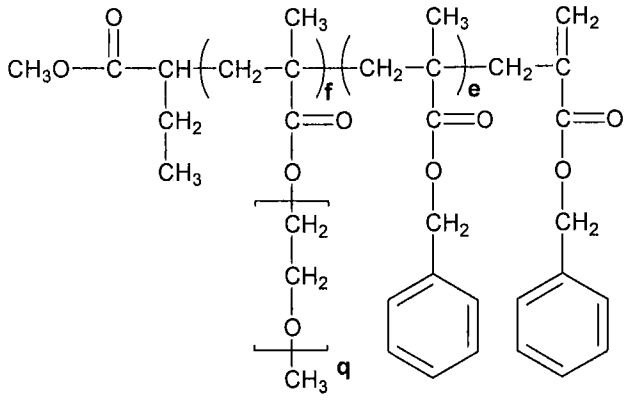
recombined with copper(I) halide, amine ligand and solvent, and the second methacrylate monomer is added. In both cases, once the target copolymer molecular weight has been obtained, an end-capping agent may added to produce a methacrylic polymer with desired end group functionality.

Likewise, these methodologies may be used to prepare macromonomers [3] using more than one monomer to create block and gradient macromonomers. For example, as is recognized in the art, gradient polymerization methods are known to produce some contamination in cases where monomer of the first block is present during the polymerization of the second block monomer. For convenience, the structure of [3] is drawn as shown but encompasses macromers of [3] made by either gradient or di-block methods.

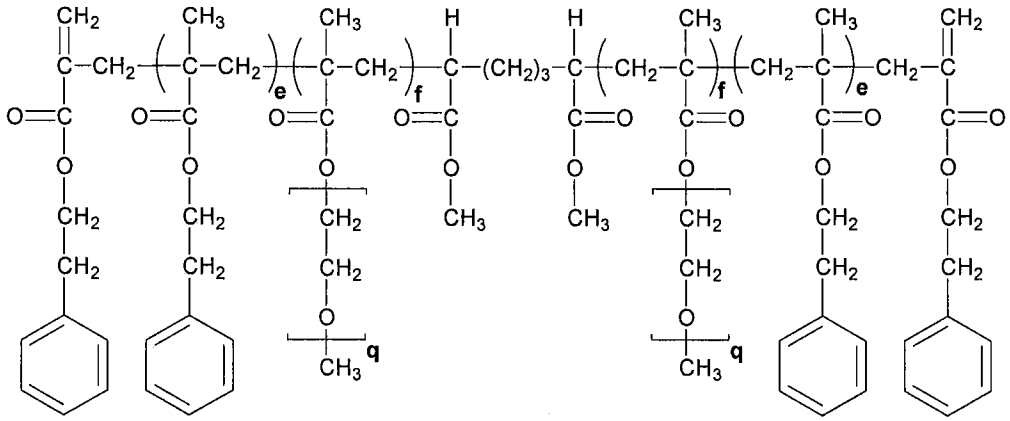
Gradient or tapered block copolymers are typically prepared in one-pot where the monomer of the first block is polymerized to selected conversion, at which point a second monomer with identical polymerizable functionality is added without removing the excess first monomer from the polymerization mixture. The copolymerization is continued until the target molecular weight is achieved, or if desired, additional portions of the second monomer may be added to further the tapered copolymer structure. Furthermore, controlled addition of the second monomer to the polymerization mixture, for example by use of a programmable syringe pump, will result in products with prescribed gradient (or tapered) copolymer structure.

By contrast, a di-block copolymer is prepared by stopping the polymerization of the first monomer at the desired molecular weight. The polymer is then isolated and purified to remove all unreacted monomer in a manner that preserves the reactive chain end functionality. This is then used to initiate polymerization of a second monomer, which, after quenching, produces a copolymer with two discrete monomer blocks.

For example, a preferred macromer [3] (shown below) is prepared from poly(ethylene glycol)200 monomethyl ether monomethacrylate and benzyl methacrylate (**X**, $\mathbf{X_1}$ = O, **Y** = $(CH_2CH_2)_qOCH_3$, $\mathbf{Y_1}$ = $CH_2C_6H_5$), with **f** ~ 15 and **e** ~ 45). This is combined in a minor amount (< 30 wt%) with aromatic acrylate or methacrylate monomer(s) [1] and cross-linker(s) [2] to create a high refractive index hydrophobic foldable intraocular lens that is resistant to temperature induced glistening formation.



Another preferred macromer [3] is prepared from poly(ethylene glycol)200 monomethyl ether monomethacrylate and 2-phenylethyl methacrylate (**X**, $\mathbf{X_1}$ = O, **Y** = $(CH_2CH_2)_qOCH_3$, $\mathbf{Y_1}$ = $CH_2CH_2C_6H_5$), with **f** ~ 8 and **e** ~ 23. This is combined in a minor amount (< 30 wt%) with aromatic acrylate or methacrylate monomer(s) [1] and cross-linker(s) [2] to create a high refractive index hydrophobic foldable intraocular lens that is resistant to temperature induced glistening formation.



The copolymeric materials of the present invention contain a total amount of monomer [1] in an amount from 65 to 95 %, preferably from 70 to 90 %. The difunctional cross-linker [2] concentration can be on the order of 0.5 to 3 % of the total concentration, and preferably from 1 to 2 %.

The materials of the present invention have at least one macromer of [3]. The total amount of macromer [3] depends on the desired physical properties for the device materials. The copolymeric materials of the present invention contain a total of at least 5 wt % and can contain as much as 35 % of macromer [3]. Preferably, the copolymeric device materials will contain 10 – 30 wt% of macromer [3]. Most preferably, the copolymeric device materials will contain 10 – 20 wt% of macromer [3].

The copolymeric device materials of the present invention optionally contain one or more ingredients selected from the group consisting of polymerizable UV absorbers and polymerizable colorants. Preferably, the device material of the present invention contains no other ingredients besides the monomers of formulas [1] and [2], the macromer [3], and the optional polymerizable UV absorbers and polymerizable colorants.

Reactive UV absorbers are known. A suitable reactive UV absorber is 2-(2'-hydroxy-3'-methallyl-5'-methylphenyl)benzotriazole, commercially available as o-Methallyl Tinuvin P ("oMTP") from Polysciences, Inc., Warrington, Pennsylvania. UV absorbers are typically present in an amount from about 0.1 - 5 %. Suitable reactive blue-light absorbing compounds include those described in U.S. Patent No. 5,470,932. Blue-light absorbers are typically present in an amount from about 0.01 - 0.5 %. When used to make IOLs, the device materials of the present invention preferably contain both a reactive UV absorber and a reactive colorant.

In order to form the device material of the present invention, the chosen ingredients [1], [2], and [3], along with any of the optional ingredients, are combined and polymerized using a radical initiator to initiate polymerization by the action of either heat or radiation. The device material is preferably polymerized in de-gassed polypropylene molds under nitrogen or in glass molds.

Suitable polymerization initiators include thermal initiators and photoinitiators. Preferred thermal initiators include peroxy free-radical initiators, such as t-butyl (peroxy-2-ethyl)hexanoate and di-(tert-butylcyclohexyl) peroxydicarbonate (commercially available as Perkadox® 16 from Akzo Chemicals Inc., Chicago, Illinois). Particularly in cases where the materials of the present invention do not contain a blue-light absorbing chromophore, preferred photoinitiators include benzoylphosphine oxide initiators, such as 2,4,6-trimethyl-benzoyldiphenyl-phosphine oxide, commercially available as Lucirin® TPO from BASF Corporation (Charlotte, North Carolina). Initiators are typically present in an amount equal to about 5 % or less of the total formulation weight, and more preferably less than 2 % of the total formulation. As is customary for purposes of calculating component amounts, the initiator weight is not included in the formulation weight % calculation.

The particular combination of the ingredients described above and the identity and amount of any additional components are determined by the desired properties of the finished device material. In a preferred embodiment, the device materials of the present invention are used to make IOLs having an optic diameter of 5.5 or 6 mm that are designed to be compressed or stretched and inserted through surgical incision sizes of 2 mm or less. For example, the macromonomer [3] is combined with a mono-functional acrylate or methacrylate monomer [1], a multifunctional acrylate or methacrylate cross-linker [2], a reactive UV absorber and a reactive colorant and copolymerized using a radical initiator in a suitable lens mold.

The device material preferably has a refractive index in the hydrated state of at least about 1.50, and more preferably at least about 1.53, as measured by an Abbe' refractometer at 589 nm (Na light source) and 25 °C. Optics made from materials having a refractive index lower than 1.50 are necessarily thicker than optics of the same power which are made from materials having a higher refractive index. As such, IOL optics made from materials with comparable mechanical properties and a refractive index lower than about 1.50 generally require relatively larger incisions for IOL implantation.

The proportions of the monomers and macromer to be included in the copolymers of the present invention should be chosen so that the copolymer has a glass transition temperature (T_g) not greater than about 37 °C, which is normal human body temperature. Copolymers having glass transition temperatures higher than 37 °C are not suitable for use in foldable IOLs; such lenses could only be rolled or folded at temperatures above 37 °C and would not unroll or unfold at normal body temperature. It is preferred to use copolymers having a glass transition temperature somewhat below normal body temperature and no greater than normal room temperature, e.g., about 20 - 25 °C, in order that IOLs made of such copolymers can be rolled or folded conveniently at room temperature. T_g is measured by differential scanning calorimetry at 10 °C/min., and is determined at the midpoint of the transition of the heat flux curve.

For IOLs and other applications, the materials of the present invention must exhibit sufficient strength to allow devices made of them to be folded or manipulated without fracturing. Thus the copolymers of the present invention will have an elongation of at least 80%, preferably at least 100%, and most preferably greater than 110%. This property indicates that lenses made of such materials generally will not crack, tear or split when folded. Elongation of polymer samples is determined on dumbbell shaped tension test specimens with a 20 mm total length, length in the grip area of 4.88 mm, overall width of

2.49 mm, 0.833 mm width of the narrow section, a fillet radius of 8.83 mm, and a thickness of 0.9 mm. Testing is performed on samples at ambient conditions using an Instron Material Tester (Model No. 4442 or equivalent) with a 50 Newton load cell. The grip distance is set at 14 mm and a crosshead speed is set at 500 mm/minute and the sample is pulled until failure. The elongation (strain) is reported as a fraction of the displacement at failure to the original grip distance. Since the materials to be tested are essentially soft elastomers, loading them into the Instron machine tends to make them buckle. To remove the slack in the material sample a pre-load is placed upon the sample. This helps to reduce the slack and provide a more consistent reading. Once the sample is pre-loaded to a desired value (typically 0.03 to 0.05 N) the strain is set to zero and the test begun. The modulus is calculated as the instantaneous slope of the stress-strain curve at 0% strain ("Young's modulus"), 25% strain ("25% modulus") and 100 % strain ("100% modulus).

IOLs made of the ophthalmic device materials of the present invention are more resistant to glistenings than other materials. Glistenings are measured according to the following test. The presence of glistenings is measured by placement of a lens or disk sample into a vial or sealed glass chamber and adding deionized water or a balanced salt solution. The vial or glass chamber is then placed into a water bath preheated to 45 °C. Samples are to be maintained in the bath for a minimum of 16 hours and preferably 24 ± 2 hours. The vial or glass chamber is then cooled to ambient temperature for a minimum of 60 minutes and preferably 90 ± 30 minutes. The sample is inspected visually in various on angle or off angle lighting to evaluate clarity. Visualization of glistenings is carried out at ambient temperature with a light microscope using a magnification of 50 to 200x. A sample is judged to have many glistenings if, at 50 – 200x magnification, there are approximately 50 to 100 % as many glistenings as observed in control samples based on 65 weight % 2-phenylethyl acrylate, 30 weight % 2-phenylethyl methacrylate, 3.2 weight % BDDA, and 1.8 weight % OMTP. Similarly, a sample is judged to

have few glistenings if there are approximately 10 % or more glistenings relative to the quantity observed in control samples. A sample is judged to have very few glistenings if there are approximately 1 % or more glistenings relative to a control sample. A sample is judged to be free of glistenings if the number of glistenings detected in the eyepiece is zero. A sample is judged to be substantially free of glistenings if, at 50 - 200x magnification, the number of glistenings detected in the eyepiece is less than about $2/mm^3$. It is often very difficult to detect glistenings, especially at surfaces and edges where more defects and debris have formed, so the sample is rastered throughout the entire volume of the lens, varying the magnification levels (50 - 200x), the aperture iris diaphragm, and the field conditions (using both bright field and dark field conditions) in an attempt to detect the presence of glistenings.

The copolymers of the present invention most preferably have an equilibrium water content (EWC) of 0.5 – 3.0%. EWC may be gravimetrically determined by comparison of dry and hydrated sample weight. First, the dry sample weight is obtained, then the sample is placed in a suitable container and equilibrated in de-ionized H_2O at a prescribed temperature for at least 24 h. The sample is then removed from the de-ionized H_2O, excess surface water is removed and the sample is weighed. EWC is determined by the following formula: $\%EWC = [(wt_{hyd} - wt_{dry}) / wt_{hyd}] \times 100$

IOLs constructed of the device materials of the present invention can be of any design capable of being stretched or compressed into a small cross section that can fit through a 2-mm incision. For example, the IOLs can be of what is known as a one-piece or multi-piece design, and comprise optic and haptic components. The optic is that portion which serves as the lens and the haptics are attached to the optic and are like arms that hold the optic in its proper place in the eye. The optic and haptic(s) can be of the same or different material. A multi-piece lens is so called because the optic and the haptic(s) are made separately and then the haptics are attached to the optic. In a single piece lens, the optic and the haptics are formed out of one piece of material.

Depending on the material, the haptics are then cut, or lathed, out of the material to produce the IOL.

In addition to IOLs, the materials of the present invention are also suitable for use as other ophthalmic or otorhinolaryngological devices such as contact lenses, keratoprostheses, corneal inlays or rings, otological ventilation tubes and nasal implants.

The invention will be further illustrated by the following examples, which are intended to be illustrative, but not limiting.

EXAMPLES

All monomers, cross-linkers and initiators were purchased from commercial sources. Polyethylene glycol(200) monomethylether monomethacrylate (PEG200-MA), 2-phenylethyl methacrylate (PEMA) and benzyl methacrylate (BzMA) were each passed through basic alumina and degassed with N_2 prior to use. 2-Phenylethyl acrylate (PEA), benzyl acrylate (BzA) and 1,4-butanediol diacrylate (BDDA) were purified by column chromatography prior to use. N,N,N',N',N"-pentamethyldiethylene triamine (PMDETA) was dried over calcium hydride and vacuum distilled prior to use. Acetone and toluene were each bubbled with N_2 and stored in the glove box. 2-Bromo-2-methyl-propionic acid 2-(2-bromo-2-methyl-propionyloxy)-ethyl ester was synthesized by esterification of ethylene glycol with 2-bromoisobutyryl bromide in the presence of pyridine. All other chemicals were of highest purity available and used as received. All reaction manipulations were performed in a N_2-filled glove box.2,2-Azobisisobutyronitrile (AIBN) was recrystallized from methanol prior to use.

Polypropylene molds were vacuum de-gassed at 90 °C prior to use. The molds were placed in a nitrogen atmosphere glove box immediately after degassing. The monomer(s), macromer, cross-linker and initiator were

combined as indicated in Table 1, then placed under low vacuum to remove any trapped air bubbles, back-flushed with nitrogen, and immediately placed in the glove box. The monomer formulation was dispensed into vacuum de-gassed polypropylene molds using a syringe equipped with a 0.2-μm PTFE filter. The filled molds were placed in a convection oven for 1 h at 70 °C, then 2 hrs at 110 °C. The resulting polymer samples were removed from the molds and extracted in refluxing acetone for 6 hours, rinsed and air dried, then placed under vacuum at 70 °C for at least 15 hrs. Tensile properties, T_g, EWC, and glistening resistance were determined according to the methods described above. The results are listed in Table 2.

Table 1. Formulation Component Detail

ID	PEA (wt%)	BzA (wt%)	PEMA (wt%)	BzMA (wt%)	cross-linker (wt%)	PEG200-MA (wt%)	EX. 1 (wt%)	EX. 2 (wt%)	EX. 3 (wt%)	EX. 4 (wt%)
0	65.0	30.0	–	3.2	1.8	–	–	–	–	–
1	58.98	–	16.58	20.02	BDDA (1.02)	3.40	–	–	–	–
2	88.97	–	–	–	BDDA (1.02)	–	10.01	–	–	–
3	79.00	–	–	–	BDDA (1.00)	–	20.00	–	–	–
4	78.70	–	–	–	1,3-BDMDA(1.33)	–	19.98	–	–	–
5	78.76	–	–	–	1,4-BDMDA (1.24)	–	20.00	–	–	–
6	68.95	–	–	19.99	BDDA (1.02)	–	10.04	–	–	–
7	68.98	–	–	10.00	BDDA (1.00)	–	20.02	–	–	–
8	58.98	–	–	19.99	BDDA (1.01)	–	20.03	–	–	–
9	58.47	–	–	19.99	BDDA (1.52)	–	20.02	–	–	–
10	78.97	–	–	–	BDDA (1.01)	–	–	20.01	–	–
11	68.48	–	–	19.99	BDDA (1.50)	–	–	10.03	–	–
12	58.47	–	–	20.00	BDDA (1.50)	–	–	20.02	–	–
13	–	88.47	–	–	BDDA (1.50)	–	–	10.03	–	–
14	–	87.98	–	–	BDDA (2.02)	–	–	10.01	–	–
15	–	83.46	–	5.04	BDDA (1.51)	–	–	9.99	–	–
16	–	78.97	–	–	BDDA (1.02)	–	–	–	20.01	–
17	–	88.49	–	–	BDDA (1.50)	–	–	–	10.01	–
18	–	78.48	–	–	BDDA (1.50)	–	–	–	20.02	–
19	–	93.49	–	–	BDDA (1.51)	–	–	–	–	5.00
20	–	88.48	–	–	BDDA (1.50)	–	–	–	–	10.02
21	–	78.50	–	–	BDDA (1.51)	–	–	–	–	20.00
22	–	87.48	–	1.00	BDDA (1.50)	–	–	10.02	–	–
23	–	86.98	–	1.50	BDDA (1.50)	–	–	10.02	–	–
24	–	86.49	–	2.01	BDDA (1.50)	–	–	10.00	–	–
25	–	88.49	–	–	BDDA (1.51)	–	–	10.00	–	–

Table 2. Tensile and Thermal Properties, %EWC, RI, and ΔT Microvacuole Test Results

ID	Stress at Break (MPa)	Strain at Break (MPa)	Young's Modulus (MPa)	100% Secant Modulus (MPa)	T_g (mid, °C)	Tg (end, °C)	Glistenings	EWC (%)	RI (hydrated, 22 °C)
0	8.12	104	57.30	7.51	–	–	Many	0.30	–
1	8.67	202	58.91	3.63	–	–	Many	0.42	–
2	2.95	185	3.20	0.79	–	–	None	0.56	–
3	3.28	184	4.05	0.89	–	–	None	0.91	–
4	3.74	181	4.65	0.99	–	–	None	0.86	–
5	3.89	174	4.55	1.06	–	–	None	0.90	–
6	7.42	211	34.16	2.44	–	–	Very Few	0.54	–
7	5.36	198	11.96	1.39	–	–	None	0.81	–
8	8.06	206	45.19	3.04	–	–	None	0.84	–
9	9.22	166	58.27	4.36	–	–	None	1.01	–
10	2.90	176	3.85	0.90	-2.1	1.6	None	2.06	–
11	7.28	167	28.98	2.86	7.7	12.7	None	1.16	–
12	8.33	165	39.48	3.56	8.3	14.3	None	1.91	–
13	6.01	178	14.40	1.76	7.9	12.2	None	1.28	–
14	6.70	154	16.37	2.41	–	–	None	1.23	–
15	11.29	179	97.32	5.07	–	–	None	1.06	–
16	3.92	193	5.39	0.95	–	–	None	1.62	–
17	9.62	188	64.88	3.80	–	–	None	1.09	–
18	9.91	184	62.34	4.07	–	–	None	1.99	–
19	9.68	189	64.11	3.71	–	–	Very Few	0.58	1.5633
20	10.23	186	72.68	4.31	–	–	None	1.13	1.5610
21	10.48	164	83.97	5.69	–	–	None	1.75	1.5557
22	9.69	184	64.69	3.74	–	–	None	1.32	–
23	10.03	186	70.50	3.88	–	–	None	1.41	–
24	9.81	181	77.82	4.05	–	–	None	1.29	–
25	9.20	189	42.11	2.83	–	–	None	1.29	–

Ex. 1. PEMA-PEG200MA-PEMA Triblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.5819 g (5.88 mmol) of CuCl, 1.4923 g (8.42 mmol) of PMDETA, and 11.9253 g (41.69 mmol) of PEG200-MA. Acetone (25 mL) was added, and the mixture was stirred to disperse the solids. 2-Bromo-2-methyl-propionic acid 2-(2-bromo-2-methyl-propionyloxy)-ethyl ester (1.0336 g, 2.87 mmol) was dissolved in acetone and added and the reaction mixture. The reaction was stirred at ambient temperature for 30 min. PEMA (25.3413 g, 133.21 mmol) was added to the polymerization along with an additional 25 mL of acetone. The reaction was stirred 2.5 hr at ambient temperature. 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) was weighed in a vial (0.9127 g, 5.84 mmol), dissolved in 2 mL of acetone and added to the reaction mixture. The flask was immersed in an oil bath and heated at 50 °C for 14 hr, then cooled to room temperature. The reaction flask was removed from the glove box and bubbled with air for 30 min. The product was purified by passing through a short column of basic alumina column prepared in CH_2Cl_2. The product was eluted with CH_2Cl_2, the solvent was rotovapped and the product collected by precipitation into n-propanol. The resulting polymer was rinsed with fresh n-propanol, then dried under vacuum at room temperature overnight. Yield 16.37 g (44%) of a colorless gummy solid. GPC (THF, polystyrene standards) M_n 16,565, M_w/M_n 1.29.

Ex. 2. PEMA-PEG200MA-PEMA Triblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.6041 g (6.10 mmol) of CuCl, 1.5638 g (8.82 mmol) of PMDETA, and 12.9677 g (45.33 mmol) of PEG200-MA. Acetone (25 mL) was added, and the mixture was stirred to disperse the solids. Dimethyl-2,6-dibromoheptanedioate (DMDBH) (1.0182 g, 2.94 mmol) was added and the reaction was stirred at ambient temperature for 1.75 hr. PEMA (24.7718 g, 130.21 mmol) was added to the polymerization along with 50 mL of acetone. The reaction was stirred 4.25 hr at ambient temperature. 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) was weighed in a vial (0.9515 g, 6.09 mmol),

dissolved in 2 mL of acetone and added to the reaction mixture. The flask was immersed in an oil bath and heated at 50 °C for 15.5 hr, then cooled to room temperature. The reaction flask was removed from the glove box and bubbled with air for 30 min. The product was purified by passing through a short column of basic alumina column prepared in CH_2Cl_2. The product was eluted with CH_2Cl_2, the solvent was rotovapped and the product collected by precipitation into 5 °C n-propanol. The resulting polymer was rinsed with fresh n-propanol, then dried under vacuum at room temperature overnight. Yield 11.97 g (32%) of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 15,618 M_w/M_n 1.34.

Ex. 3. PEG200MA-PEMA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.3173 g (3.21 mmol) of CuCl, 0.7866 g (4.44 mmol) of PMDETA, and 12.6677 g of PEG200-MA. Acetone (25 mL) was added, and the mixture was stirred to disperse the solids. Methyl 2-bromopropionate (0.5507 g, 3.30 mmol) was added and the reaction was stirred at ambient temperature for 2 hr. PEMA (25.0914 g, 131.89 mmol) was added to the polymerization along with 50 mL of acetone. The reaction was stirred overnight at ambient temperature. 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) was weighed in a vial (0.4978 g, 3.19 mmol), dissolved in 2 mL of acetone and added to the reaction mixture. The flask was immersed in an oil bath and heated to 50 °C for 6 hr, then cooled to room temperature. The reaction flask was removed from the glove box and bubbled with air for 30 min. The product was purified by passing through a short column of basic alumina column prepared in CH_2Cl_2. The product was eluted with CH_2Cl_2, the solvent was rotovapped and the product collected by precipitation into 5 °C isopropanol. The resulting polymer was rinsed with fresh IPA, then dried under vacuum at room temperature overnight. Yield 21.41 g (64%) of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 22,490, M_w/M_n 1.28.

Ex. 4. PEG200MA-BzMA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.3195 g (3.23 mmol) of CuCl, 0.5928 (3.34 mmol) of PMDETA, and 12.8104 g (44.78 mmol) of PEG200-MA. Toluene (25 mL) was added and the reaction mixture was immersed in a 60 °C oil bath. Once the solids had dispersed, methyl 2-bromobutyrate (0.4697 g, 2.59 mmol) was added. The reaction was stirred at 60 °C for 1 hr, followed by addition of 22.8213 g (129.51 mmol) of BzMA and 45 mL of toluene. After 6.5 hr further reaction, TEMPO (0.5231 g, 3.35 mmol) was dissolved in toluene and added. Heating was continued for 16 hr, then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and bubbled with air for 30 min. The product was purified by passing through a short column of basic alumina column prepared in CH_2Cl_2. The product was eluted with CH_2Cl_2, the solvent was rotovapped and the product collected by precipitation into 0 °C isopropanol. The resulting polymer was rinsed with fresh IPA, then dried under vacuum at room temperature overnight. Yield 8.93 g (25%) of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 23,337, M_w/M_n 1.19.

Ex. 5. PEG200MA-POEMA Triblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.6018 g (6.08 mmol) of CuCl, 1.5726 g (8.87 mmol) of PMDETA, 12.5997 g (44.05 mmol) of PEG200-MA, and 25 mL of acetone. Once the solids had dispersed, 0.9157 g (2.65 mmol) of dimethyl -2,6-dibromoheptanedioate was added. The reaction was stirred at ambient temperature (22 °C) for 1 hr 40 min, then 37.4515 g (181.59 mmol) of phenoxyethyl methacrylate (POEMA) and 25 mL of acetone was added. After 3.5 hr further reaction time, 0.9841 g (6.29 mmol) of TEMPO was dissolved in acetone and added to the reaction mixture. The reaction flask was immersed in a 50 °C oil bath for 15.5 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and bubbled with air for 30 min. The product was purified by passing through a

short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product collected by precipitation into -5 °C n-propanol. The resulting polymer was rinsed with fresh n-propanol, then dried under vacuum at room temperature overnight. Yield 14.18 g of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 41,833, M_w/M_n 2.06.

Ex. 6. PEG200MA-PEMA Triblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.6078 g (6.14 mmol) of CuCl, 1.5574 g (8.78 mmol) of PMDETA, 12.3783 g (43.27 mmol) of PEG200-MA, and 25 mL of acetone (25 mL). Once the solids had dispersed, 0.9257 g (2.68 mmol) of dimethyl -2,6-dibromoheptanedioate was added. The reaction was stirred at ambient temperature (22 °C) for 1 hr, then 34.6909 g (182.35 mmol) of PEMA and 25 mL of acetone was added. After 4 hr further reaction time, 0.9702 g (6.21 mmol) of TEMPO was dissolved in acetone and added to the reaction mixture. The reaction flask was immersed in a 50 °C oil bath for 2.5 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and bubbled with air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product purified further by precipitation into -5 °C n-propanol and -5 °C hexane. The resulting polymer was rinsed with fresh hexane, and then dried under vacuum at room temperature overnight. Yield 22.92 g of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 27,186, M_w/M_n 1.35.

Ex. 7. PEG200MA-PEMA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.3146 g (3.18 mmol) of CuCl, 0.8080 g (4.56 mmol) of PMDETA, 12.8199 g (44.82 mmol) of PEG200-MA, and 25 mL of toluene. Once the solids had dispersed, 0.5620 g (2.88 mmol) of ethyl 2-bromoisobutyrate was added. The reaction was stirred at ambient temperature (22 °C) for 2 hr 10 min, then 25.5059 g (134.07 mmol) of PEMA and 50 mL of toluene was

added. After 3 hr further reaction time, 0.5045 g (3.23 mmol) of TEMPO was dissolved in toluene and added to the reaction mixture. The reaction flask was immersed in a 50 °C oil bath for 15 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and exposed to air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product was collected by precipitation into 0 °C isopropanol. The resulting polymer was rinsed with fresh isopropanol, and then dried under vacuum at room temperature overnight. Yield 12.14 g of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 17,536, M_w/M_n 1.29.

Ex. 8. PEG200MA-PEMA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.4039 g (4.08 mmol) of CuCl, 0.7344 g (4.14 mmol) of PMDETA, 12.7295 g (44.50 mmol) of PEG200-MA, and 25 mL of toluene. The flask was stirred at room temperature until the solids dispersed, then immersed in a 60 °C oil bath and 0.7330 g (3.76 mmol) of ethyl 2-bromoisobutyrate was added. The reaction was stirred at 60 °C for 2 hr 20 min, then 33.9764 g (178.60 mmol) of PEMA and 50 mL of toluene was added. After 5.5 hr further reaction time, 0.6390 g (4.09 mmol) of TEMPO was dissolved in toluene and added to the reaction mixture. The reaction flask was heated in a 60 °C oil bath for an additional 16 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and exposed to air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product was collected by precipitation into 0 °C isopropanol. The resulting polymer was dissolved in CH_2Cl_2 and precipitated into 0 °C hexane and rinsed with fresh hexane, and then dried under vacuum at room temperature overnight. Yield 16.74 g of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 21,039, M_w/M_n 1.19.

Ex. 9. DEGMA-BzMA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.4654g (4.70 mmol) of CuCl, 0.8505 g (4.80 mmol) of PMDETA, 12.3379 g (65.55 mmol) of diethyleneglycol monomethylether methacrylate (DEGMA), and 25 mL of acetone. The flask was stirred at room temperature until the solids dispersed and 0.7222 g (3.99 mmol) of methyl 2-bromobutyrate was added. The reaction was stirred at ambient temperature (22 °C) for 1 hr, and then 18.9499 g (107.54 mmol) of BzMA and 40 mL of acetone was added. After 4 hr further reaction, 0.7345 g (4.70 mmol) of TEMPO was dissolved in acetone and added to the reaction mixture. The reaction flask was immersed in a 50 °C oil bath for 14 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and exposed to air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product was collected by precipitation into 0 °C isopropanol, and rinsed with fresh isopropanol, and then dried under vacuum at room temperature overnight. Yield 4.38 g of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 13,807, M_w/M_n 1.33.

Ex. 10. BzMA-PEG200MA Diblock Copolymer (Reverse Addition)

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.3169 g (3.20 mmol) of CuCl, 0.6001 g (3.38 mmol) of PMDETA, 23.0942 g (131.06 mmol) of benzyl methacrylate (BzMA), and 45 mL of acetone. The flask was stirred at room temperature until the solids dispersed and 0.4769 g (2.63 mmol) of methyl 2-bromobutyrate was added. The reaction was stirred at ambient temperature (22 °C) for 2.5 hr, and then 12.8530 g (44.93 mmol) of PEG200-MA and 25 mL of acetone was added. After 3.5 hr further reaction time, 0.4855 g (3.11 mmol) of TEMPO was dissolved in acetone and added to the reaction mixture. The reaction flask

was immersed in a 50 °C oil bath for 15 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and exposed to air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product was precipitated twice into cold (15 °C) isopropanol, rinsed with fresh isopropanol, and then dried under vacuum at room temperature overnight. Yield 9.29 g of a colorless solid. GPC (THF, polystyrene standards) M_n 10,646, M_w/M_n 1.63.

Ex. 11. BzMA-PEG400MA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.3200 g (3.23 mmol) of CuCl, 0.5787 g (3.26 mmol) of PMDETA, 12.7206 g (25.39 mmol) of PEG400-MA, and 25 mL of acetone. The flask was stirred at room temperature until the solids dispersed and 0.4907 g (2.71 mmol) of methyl 2-bromobutyrate was added. The reaction was stirred at ambient temperature (22 °C) for 1.25 hr, and then 23.8229 g (135.20 mmol) of BzMA and 45 mL of acetone was added. After 5.5 hr further reaction time, 0.4915 g (3.15 mmol) of TEMPO was dissolved in acetone and added to the reaction mixture. The reaction flask was immersed in a 50 °C oil bath for 15 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and exposed to air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product was precipitated into 15 °C isopropanol, rinsed with fresh isopropanol, and then dried under vacuum at room temperature overnight. Yield 9.17 g of a colorless solid. GPC (THF, polystyrene standards) M_n 27,641, M_w/M_n 1.26.

Ex. 12. DEGMA-BzMA Diblock Copolymer

A 200-mL round bottom flask containing a PTFE coated stir bar was charged with 0.4916 g (4.97 mmol) of CuCl, 0.8818 g (4.97 mmol) of PMDETA, 25.2357 g (134.08 mmol) of diethyleneglycol monomethylether methacrylate (DEGMA), and 50 mL of acetone. The flask was stirred at room temperature

until the solids dispersed and 0.7535 g (4.16 mmol) of methyl 2-bromobutyrate was added. The reaction was stirred at ambient temperature (22 °C) for 2 hr, and then 24.6653 g (139.98 mmol) of BzMA and 50 mL of acetone was added. After 4.5 hr further reaction, 0.7546 g (4.83 mmol) of TEMPO was dissolved in acetone and added to the reaction mixture. The reaction flask was immersed in a 50 °C oil bath for 15 hr, and then the reaction was allowed to cool to room temperature. The reaction flask was removed from the glove box and exposed to air for 30 min. The product was purified by passing through a short column of basic alumina and eluted with CH_2Cl_2. The solvent was rotovapped and the product was precipitated into 5 °C isopropanol, rinsed with fresh isopropanol, and then dried under vacuum at room temperature overnight. Yield 7.89 g of a colorless glassy solid. GPC (THF, polystyrene standards) M_n 19,672, M_w/M_n 1.17.

Table 3. Formulation Component Detail

ID	PEA (wt%)	BzA (wt%)	PEMA (wt%)	BzMA (wt%)	BDDA (wt%)	EX. 5 (wt%)	EX. 6 (wt%)	EX. 7 (wt%)	EX. 8 (wt%)
26	88.99	–	–	–	1.02	10.00	–	–	–
27	78.99	–	–	–	1.00	20.01	–	–	–
28	68.98	–	–	–	1.00	30.01	–	–	–
29	78.99	–	–	–	1.01	–	20.00	–	–
30	68.97	–	–	–	1.01	–	30.03	–	–
31	–	78.96	–	–	1.00	–	–	20.04	–
32	–	88.45	–	–	1.53	–	–	–	10.01
33	–	78.47	–	–	1.53	–	–	–	20.00
34	–	68.49	–	–	1.51	–	–	–	30.00

Table 4. Tensile and Thermal Properties, %EWC, RI, and ΔT Microvacuole Test Results

ID	Stress at Break (MPa)	Strain at Break (MPa)	Young's Modulus (MPa)	100% Secant Modulus (MPa)	Glistenings)	EWC (%)
26	4.22	189	4.30	1.16	Very Few	0.83
27	5.16	175	8.82	2.06	Very Few	1.49
28	6.56	166	18.67	3.36	Very Few	2.14
29	4.22	196	6.24	1.06	Very Few	1.37
30	4.80	194	8.92	1.33	Very Few	1.85
31	3.19	185	4.11	0.87	None	2.44
32	11.26	186	62.20	3.93	None	0.97
33	10.55	175	69.76	4.35	None	1.64
34	10.08	156	85.35	5.47	Very Few	2.08

Table 5. Formulation Component Detail

ID	PEA (wt%)	BzA (wt%)	PEMA (wt%)	BzMA (wt%)	BDDA (wt%)	EX. 9 (wt%)	EX. 10 (wt%)	EX. 11 (wt%)	EX. 12 (wt%)
35	78.97	–	–	–	1.00	20.03	–	–	–
36	68.98	–	–	–	1.00	30.02	–	–	–
37	–	88.49	–	–	1.51	–	10.00	–	–
38	–	88.45	–	–	1.51	–	–	10.04	–
39	–	78.50	–	–	1.50	–	–	–	20.00
40	78.97	–	–	–	1.01	–	–	–	20.01
41	–	68.96	–	–	1.01	–	–	–	30.03
42	68.96	–	–	–	1.01	–	–	–	30.03

Table 6. Tensile and Thermal Properties, %EWC, RI, and ΔT Microvacuole Test Results

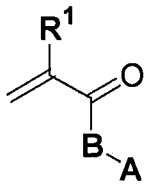
ID	Stress at Break (MPa)	Strain at Break (MPa)	Young's Modulus (MPa)	100% Secant Modulus (MPa)	Glistenings	EWC (%)
35	5.10	186	11.46	1.75	Many	0.69
36	6.70	175	25.80	3.13	Many	0.60
37	–	–	–	–	Many	0.52
38	–	–	–	–	Very Few	1.38
39	–	–	–	–	Very Few	0.59
40	–	–	–	–	Very Few	0.71
41	–	–	–	–	Very Few	0.82
42	–	–	–	–	Very Few	0.89

This invention has been described by reference to certain preferred embodiments; however, it should be understood that it may be embodied in other specific forms or variations thereof without departing from its special or essential characteristics. The embodiments described above are therefore considered to be illustrative in all respects and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description.

What is claimed is:

1. A polymeric ophthalmic or otorhinolaryngological device material comprising

a) 65 to 95 % (w/w) of a monofunctional acrylate or methacrylate monomer of formula [1]:



[1]

wherein

B = $-O(CH_2)_n-$, $-(OCH_2CH_2)_n-$; $-NH(CH_2)_n-$, or $-NCH_3(CH_2)_n-$;

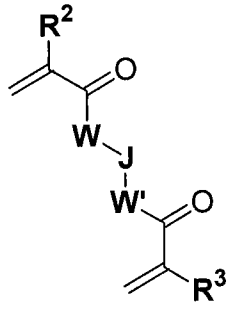
R^1 = H, CH_3, CH_2CH_3, or CH_2OH;

n = 0 - 12;

A = C_6H_5 or $O(CH_2)_mC_6H_5$, where the C_6H_5 group is optionally substituted with $-(CH_2)_nH$, $-O(CH_2)_nH$, $-CH(CH_3)_2$, $-C_6H_5$, $-OC_6H_5$, $-CH_2C_6H_5$, F, Cl, Br, or I; and

m = 0 – 18;

b) a difunctional acrylate or methacrylate cross-linking monomer of formula [2]:



[2]

wherein

R^2, R^3 independently = H, CH_3, CH_2CH_3, or CH_2OH;

W, W' independently = $O(CH_2)_d$, $NH(CH_2)_d$, $NCH_3(CH_2)_d$, $O(CH_2)_dC_6H_4$, $O(CH_2CH_2O)_dCH_2$, $O(CH_2CH_2CH_2O)_dCH_2$, $O(CH_2CH_2CH_2CH_2O)_dCH_2$, or nothing;

J = $(CH_2)_a$, $O(CH_2CH_2O)_b$, O, or nothing, provided that if W and W' = nothing, then J ≠ nothing;

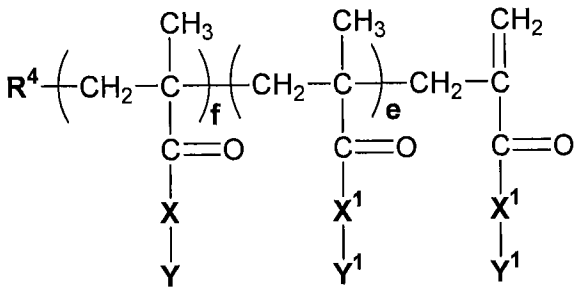
d = 0 - 12;

a = 1 – 12; and

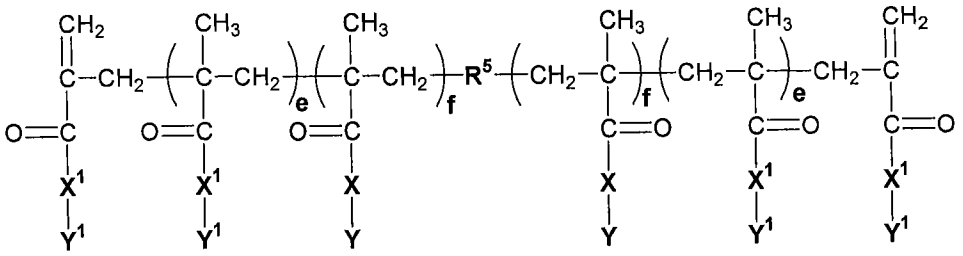
b = 1 – 24;

and

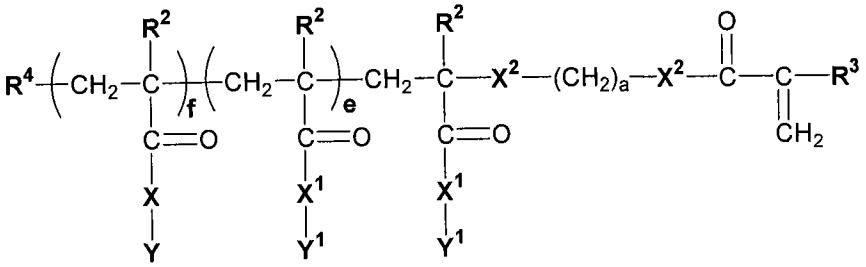
c) 5 to 35 % (w/w) of a hydrophilic side-chain macromer of formula [3a], [3b], [3c], [3d], or [3e]:



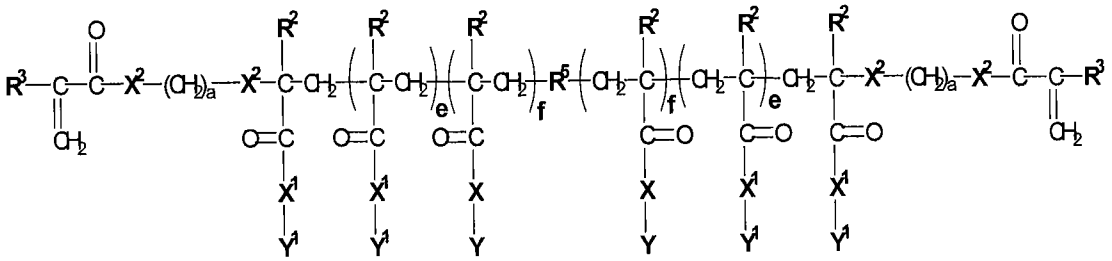
[3a]



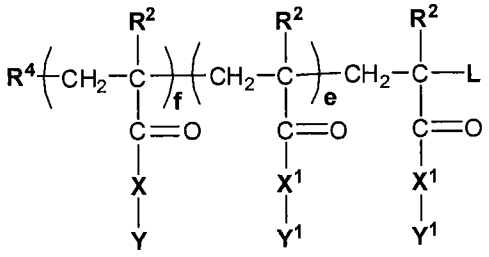
[3b]



[3c]



[3d]



[3e]

wherein for formulas [3a], [3b], [3c], [3d], and [3e]

e, f independently = 1 – 100;

X, X^1, X^2 independently = O, NH-, $N(CH_3)$-, $N(CH_2CH_3)$-, or $N(C_6H_5)$-;

Y, Y^1 independently = -H, $-(CH_2)_pH$, $-(CH_2)_pOH$, $-CHC(CH_3)_2$, $-CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $CH_2CH_2N(C_6H_5)_2$, $-CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2OC_6H_5$, $(CH_2CH_2O)_qCH_3$, $(CH_2CH(CH_3)O)_qCH_3$, $(CH_2CH_2CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qH$, $(CH_2CH(CH_3)O)_qH$, $(CH_2CH_2CH_2CH_2O)_qH$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, $(CH_2)_tOC_6H_5$, or $CH_2CH_2N(-C(O)CH_2CH_2CH_2-)$,

provided that $Y \neq Y^1$,

and further provided that at least one of Y and Y^1 = $CH_2CH_2N(CH_3)_2$, $-CH_2CH_2N(CH_2CH_3)_2$, $CH_2CH_2N(C_6H_5)_2$, $-CH_2CH(OH)CH_2OH$, $CH_2CH(OH)CH_2OC_6H_5$, $(CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qH$, $(CH_2CH_2O)_qC_6H_5$, or $CH_2CH_2N(-C(O)CH_2CH_2CH_2-)$; and the other of Y and Y^1 = -H, $-(CH_2)_pH$, , $-CHC(CH_3)_2$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, or $(CH_2)_tOC_6H_5$;

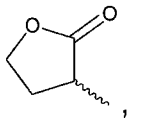
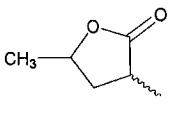
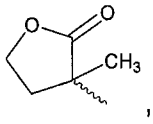
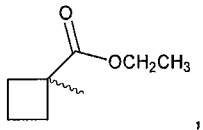
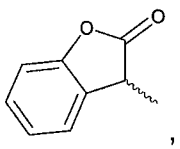
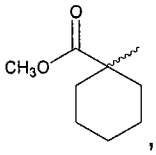
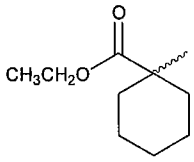
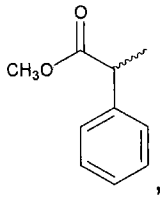
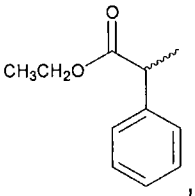
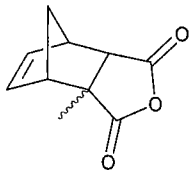
p = 1 – 18;

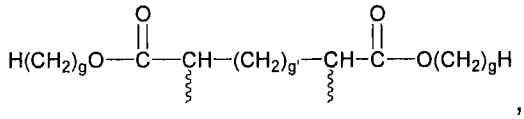
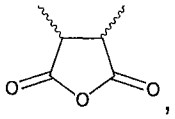
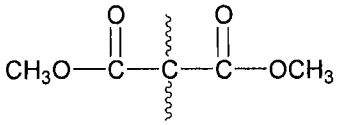
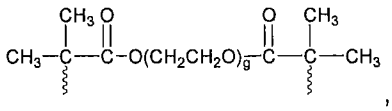
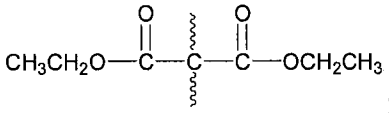
q = 1 – 230;

t = 0 – 6;

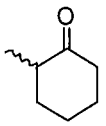
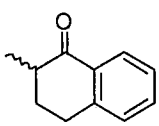
R^4 = $CH_3OC(O)CH(CH_3)$-, $CH_3OC(O)C(CH_3)_2$-, $HOCH_2CH_2OC(O)C(CH_3)_2$-, $(CH_2=C(R^3)CO_2CH_2CH_2OC(O)C(CH_3)_2$-, $CH_3CH_2OC(O)CH(CH_3)$-, $CH_3CH_2OC(O)C(CH_3)_2$-, $CH_3OC(O)CH(CH_2CH_3)$-, $CH_3CH_2OC(O)CH(CH_2CH_3)$-, $CH_2=CHCH_2OC(O)C(CH_3)_2$-, $CH_3CH_2OC(O)CH(CH_2CH_2CH_3)$-, $CH_3OC(O)CH(CH_2CH_2CH_2CH_3)$-, $[CH_3OC(O)]_2CH$-,

$[CH_3CH_2OC(O)]_2CH$-, $[CH_3CH_2OC(O)]_2C(CH_3)$-,
$CH_3CH_2OC(O)CH(CH_2CH_2CH_2CH_3)$-, $(CH_3)_3COC(O)C(CH_3)_2$-,
$CH_3CH_2OC(O)CH_2CH_3(CH_2CH_2CH_2CH_3)$-,
$CH_3CH_2OC(O)CH(CH_2CH_2CH_2CH_2CH_3)$-,
$CH_3CH_2OC(O)CH(CH_2CH_2CH_2CH_2CH_2CH_3)$-,


,

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,

,

,

,

,

,

, or

;

R^5 =

,

,

,

, or

;

g, g' independently = 1 – 12; and

L = H, Cl, Br, $-CH_2C(O)CH_3$, $CH_2C(O)C(CH_3)_3$, $-CH_2C(O)C_6H_5$, -

,

, or
$CH_2C(O)C_6H_4OH$, $-CH_2C(O)C_6H_4OCH_3$,
$CH_2CH=CH_2$.

2. The polymeric device material of Claim 1 wherein for the monomer of formula [1]:

$B = -O(CH_2)_n-$ or $-(OCH_2CH_2)_n-$;

$R^1 = -H$ or $-CH_3$;

$n = 1 - 5$;

$A = -C_6H_5$, $O(CH_2)_mC_6H_5$; and

$m = 0 – 4$.

3. The polymeric device material of Claim 1 wherein for the monomer of formula [2]:

R^2, R^3 independently = H or CH_3;

W, W' independently = $O(CH_2)_d$, $O(CH_2)_dC_6H_4$, or nothing;

$J = O(CH_2CH_2O)_b$ or nothing, provided that if W and W' = nothing, then J ≠ nothing;

$d = 0 - 6$; and

$b = 1 – 10$.

4. The polymeric device material of Claim 1 wherein for the macromer of formula [3]:

e, f independently = 5 - 75;

X, X^1, X^2 independently = O or $N(CH_3)-$;

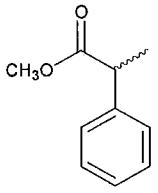
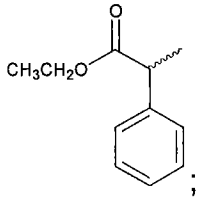
Y, Y^1 independently = $-(CH_2)_pH$, $(CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qH$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, or $(CH_2)_tOC_6H_5$;

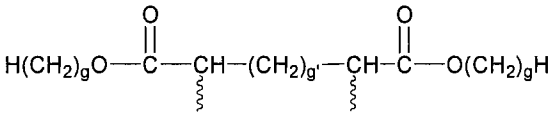
$p = 1 - 12$;

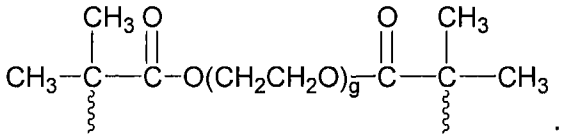
$q = 2 - 60$;

$t = 1 - 5$;

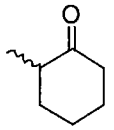
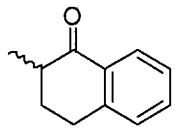
$R^4 = CH_3OC(O)CH(CH_3)-$, $CH_3OC(O)C(CH_3)_2-$, $HOCH_2CH_2OC(O)C(CH_3)_2-$, $(CH_2=C(R^3)CO_2CH_2CH_2OC(O)C(CH_3)_2-$, $CH_3CH_2OC(O)CH(CH_3)-$, $CH_3CH_2OC(O)C(CH_3)_2-$, $CH_3OC(O)CH(CH_2CH_3)-$, $CH_3CH_2OC(O)CH(CH_2CH_3)-$, $(CH_3)_3COC(O)C(CH_3)_2-$,


, or

;

R^5 =  or


;

g, g' independently = 1 – 12; and

L = H, Cl, Br, $-CH_2C(O)CH_3$, $CH_2C(O)C(CH_3)_3$, $-CH_2C(O)C_6H_5$, $CH_2C(O)C_6H_4OH$, $-CH_2C(O)C_6H_4OCH_3$, , , or $CH_2CH=CH_2$.

5. The polymeric device material of Claim 4 wherein for the macromer of formula [3]:

e, f independently = 5 - 60;

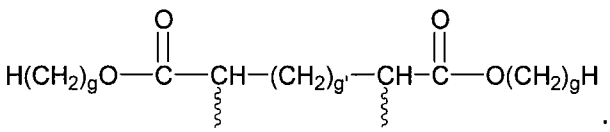
X, X^1, X^2 = O;

Y, Y^1 independently = $-(CH_2CH_2O)_qCH_3$, $(CH_2CH_2O)_qC_6H_5$, $(CH_2)_tC_6H_5$, or $(CH_2)_tOC_6H_5$;

q = 2 - 40;

t = 1-2;

R^4 = $CH_3OC(O)CH(CH_3)-$, $CH_3OC(O)C(CH_3)_2-$, $HOCH_2CH_2OC(O)C(CH_3)_2-$, $(CH_2=C(R^3)CO_2CH_2CH_2OC(O)C(CH_3)_2-$, or $CH_3OC(O)CH(CH_2CH_3)-$;

R^5 = 
;

g, g' independently = 1-6; and

L = H, $-CH_2C(O)C_6H_5$, $-CH_2C(O)C_6H_4OH$, $-CH_2C(O)C_6H_4OCH_3$, or $CH_2CH=CH_2$.

6. The polymeric device material of Claim 1 wherein the monomer of formula [1] is selected from the group consisting of benzyl methacrylate; 2-phenylethyl methacrylate; 3-phenylpropyl methacrylate; 4-phenylbutyl methacrylate; 5-phenylpentyl methacrylate; 2-phenoxyethyl methacrylate; 2-(2-phenoxyethoxy)ethyl methacrylate; 2-benzyloxyethyl methacrylate; 2-(2-(benzyloxy)ethoxy)ethyl methacrylate; 3-benzyloxypropyl methacrylate; benzyl acrylate; 2-phenylethyl acrylate; 3-phenylpropyl acrylate; 4-phenylbutyl acrylate; 5-phenylpentyl acrylate; 2-phenoxyethyl acrylate; 2-(2-phenoxyethoxy)ethyl acrylate; 2-benzyloxyethyl acrylate; 2-(2-(benzyloxy)ethoxy)ethyl acrylate; and 3-benzyloxypropyl acrylate.

7. The polymeric device material of Claim 1 wherein the monomer of formula [2] is selected from the group consisting of ethylene glycol dimethacrylate; diethylene glycol dimethacrylate; triethylene glycol dimethacrylate; 1,6-hexanediol dimethacrylate; 1,4-butanediol dimethacrylate; 1,4-benzenedimethanol dimethacrylate; ethylene glycol diacrylate; diethylene glycol diacrylate; triethylene glycol diacrylate; 1,6-hexanediol diacrylate; 1,4-butanediol diacrylate; and 1,4-benzenedimethanol diacrylate.

8. The polymeric device material of Claim 1 wherein the amount of monomer [1] is 70 to 90 % (w/w).

9. The polymeric device material of Claim 1 wherein the amount of monomer [2] is 0.5 to 3 % (w/w).

10. The polymeric device material of Claim 1 wherein the amount of hydrophilic side-chain macromer is 10 to 30 % (w/w).

11. The polymeric device material of Claim 10 wherein the amount of hydrophilic side-chain macromer is 10 to 20 % (w/w).

12. The polymeric device material of Claim 1 wherein the hydrophilic side-chain macromer is a macromer of formula [3a].

13. The polymeric device material of Claim 1 wherein the hydrophilic side-chain macromer is a macromer of formula [3b].

14. The polymeric device material of Claim 1 wherein the hydrophilic side-chain macromer is a macromer of formula [3c].

15. The polymeric device material of Claim 1 wherein the hydrophilic side-chain macromer is a macromer of formula [3d].

16. The polymeric device material of Claim 1 wherein the hydrophilic side-chain macromer is a macromer of formula [3e].

17. The polymeric device material of Claim 1 further comprising an ingredient selected from the group consisting of a polymerizable UV absorbers and a polymerizable colorants.

18. The polymeric device material of Claim 17 comprising 0.1 – 5 % (w/w) of a polymerizable UV absorber and 0.01 - 0.5 % (w/w) of a polymerizable colorant.

19. An ophthalmic or otorhinolaryngological device comprising the polymeric device material of Claim 1 wherein the ophthalmic or otorhinolaryngological device is selected from the group consisting of intraocular lenses; contact lenses; keratoprostheses; corneal inlays or rings; otological ventilation tubes; and nasal implants.

20. The ophthalmic or otorhinolaryngological device of Claim 19 wherein the ophthalmic or otorhinolaryngological device is an intraocular lens.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/078643

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61L27/16 A61L27/18 A61L27/50 A61F2/16 G02B1/04

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)
A61L A61F G02B C08F

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 practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/138213 A (ALCON INC [CH]; SCHLUETER DOUGLAS C [US]; KARAKELLE MUTLU [US]) 28 December 2006 (2006-12-28) page 4, line 4 - line 16 page 5, line 1 - page 7, line 30 examples 1-12 claims 1-20	1-20
X	WO 2006/138188 A (ALCON INC [CH]; SCHLUETER DOUGLAS C [US]) 28 December 2006 (2006-12-28) page 4, line 4 - page 6, line 13 examples 1-11 claims 1-19	1-20

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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

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 November 2008	02/12/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Menidjel, Razik

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/078643

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2004/131849 A1 (WIRES DUANE L [US]) 8 July 2004 (2004-07-08) page 1, paragraph 16 - paragraph 18 page 2, paragraph 25 - paragraph 28 page 3, paragraph 44 - page 4, paragraph 46 examples 1-6 claims 1-34	1-20
A	US 5 331 073 A (WEINSCHENK III JOSEPH I [US] ET AL) 19 July 1994 (1994-07-19) cited in the application column 2, line 19 - line 57 column 4, line 39 - column 5, line 7 examples 1-5 claims 1-22	1-20
A	WO 2006/019404 A (ALCON INC [CH]; SCHLUETER DOUGLAS C [US]) 23 February 2006 (2006-02-23) the whole document	1-20
A	WO 2004/007579 A (ALCON INC [CH]; SCHLUETER DOUGLAS C [US]; LEBOEUF ALBERT R [US]; KARAK) 22 January 2004 (2004-01-22) the whole document	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/078643

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