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(54) Title: POLYMERIC MATERIALS

(57) Abstract: A method of making a material which comprises a filler and/or fugitive compound involves forming a layer L1 of a composition comprising a polymeric material and a filler material on a substrate; subjecting the layer L1 to a temperature to melt the polymeric material; forming on layer L1, a layer L2 of a composition comprising a polymeric material and a filler material; subjecting layer L2 to a temperature above the melting temperature of the polymeric material; and continuing forming layers as aforesaid as required. Subsequently, the material prepared may be removed from the substrate and/or the fugitive material may be removed, thereby to define a porous material which may be machined or otherwise further processed to produce medical implants or parts thereof.



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POLYMERIC MATERIALS

This invention relates to a polymeric material and particularly, although not exclusively, relates to a material comprising a polymeric material and a filler, for example a fugitive material, wherein the filler may be removable in order to define a porous structure defined by the polymeric material. In preferred embodiments, the material defines an osseoconductive polymeric material and/or is suitable for medical use such as for making medical implants or parts thereof. Preferred embodiments relate to materials comprising polyaryletherketones, for example polyetheretherketone (PEEK).

Production scale methods of fabricating porous polyetheretherketones (PEEK) are limited. One known method involves gas assisted injection moulding (Mucell®, Trexel, USA). This Mucell process introduces a supercritical gas such as nitrogen during the screw-recovery phase in extrusion or injection moulding. However, the porosity formed is closed cell and limited to pore diameters up to 100µm. Consequently, its application for any osseoconductivity in medical devices requiring bone ingrowth is restricted. To overcome this, variations on the technology have been reported for biodegradable PLA polymers, which have combined well known methods such as salt-leaching with the supercritical process in order to achieve the interconnected porosity (Kramschuster, A. and Turng, L.S., "Highly Porous Injection-Moulded Biodegradable Polymer Foams for Tissue Engineering Scaffolds," Biofoams 2007, Capri, Italy, September 26-28, 2007).

The high melt temperature (400°C) required to process PEEK provides additional challenges, as does the incorporation of fillers that will affect viscosity. Porosity achieved through traditional, well-known methods of compression moulding and salt leaching has been described for PEEK (see for example, WO2007/051307) and other members of the polyaryletherketone family. However, such methods have significant limitations when applied in the context of medical devices. For example, compression moulding can result in brittle parts, voids and difficulties in making complex shapes. It may also be difficult to release the moulded material without the use of undesirable mould release agents. Also, the fugitive material (e.g. salt) may become encapsulated during compression moulding meaning that it cannot be completely removed in a leaching process. Disadvantageously, there may be as much as 3wt% of salt in such compression moulded materials.

Other methods of creating porous osseoconductive PEEK, allegedly suitable for medical use, have also been described and include heat sintering of particles (see WO200909959). In heat sintering, particles of polymer are held in a mould in contact with each other and the polymer heated to just allow thermal bonding of the adjacent polymer particles at their contact points. However, disadvantageously, the pore diameter is dictated by the particle sizes of the selected

polymer and this may not be optimal for bone ingrowth. Also, the final porous shape is dictated by the mould used since machining post-sintering is generally difficult. Furthermore, since the sintered particles are only bonded at their contact points, the bond between the particles may be relatively weak leading to potential friability of the porous material.

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It is an object of the present invention to address the above described problems.

According to a first aspect of the invention, there is provided a method of making a material comprising the steps of:

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- (i) forming a layer L1 of a composition comprising a polymeric material and a filler material;
- (ii) subjecting the layer L1 to a temperature above the melting temperature of the polymeric material in order to melt the polymeric material in layer L1;
- (iii) forming on layer L1 a layer L2 of a composition comprising a polymeric material and a filler material;
- (iv) subjecting layer L2 to a temperature above the melting temperature of the polymeric material in order to melt the polymeric material in layer L2.

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Said method preferably comprises selecting first particles which comprise said polymeric material and selecting second particles which comprise said filler material. Said composition may be formed by blending, preferably dry-blending, said first particles and said second particles. A substantially homogenous blend is preferably formed. Blending is preferably undertaken in the absence of any solvent. It is preferably carried out at a temperature in the range 5 to 50°C, more preferably 10 to 35°C, especially at ambient temperature.

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Said first particles may include particles having a volume in the range 0.001 to 3mm³, preferably in the range 0.01 to 2.5mm³, more preferably in the range 0.05 to 1.0 mm³, especially 0.1 to 0.5mm³. Preferably substantially all of said first particles have a volume as aforesaid.

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The average volume of said first particles (total volume of first particles divided by the total number of said first particles) may be at least 0.001mm³, preferably at least 0.01mm³, more preferably at least 0.1mm³. The average volume (as described) may be less than 1mm³.

Said first particles may include particles having a maximum dimension in one direction of at least 0.1mm, preferably at least 0.2mm, more preferably at least 0.3mm. The maximum

dimension may be less than 2mm, preferably less than 1mm, more preferably less than 0.8mm. Preferably, substantially all particles in the mass have maximum dimensions as aforesaid.

- 5 The average of the maximum dimensions (sum of maximum dimensions of all particles divided by the total number of said particles) may be at least 0.1mm, preferably at least 0.3mm. The average may be less than 2mm, preferably less than 1mm, more preferably less than 0.8mm.

- 10 The ratio of the average volume of the first particles to the average volume of the second particles may be in the range 0.2 to 5, preferably in the range 0.3 to 3, more preferably in the range 0.5 to 2.

- 15 Said second particles may be a D_{50} in the range 1 to 20000 μm . Preferably, the D_{50} is in the range 10 to 2000 μm . In some embodiments wherein, for example, the second particles are arranged to produce a material to be used in an osseoconductive capacity, the D_{50} may be in the range 10 to 1200 μm to allow pores to be produced which are suitable for bone ingrowth. In other embodiments, lower porosity may be required in which case the D_{50} may be in the range 10 to 100 μm .

- 20 Said filler material could comprise filaments, which may be cylindrical. Such filaments may have an average diameter of 0.2 to 1mm, suitably 0.4 to 0.8mm and an average length of at least 1.0mm, for example at least 1.4mm. The average length may be less than 5mm or less than 3mm or less than 2mm. Non-filamentous filler is preferred.

- 25 Said composition may include at least 30 wt%, preferably at least 40wt%, more preferably at least 45 wt% of said polymeric material. Said composition may include less than 65 wt% or less than 60 wt% of said polymeric material. Said composition may include at least 30 wt%, preferably at least 40 wt%, more preferably at least 45 wt% of said filler material. Said composition may include less than 65 wt% or less than 60 wt% of said filler material. Said composition preferably includes 40 to 60 wt%, more preferably 45 to 55 wt%, of said polymeric material and 40 to 60 wt%, more preferably 45 to 55 wt% of said filler material. The ratio of the wt% of said polymeric material to said filler material is preferably in the range 0.6 to 1.3.
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- 35 Preferably at least 90 wt%, preferably at least 95 wt%, more preferably about 100 wt% of said composition is made up of said polymeric material and filler material.

Said polymeric material preferably comprises a bio-compatible polymeric material. Said polymeric material preferably comprises a thermoplastic polymer.

Said polymeric material may have a Notched Izod Impact Strength (specimen 80mm x 10mm x 4mm with a cut 0.25mm notch (Type A), tested at 23°C, in accordance with ISO180) of at least 4KJm^{-2} , preferably at least 5KJm^{-2} , more preferably at least 6KJm^{-2} . Said Notched Izod Impact Strength, measured as aforesaid, may be less than 10KJm^{-2} , suitably less than 8KJm^{-2} .

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The Notched Izod Impact Strength, measured as aforesaid, may be at least 3KJm^{-2} , suitably at least 4KJm^{-2} , preferably at least 5KJm^{-2} . Said impact strength may be less than 50KJm^{-2} , suitably less than 30KJm^{-2} .

- 10 Said polymeric material suitably has a melt viscosity (MV) of at least 0.06 kNsm^{-2} , preferably has a MV of at least 0.09 kNsm^{-2} , more preferably at least 0.12 kNsm^{-2} , especially at least 0.15 kNsm^{-2} .

- 15 MV is suitably measured using capillary rheometry operating at 400°C at a shear rate of 1000s^{-1} using a tungsten carbide die, $0.5\times 3.175\text{mm}$.

Said polymeric material may have a MV of less than 1.00 kNsm^{-2} , preferably less than 0.5 kNsm^{-2} .

- 20 Said polymeric material may have a MV in the range 0.09 to 0.5 kNsm^{-2} , preferably in the range 0.14 to 0.5 kNsm^{-2} , more preferably in the range 0.3 to 0.5 kNsm^{-2} .

- 25 Said polymeric material may have a tensile strength, measured in accordance with ISO527 (specimen type 1b) tested at 23°C at a rate of 50mm/minute of at least 20 MPa , preferably at least 60 MPa , more preferably at least 80 MPa . The tensile strength is preferably in the range 80 - 110 MPa , more preferably in the range 80 - 100 MPa .

- 30 Said polymeric material may have a flexural strength, measured in accordance with ISO178 ($80\text{mm} \times 10\text{mm} \times 4\text{mm}$ specimen, tested in three-point-bend at 23°C at a rate of 2mm/minute) of at least 50 MPa , preferably at least 100 MPa , more preferably at least 145 MPa . The flexural strength is preferably in the range 145 - 180MPa , more preferably in the range 145 - 164 MPa .

- 35 Said polymeric material may have a flexural modulus, measured in accordance with ISO178 ($80\text{mm} \times 10\text{mm} \times 4\text{mm}$ specimen, tested in three-point-bend at 23°C at a rate of 2mm/minute) of at least 1 GPa , suitably at least 2 GPa , preferably at least 3 GPa , more preferably at least 3.5 GPa . The flexural modulus is preferably in the range 3.5 - 4.5 GPa , more preferably in the range 3.5 - 4.1 GPa .

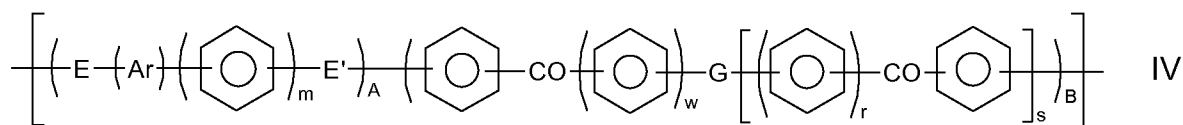
Said polymeric material may be amorphous or semi-crystalline. It is preferably semi-crystalline.

The level and extent of crystallinity in a polymer is preferably measured by wide angle X-ray diffraction (also referred to as Wide Angle X-ray Scattering or WAXS), for example as
 5 described by Blundell and Osborn (Polymer 24, 953, 1983). Alternatively, crystallinity may be assessed by Differential Scanning Calorimetry (DSC).

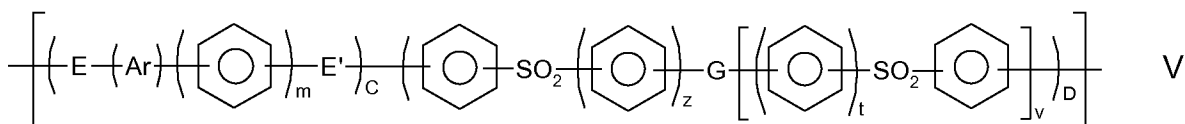
The level of crystallinity of said polymeric material may be at least 1%, suitably at least 3%, preferably at least 5% and more preferably at least 10%. In especially preferred embodiments,
 10 the crystallinity may be greater than 25%.

The main peak of the melting endotherm (T_m) of said polymeric material (if crystalline) may be at least 300°C.

15 Said polymeric material may include a repeat unit of general formula



or a repeat unit of general formula

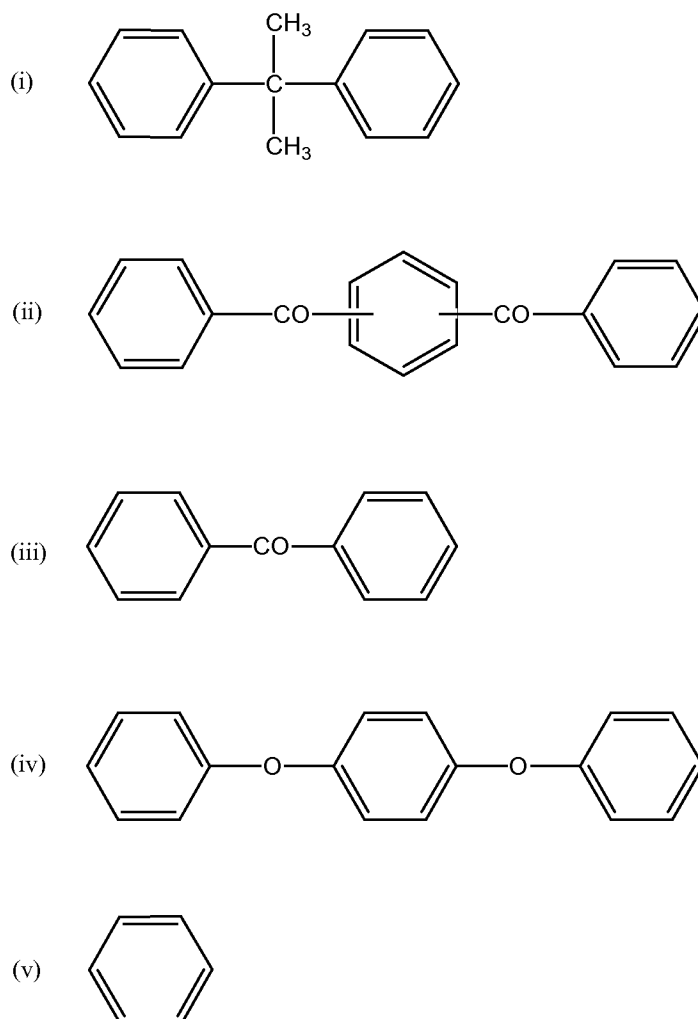


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wherein A, B, C and D independently represent 0 or 1, E and E' independently represent an oxygen or a sulphur atom or a direct link, G represents an oxygen or sulphur atom, a direct link or a -O-Ph-O- moiety where Ph represents a phenyl group, m, r, s, t, v, w, and z represent zero or 1 and Ar is selected from one of the following moieties (i) to (v) which is bonded via one or more of

25 its phenyl moieties to adjacent moieties

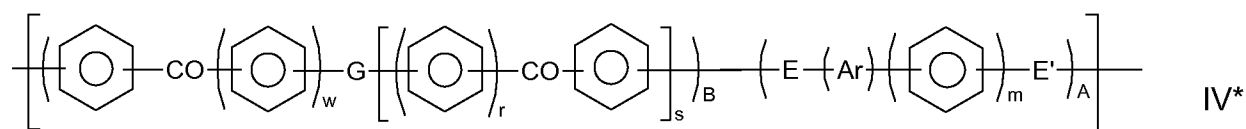
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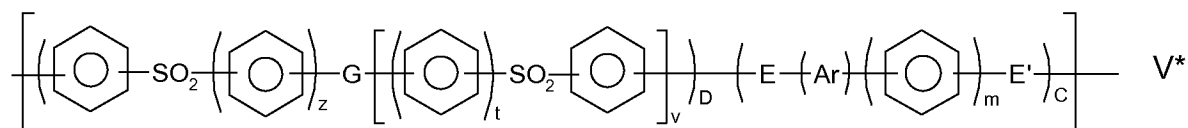
5 Unless otherwise stated in this specification, a phenyl moiety has 1,4-, linkages to moieties to which it is bonded.

Said polymeric material may be a homopolymer which includes a repeat unit of IV or V or may be a random or block copolymer of at least two different units of IV and/or V.

10 As an alternative to a polymeric material comprising units IV and/or V discussed above, said polymeric material may include a repeat unit of general formula



or a homopolymer having a repeat unit of general formula

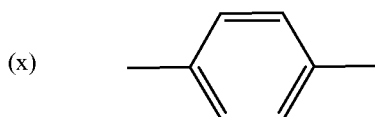
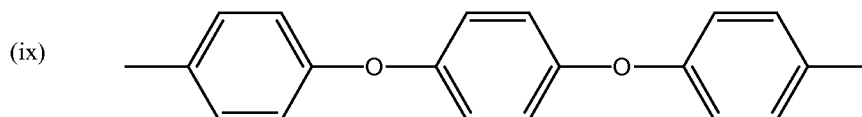
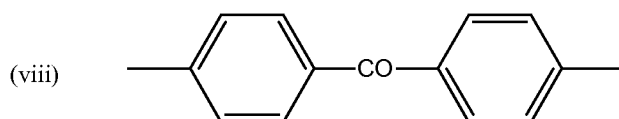
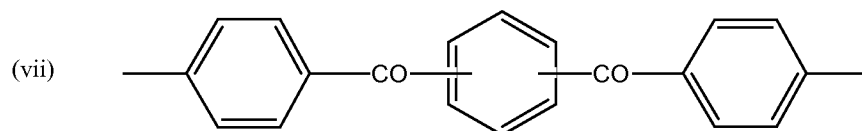
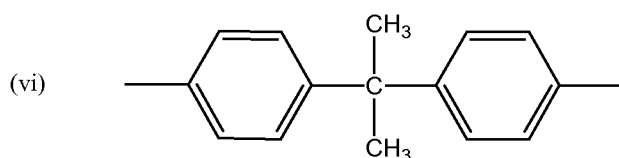


wherein A, B, C, and D independently represent 0 or 1 and E, E', G, Ar, m, r, s, t, v, w and z are as described in any statement herein.

- 5 Said polymeric material may be a homopolymer which includes a repeat unit of IV* or V* or a random or block copolymer of at least two different units of IV* and/or V*.

Preferably, said polymeric material is a homopolymer having a repeat unit of general formula IV.

- 10 Preferably Ar is selected from the following moieties (vi) to (x)



In (vii), the middle phenyl may be 1,4- or 1,3-substituted. It is preferably 1,4-substituted.

Suitable moieties Ar are moieties (ii), (iii), (iv) and (v) and, of these, moieties, (ii), (iii) and (v) are preferred. Other preferred moieties Ar are moieties (vii), (viii), (ix) and (x) and, of these, moieties (vii), (viii) and (x) are especially preferred.

An especially preferred class of polymeric materials are polymers (or copolymers) which consist essentially of phenyl moieties in conjunction with ketone and/or ether moieties. That is, in the preferred class, the polymer material does not include repeat units which include $-S-$, $-SO_2-$ or aromatic groups other than phenyl. Preferred bio-compatible polymeric materials of the type described include:

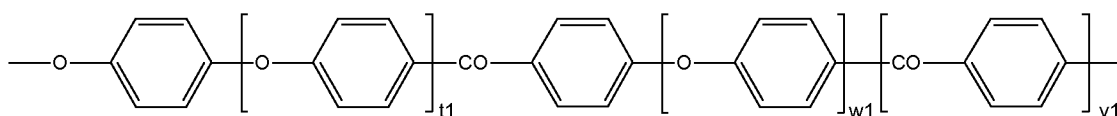
- (a) a polymer consisting essentially of units of formula IV wherein Ar represents moiety (v), E and E' represent oxygen atoms, m represents 0, w represents 1, G represents a direct link, s represents 0, and A and B represent 1 (i.e. polyetheretherketone).
- (b) a polymer consisting essentially of units of formula IV wherein E represents an oxygen atom, E' represents a direct link, Ar represents a moiety of structure (ii), m represents 0, A represents 1, B represents 0 (i.e. polyetherketone);
- (c) a polymer consisting essentially of units of formula IV wherein E represents an oxygen atom, Ar represents moiety (ii), m represents 0, E' represents a direct link, A represents 1, B represents 0, (i.e. polyetherketoneketone).
- (d) a polymer consisting essentially of units of formula IV wherein Ar represents moiety (ii), E and E' represent oxygen atoms, G represents a direct link, m represents 0, w represents 1, r represents 0, s represents 1 and A and B represent 1. (i.e. polyetherketoneetherketoneketone).
- (e) a polymer consisting essentially of units of formula IV, wherein Ar represents moiety (v), E and E' represents oxygen atoms, G represents a direct link, m represents 0, w represents 0, s, r, A and B represent 1 (i.e. polyetheretherketoneketone).
- (f) a polymer comprising units of formula IV, wherein Ar represents moiety (v), E and E' represent oxygen atoms, m represents 1, w represents 1, A represents 1, B

represents 1, r and s represent 0 and G represents a direct link (i.e. polyether-diphenyl-ether-phenyl-ketone-phenyl-).

Said polymeric material may consist essentially of one of units (a) to (f) defined above.

- 5 Alternatively, said polymeric material may comprise a copolymer comprising at least two units selected from (a) to (f) defined above. Preferred copolymers include units (a). For example, a copolymer may comprise units (a) and (f); or may comprise units (a) and (e).

- 10 Said polymeric material preferably comprises, more preferably consists essentially of, a repeat unit of formula (XX)



- 15 where t_1 , and w_1 independently represent 0 or 1 and v_1 represents 0, 1 or 2. Preferred polymeric materials have a said repeat unit wherein $t_1=1$, $v_1=0$ and $w_1=0$; $t_1=0$, $v_1=0$ and $w_1=0$; $t_1=0$, $w_1=1$, $v_1=2$; or $t_1=0$, $v_1=1$ and $w_1=0$. More preferred have $t_1=1$, $v_1=0$ and $w_1=0$; or $t_1=0$, $v_1=0$ and $w_1=0$. The most preferred has $t_1=1$, $v_1=0$ and $w_1=0$.

- 20 In preferred embodiments, said polymeric material is selected from polyetheretherketone, polyetherketone, polyetherketoneetherketoneketone and polyetherketoneketone. In a more preferred embodiment, said polymeric material is selected from polyetherketone and polyetheretherketone. In an especially preferred embodiment, said polymeric material is polyetheretherketone.

- 25 Said first particles may comprise said polymeric material and other optional additives, suitably so that said first particles are homogenous particles. Said first particles may comprise 40 to 100 wt% (preferably 60 to 100 wt%) of said polymeric material and 0 to 60 wt% of other additives.

- 30 Other additives may comprise reinforcing agents and may comprise additives which are arranged to improve mechanical properties of components made from the mass of material. Preferred reinforcing agents comprise fibres.

- 35 Said fibres may comprise a fibrous filler or a non-fibrous filler. Said fibres may include both a fibrous filler and a non-fibrous filler.

A said fibrous filler may be continuous or discontinuous. In preferred embodiments, a said fibrous filler is discontinuous.

5 Preferably, fibres which are discontinuous have an average length of less than 10mm, preferably less than 7mm.

A said fibrous filler may be selected from inorganic fibrous materials, high-melting organic fibrous materials and carbon fibre.

10 A said fibrous filler may be selected from inorganic fibrous materials, non-melting and high-melting organic fibrous materials, such as aramid fibres, and carbon fibre.

A said fibrous filler may be selected from glass fiber, carbon fibre, asbestos fiber, silica fiber, alumina fiber, zirconia fiber, boron nitride fiber, silicon nitride fiber, boron fiber, fluorocarbon
15 resin fibre and potassium titanate fiber. Preferred fibrous fillers are glass fibre and carbon fibre.

A fibrous filler may comprise nanofibres.

20 A said non-fibrous filler may be selected from mica, silica, talc, alumina, kaolin, calcium sulfate, calcium carbonate, titanium oxide, ferrite, clay, glass powder, zinc oxide, nickel carbonate, iron oxide, quartz powder, magnesium carbonate, fluorocarbon resin and barium sulfate. The list of non-fibrous fillers may further include graphite, carbon powder and nanotubes. The non-fibrous fillers may be introduced in the form of powder or flaky particles.

25 Preferred reinforcing agents are glass fibre and/or carbon fibre.

Other additives may comprise radiopacifiers, for example barium sulphate and any other radiopacifiers described in co-pending application PCT/GB2006/003947. Up to 20wt%, or up
30 to 5wt% of radiopacifiers may be included. Preferably, less than 1wt%, more preferably no radiopacifier is included.

Other additives may include colourants, for example titanium dioxide. Up to 3wt% of colourant may be included but preferably less than 1wt%, more preferably no, colourant is included.

35 80 wt%, 90 wt% , 95 wt% or about 100 wt% of said first particles are made up of said polymeric material, especially a polymeric material having a repeat unit of formula (XX), especially of polyetheretherketones.

Said filler material suitably has a melting point which is greater than the T_m of the polymeric material, suitably by at least 50°C, preferably by at least 100°C, more preferably by at least 250°C, especially by at least 400°C

- 5 In the method, a said composition comprising a said polymeric material and filler material is suitably selected and contacted with a surface S1 for defining layer L1. Said composition preferably consists essentially of dry solid material; it preferably does not include any solvent. A thin layer L1 of said composition is preferably formed on the surface S1. The thin layer L1 may have a thickness across at least 50%, 75%, 90%, 95% or about 100% of its area of less
10 than 3mm, more preferably less than 1.0mm. The thickness across said area may be at least 0.1mm, 0.2mm, 0.3mm or 0.4mm. Said thin layer L1 is suitably no more than four, preferably no more than three, particles thick at any point across its extent.

- Said thin layer L1 is suitably heated, in step (ii), after it has been laid down. Preferably, it is
15 heated so that it reaches a temperature above the T_m of the polymeric material. It is preferably heated so the polymeric material melts and is able to flow, suitably so that a continuum is formed between particles of polymeric material by coalescence of the polymeric material of said particles. Said polymeric material is preferably able to flow in a direction parallel to the surface of layer L1. In the method, particles of said polymeric material
20 (preferably substantially the entirety thereof) are heated so that substantially the entirety of the particles melt, including a central core thereof, rather than the particles only being heated close to their surfaces as in sintering.

- Said thin layer L1 is suitably heated by being subjected to a temperature of at least 5°C,
25 preferably at least 10°C, more preferably at least 20°C, greater than the T_m of said polymeric material. Said thin layer may be subjected to a temperature of at least 350°C, preferably at least 380°C, more preferably at least 400°C.

- Said thin layer L1 is preferably heated to a temperature less than the decomposition
30 temperature of said polymeric material. Said thin layer L1 is suitably heated to a temperature which is less than the melting temperature of the filler material. Preferably, it is heated to a temperature which is at least 50°C, preferably at least 100°C less than said melting temperature.

- 35 Heating of said thin layer L1 may be carried out using a heating means. Said heating means may include a heat emitting face under which said thin layer L1 is arranged. Said heating means may comprise a radiant heat source which is suitably arranged to radiate heat and direct it towards said thin layer. Heating of said layer is preferably not dependent on absorbance of radiation (e.g. from a laser) by a black body absorber included into composition.

Preferably said composition includes no such black body absorber. Said heating means is preferably arranged preferentially to direct heat towards an exposed, suitably upwardly facing, surface of said thin layer L1, suitably so that said exposed surface is heated at a faster rate compared to the rate of heating of a surface of said thin layer L1 which is in contact with a surface on which the thin layer is laid down. Said heating means suitably emits blanket radiation, rather than focussed and targeted radiation as may be emitted by a laser. Said heating means is preferably arranged to heat all particles in said thin layer L1.

Said thin layer L1 may be subjected to said heating means for a time sufficient to fully melt the polymeric material but not so long that there is any significant degradation of the polymeric material. Suitably, said layer L1 is subject to a temperature above the T_m of the polymeric material for less than 10, 7, 5, 4, 3 or 2 minutes. The time is also suitably selected so there is no significant degradation of the filler material and/or any component within the composition used to make layer L1.

After heating in step (ii) of the method, a composition comprising a said polymeric material and filler material is suitably selected and contacted with said layer L1, during step (iii) of the method. Said composition may be substantially the same as the composition used to form layer L1 or it may be different, for example including more or less filler material. In step (iii), said composition may be contacted with layer L1 whilst layer L1 is at a temperature above ambient temperature, for example at least 25°C, 50°C or 100°C above ambient temperature. Suitably, layer L1 is tacky when contacted with said composition in step (iii), suitably so particles in said composition are able to stick to layer L1.

Said composition used in step (iii) preferably consists essentially of dry solid material; it preferably does not include any solvent. A thin layer L2 of said composition is preferably formed on the surface of layer L1. The thin layer L2 may have a thickness across at least 50%, 75%, 90%, 95% or about 100% of its area of less than 3mm, suitably less than 2.0mm, preferably less than 1.5mm, more preferably less than 1.0mm. The thickness across said area may be at least 0.2mm, 0.3mm or 0.4mm. Said thin layer L2 preferably is suitably no more than four, preferably no more than three particles thick at any point across its extent.

Said thin layer L2 is suitably heated, in step (iv), after it has been laid down. Preferably, it is heated so that it reaches a temperature above the T_m of the polymeric material. It is preferably heated so the polymeric material melts and is able to flow, suitably so that a continuum is formed between particles of the polymeric material by coalescence of the polymeric material of said particles. In the method, particles of said polymeric material (preferably substantially the entirety thereof) are heated so that the entirety of the particles

melt, including a central core thereof, rather than the particles only being heated close to their surfaces as in sintering.

5 Said thin layer L2 is suitably heated by being subjected to a temperature of at least 5°C, preferably at least 10°C, more preferably at least 20°C greater than the T_m of said polymeric material. Said thin layer L2 may be subjected to a temperature of at least 350°C, preferably at least 380°C, more preferably at least 400°C.

10 Said thin layer L2 is preferably heated to a temperature which is less than the decomposition temperature of said polymeric material.

15 Said thin layer L2 is suitably heated to a temperature which is less than the melting temperature of the filler material. Preferably, it is heated to a temperature which is at least 50°C, preferably at least 100°C, less than said melting temperature. Heating of said thin layer L2 may be carried out using a heating means as described in relation to heating of layer L1.

20 The method may include repeating steps (iii) and (iv) in order to form additional layers. The method may include forming layers L1 to L_n wherein n is at least 10, at least 20 at least 30 or at least 40. Preferably, layers L1 and L2 include the same polymeric material. They preferably include at least 20 wt% or at least 30 wt% of the same polymeric material. Preferably at least 3, 4, 5, 6, or 7 layers formed in the method include the same polymeric material. Preferably, at least n minus 2 layers, more preferably each layer formed in the method includes the same polymeric material.

25 The material made in the method may have a thickness of at least 10mm or at least 15mm. There is generally no limit to the thickness that can be achieved in the method. Typically, the material will have a thickness less than 50mm, or less than 25mm.

30 The material made in the method may have a volume of at least 500mm³, although materials having much greater volumes can readily be achieved.

35 The volume occupied by filler material in the material made in the method may be at least 10 vol%, suitably at least 20 vol%, preferably at least 30 vol%, or even 40 vol%. The volume occupied by filler material may be less than 80 vol%, 70 vol% or 60 vol%.

Surface S1 on which layer L1 is formed may comprise a heat resistant surface, for example of a mould or other surface, which is not incorporated into a material made in the method. In this case, the method includes a step of disengaging material from surface S1 after its formation. Alternatively, surface S1 may form a part of the material made in the method. For example,

surface S1 may be defined by a part comprising a said polymeric material. The polymeric material may not be part of a composition which includes fillers as described herein. Said part may be defined by at least 80, 90, 95 or about 100% of said polymeric material, for example polyetheretherketone.

5

The method may include a step of altering the shape of the material, suitably after the last layer (e.g. layer Ln) has been laid down. In one embodiment, the material may be machined to alter its shape and/or to form the shape of at least part of a desired medical implant. In another embodiment, the material could be thermoformed, for example whilst the material is

10

still at a temperature above ambient temperature after formation of last layer Ln.

The method may include forming the material into a medical implant or a part thereof.

15

The method may include the step of treating the material to remove at least some of said filler material. Suitably, such treatment is undertaken after altering the shape of the material as described. The treatment may be arranged to define porosity in the material.

20

Means for removing filler material may be arranged to solubilise said filler material. Said means suitably comprises a solvent. Said solvent preferably comprises water and more preferably includes at least 80wt%, preferably at least 95wt%, especially at least 99wt% water. The solvent preferably consists essentially of water.

25

Means for removing the filler material may comprise contacting the material with a solvent formulation (preferably comprising water as aforesaid) which is at a temperature of 100°C or greater and a pressure at or above ambient pressure thereby to charge the solvent formulation with filler material and separating the charged solvent from the product.

30

In the method, said solvent formulation may be at a temperature of greater than 150°C, suitably greater than 200°C when contacted with said material. Said solvent formulation may be at a temperature of less than 500°C, suitably less than 450°C, preferably less than 400°C, more preferably less than 350°C when contacted with said material.

35

The solvent formulation may be under a pressure of at least 4 bar, suitably at least 8 bar, preferably at least 10 bar when contacted with said material. The pressure may be less than 300 bar, preferably less than 200 bar, more preferably less than 100 bar, especially less than 50 bar. The pressure is preferably selected to maintain the solvent formulation in the liquid state when in contact with said material.

Preferably, in the method, the solvent formulation is arranged to flow from a first region to a third region via a second region in which said material is arranged.

5 Said filler material may have a solubility in water of at least 5g/100ml, suitably at least 15g/100ml, preferably at least 20g/100ml, more preferably at least 25g/100ml, especially at least 30g/100ml, wherein in each case solubility is measured at 25°C.

10 In the method, a component (or part thereof) may be made which includes regions of different porosities or regions which include different levels of filler material (and may later define regions of different porosities). For example, a first region may be made by laying down one or more layers of a composition which includes a first amount of filler material; and a second region may be made by laying down one or more layers of a composition which includes a second amount of filler material, wherein said first and second amounts are different. The component (or part thereof) may include one or a plurality of further regions. Thus, the method
15 may be used to produce a component (or part thereof) which includes different levels of filler material (or porosity if the filler material is removed). For example, a component (or part thereof) may include gradually increasing or stepped levels of filler material (or porosity) on moving from one position to another position.

20 In a first embodiment, a component (or part thereof) made in the method may be used, for example as a part or the whole of a device which may be incorporated into or associated with a human body, only after filler material has been removed.. In this case, the method may be used to define a component (or part thereof) which is porous prior to use. The filler material's sole purpose in the method may be to facilitate such pore formation.

25 In a second embodiment, a component (or part thereof) made in the method may be arranged to be used, for example as a part or the whole of a device which may be incorporated into or associated with a human body, whilst filler material remains associated with the device and/or prior to any removal of filler material. Thus, the filler material is suitably of a type which has no detrimental effects when present in a human body. Preferably, such a filler material is
30 arranged to leach out of the component (or part thereof) in vivo. The material leaching out is suitably an active ingredient which may have a positive effect within the body. Suitably, leaching of said filler material is arranged to produce increasing levels of porosity in said component (or part thereof) in vivo. Such porosity may also be arranged to have a positive
35 effect.

In a third embodiment, a component (or part thereof) made in the method may be treated to remove its filler material as described in accordance with the first embodiment. Thereafter, porous regions of the component (or part thereof) may be impregnated with another material.

Such a material may be arranged to leach from the component (or part thereof) in vivo or may be arranged to remain within pores in the component (or part thereof) and exert an effect, for example a biological effect, when present. An example of a material which may be impregnated as aforesaid is collagen or a drug loaded bio-absorbable polymer.

5

The invention extends to a method of making a medical implant or part thereof, the method being as described according to the first aspect.

10 The invention extends to the use of a material formed as described according to the first aspect in making a medical implant or part thereof.

The invention extends to a material, for example a medical implant, made as described herein.

15 According to a second aspect of the invention, there is provided a material comprising a polymeric material and filler material as described according to the first aspect.

20 As described according to the first aspect, said filler material may be partially or substantially wholly removed to define a material which is porous. In a third aspect, the invention provides a porous material comprising a porous polymeric material as described herein. The material may have a porous volume fraction of at least 40%, suitably at least 45%, preferably at least 50%, more preferably at least 54%. The porous volume fraction may be less than 75%, less than 70%, less than 65% or less than 60%.

25 Said material may have a solid volume fraction of less than 60%, less than 56%, less than 50% or less than 45%. The solid volume fraction may be at least 25%, preferably at least 30%, more preferably at least 35%, especially at least 40%.

30 Said material may have an average connectivity density of solid phase of 0.5 to 5mm^3 , suitably 1 to 3mm^3 , preferably 1.5 to 2.5mm^3 , more preferably 1.6 to 2.3mm^3

Said material may have an average degree of anisotropy, in the range 1 to 2 , preferably 1 to 1.5 , more preferably 1 to 1.2 .

35 Said material preferably has a pore size mean in the range 500 - $1500\mu\text{m}$. This can be controlled by the filler used. Suitably, the pore size mean is in the range 500 - $1000\mu\text{m}$, preferably 550 - $800\mu\text{m}$.

Said material may have a flex strength determined in accordance with BS EN ISO 178:2003 as described herein of at least 5 MPa, preferably at least 9 MPa, The flex strength may be less than 20 MPa, less than 15 MPa or less than 12 MPa.

- 5 Said material may have a flex modulus measured in accordance with BS EN ISO 178:2003 as described herein of at least 250 MPa, preferably at least 290 MPa, especially at least 305 MPa. The flex modulus may be less than 400 MPa or less than 350 MPa.

Said material may have a compressive strength of at least 20 MPa, preferably at least 25 MPa.

- 10 The compressive strength may be in the range 20 to 50 MPa, for example 25 to 50 MPa, or 33-44 MPa, which is in the range of that for trabecular bone. Compressive strength may be measured as described in ASTM D695.

- 15 An irregular shaped porous network is suitably defined throughout the method. The material preferably comprises a continuous network of said polymeric material wherein said network does not comprise fused particles of polymeric material but rather comprises a continuum of polymeric material. Said material preferably includes less than 3 wt%, less than 2 wt%, less than 1 wt%, less than 0.5 wt% of a filler material, for example fugitive material (e.g. salt). Advantageously, the material includes a negligible amount of filler material which has a
20 solubility in water as described herein. Thus, the majority of filler material intended to be removed in defining the material of the second aspect has been removed and, therefore, it is not present in the material formed in the method described herein. Alternatively, in some cases, a small amount of filler material may be intentionally left in the material within its pores. For example, where the filler material is Ca or P-containing, for example as in hydroxyapatite,
25 residual filler material may advantageously encourage formation of new bone within the pore material.

- In an especially preferred embodiment, said material comprises a porous material comprising porous polymeric material of formula XX, especially of polyetheretheketone, which has a
30 porous volume fraction of less than 65% and at least 54%; and/or a solid volume fraction of less than 50% and at least 40%; and/or an average connectivity of 1.5 to 2.5mm³, and/or an average pore size in the range 550 to 800µm.

- Porosity characteristics described herein may be assessed by Micro CT analysis.
35

Any invention or embodiment described herein may be combined with any feature of any other invention of embodiment described herein mutatis mutandis.

Specific embodiments of the invention will now be described, by way of example, with reference to the accompanying figures in which:

- Figure 1a is a plan view of a blend of PEEK and filler on a surface prior to heating;
- 5 Figure 1b is a plan view of the blend of Figure 1a after heating;
- Figures 2a and 2b are cross-sections along lines II-II of Figures 1a and 1b;
- Figures 3a-3e are photographs of a porous part;
- Figures 4a and 4b are electron-micrographs of the porous part.
- Figure 5 shows part of a craniomaxillofacial implant;
- 10 Figure 6 shows a hip cup with a porous backing; and
- Figure 7 shows a half solid/half porous material.

The following materials are referred to hereinafter:

- 15 PEEK LT1 – polyetheretherketone polymer obtained from Invibio Limited, UK.

Soluble Bioglass – refers to Phosphate-based glass obtained from MO-SCI having maximum particle sizes in the range 500-1000nm.

- 20 In general terms, a polymeric material comprising polyetheretherketone (PEEK) and a fugitive material is made in a process comprising:
- (i) mixing uniformly sized microgranules of PEEK with a selected fugitive material;
 - (ii) forming an approximately one particle thick first layer of the mixture on a surface;
 - 25 (iii) heating the entire first layer to melt the PEEK;
 - (iv) forming an approximately one particle thick second layer of the mixture on the surface of the first layer;
 - (v) heating the entire second layer to melt the PEEK in the second layer;
 - (vi) repeating steps (ii)-(v) to build up the desired thickness;
 - 30 (vii) allowing the material formed to cool. As a result a coral-like structure of PEEK/fugitive material is created, wherein the microgranules of PEEK have flowed into more elongated shapes and have contacted one another;
 - (viii) optionally, heating the entire material in an oven to ensure total melt through so that the material does not include any sintered portions. The step may ensure the material is
 - 35 not friable;
 - (ix) machining the material to the desired shape;
 - (x) optionally, leaching the material to remove some or all of the fugitive material.

Further detail is provided below in the following examples.

Example 1 – Manufacture of microgranules

A method analogous to that described in WO2006/0118407 and US 6030558 was used. In the method, 3mm granules of PEEK LT1 were introduced into a twin-screw extruder extruded under the following conditions:

Extrusion rate	3 Kg/hr
Screw speed	100rpm
Torque	200%
Barrel temperature	250, 360, 350°C

A pelletiser blade having 82 teeth, rotating at a speed of 5.5 was used to cut the extrudate, exiting a 3-hole die to produce substantially cylindrical microgranules of PEEK of approximately 600µm diameter and 600µm length. By selection of appropriate conditions, in particular the cooling rate of the extrudate, amorphous or semi-crystalline microgranules can be produced and used in the examples which follow.

Example 2 – Preparation of layered polymeric material

A polymeric material comprising a blend of the microgranules prepared in Example 1 (50wt%) and soluble Bioglass (50wt%) was prepared by dry tumbling the materials until a homogenous blend was obtained.

A foundation layer was formed in a mould or on another heat-resistant surface, by spreading the blend to define a layer of one particle thickness on the selected surface. The material may be pressed down slightly to cause it to spread and define an open spread of the blend on the surface. The foundation layer could, as an alternative to use of the blend, be defined by PEEK microgranules in the absence of the soluble Bioglass.

The foundation layer was then heated at 400°C until it melted. Heat was supplied from one direction only (i.e. in a direction perpendicular to the foundation layer and from a side opposite the exposed, upper surface of the foundation layer) using a domestic grill-type arrangement, under which the foundation layer may be positioned. Melting is characterised by a colour-change in the PEEK - nature/beige to sugar brown (when the material is beginning to melt and/or PEEK microgranules start to sinter) to a darker colour when the PEEK becomes hotter and is truly molten. When molten there will be some flow of the PEEK microgranules as a

result of which they contact one another. Since the microgranules/blend is not tightly packed within a mould but is loosely arranged whether within a mould or on a surface, the layer of the microgranules/blend can spread out and create a mesh/web/netting-like structure.

- 5 The foundation layer which is still partially or fully molten was then covered with an even spread of the blend of one, two or three particles thickness to define a first layer. The cold particles of the blend stick to the upper surface of the partially or fully molten foundation layer. Heat may be supplied to the new first layer as described for the foundation layer so that the layer becomes molten and is able to flow. The presence of the filler in the blend prevents
- 10 PEEK accumulating and forming a solid region consisting essentially of PEEK and no Bioglass.

- Second and subsequent layers of the blend are spread on hot partially or fully molten underlying layers to define layers one, two or three particles thick followed by heating as
- 15 described to build up a layered polymeric material of desired thickness. After the final layer has been laid down, the layered polymeric material construct may be at a temperature which may allow it to be immediately formed into a new shape (e.g. in a thermoforming step) whereby a mould may press into the construct to create the shape.

- 20 Typically, the thickness of the construct may be in the range of from 2mm (to allow minimal tissue ingrowth) or to sizes of, for example 20mm in depth to provide near net shapes for machining of spinal fusion cages and may include 40, 50, 60 or more layers of the blend laid down and caused to flow as described.

- 25 If the construct is not formed into a new shape, for example by thermoforming, the construct may be removed from the surface on which it was formed and allowed to cool. A coral-like structure of PEEK and Bioglass is created. The microgranules of uniform sizes have flowed into more elongated shapes and contacted one another. Microgranules are preferable but powder or larger granules could be used, with modifications made to the filler size to
- 30 compensate for the changes.

- The cooled construct that has the required internal configuration can be optionally placed into an oven to ensure total melt throughout the material to ensure no sintered portions remain. Also fully melting the PEEK ensures that the material is not friable. A porous part made as
- 35 described herein is shown in Figures 3 and 4. The figures show solid PEEK in which interconnected pores are defined.

The cooled construct can be controllably cooled to affect the extent of crystallinity in the PEEK structure. The cooled construct can be machined to the required shape to define a part. The part may, optionally, be leached to remove some or all of the Bioglass and thereby define a porous structure.

5

Formation of a layer is illustrated in Figures 1 and 2. Figures 1a/2a show a one particle thick loose layer of the blend. After heating, the PEEK 2 flows so the microgranules merge into one another to define a continuum. The high melting point filler (Bioglass) 4 particles remain intact and do not substantially flow. However, with particular soluble phosphate Bioglasses the temperature of the PEEK melt may encourage the slight flow of the glass into a more spherical form, which is beneficial in creating more rounded pores.

10

Example 3 - Preparation of an alternative layered polymeric material comprising a construct having partial porosity

15

A foundation layer of neat PEEK is laid onto a base surface. This layer is required to be solid (non-porous) so sufficient material (e.g. of microgranules of Example 1) is laid out. The granules can be melted and the foundation layer built up by adding further layers. Alternatively, a solid PEEK foundation layer can be pre-made from a solid piece of PEEK (e.g. through extrusion, compression moulding, injection moulding or machining). This solid PEEK layer could be held in a mould to retain some shape conformity with only the upper surface exposed to be heated.

20

The solid PEEK foundation layer is heated at 400°C by directing heat at its exposed side until the upper exposed surface melts. This is characterised by a colour change in the material from natural/beige to sugar brown (when the material is beginning to melt and PEEK particles are able to sinter to each other) to a darker colour when the material is hotter and is truly molten.

25

A first layer is then formed on the molten solid PEEK surface. This can be formed from the blend of Example 2. A layer of ideally one, or two/three particles thickness is spread loosely to cover the surface of the foundation layer. A colour change will denote coverage as the hot molten PEEK is covered by cooler fresh material at a new lower temperature. The lower surface of these new particles will bind to the underlying hot partially or fully molten PEEK. The upper surface of these new particles will be at a lower temperature requiring heating to melt, flow and bond to any subsequent additional layers.

30

35

The exposed upper surface of the first layer is heated at 400°C until it melts. This is characterised by a colour change in the material from natural/beige to sugar brown to a darker

colour when the material is hotter and is truly molten. Some flow will occur with the PEEK particles in the first layer so they will contact one another. The first layer is then covered with an even spread of the blend of Example 2 to define a second layer. The particles of the blend at ambient temperature stick to the molten upper surface of the first layer. This second layer is
5 heated to cause flow as for the first layer. Additional layers may be formed until the desired thickness is obtained. During formation of each layer, the PEEK flows and the filler (Bioglass) remains homogenously positioned in the PEEK and prevents a solid mass comprising regions of unfilled PEEK forming.

10 After formation of the last layer, the construct is removed and allowed to cool. A coral-like structure of PEEK and filler is created. The PEEK microgranules of uniform sizes have flowed into more elongated shapes and contacted one another.

After formation, the cooled shape may be placed in an oven, machined, heated and/or leached
15 as described in Example 2. The result is a construct having a non-porous region defined by the foundation layer and a porous region defined by the other layers.

Example 4 – Preparation of an alternative layered polymeric material comprising a construct having varying porosity

20

Blends of different soluble fillers (e.g. water soluble phosphate glass) and PEEK particles of suitable size were blended to create separate mixes of PEEK/fillers. Finer PEEK particles can be blended with larger particles of filler and/or larger particles of PEEK can be blended with finer particles of filler. These blends can be used to create gradients of porosity and pore
25 sizes. A foundation layer is laid onto a surface. This can be formed from a blend or from PEEK alone as described in Example 3. The material is then heated at 400°C as described in Examples 2 and 3 and a mesh/web/netting-like structure formed. The foundation layer is then covered with an even preferably one or two/three particles thick spread of a selected blend. The particles of the blend at ambient temperature stick to the molten upper surface of the
30 foundation layer. This layer is then heated to heat the PEEK and cause flow as described previously. This process is repeated using the same blend until the desired thickness is obtained. An alternative blend can next be selected and layers built up, in the manner described using the first blend. Other alternative blends may be used to form further layers if desired. After the last layer has been formed, the construct is removed and allowed to cool. A
35 coral-like structure of PEEK and filler is created. The PEEK particles have flowed into more elongated shape and contacted one another. After formation, the cooled shape may be placed in an oven, machined and/or leached as described in Example 2. In view of use of different blends, the construct may include, after leaching, regions of different porosities.

Example 5 – Preparation of a bioactive material that possesses structure and is arranged to define interconnected passageways through the material as the bioactive material is absorbed by surrounding bore

- 5 Bioactive fillers (e.g. Bioactive glass 45S5 or hydroxyapatite) and PEEK particles of suitable size were blended to create separate mixes of PEEK and respective fillers. Fine PEEK particles can be blended with larger particles of bioactive fillers; and larger particles of PEEK can be blended with finer particles of bioactive fillers. Differing ratios of materials can be used to accommodate different or additional fillers, shape and size of particles. These blends can be
10 used to create constructs having gradients of concentration of bioactive fillers within PEEK matrixes, as described in Examples 2 to 4. The bioactive particles may be uniform in shape (e.g. spherical hydroxyapatite (HA) beads of diameter 600 microns). The filler can be incorporated to define a construct such that the HA beads and PEEK particles interconnect. This provides channels of HA through the material and supporting interconnected channels of
15 PEEK to provide structure. Implants may be made from the constructs by machining and the implants introduced into a patient. The bioactive fillers are absorbed by the body in vivo to leave a desired interconnected porous network of suitable shape that allows bone growth through the material. This is beneficial over usual methods of compounding these bioactive materials (e.g. blending and melting a large single mass of material) as it creates deliberate
20 interconnection of the filler to provide channels.

The method described in the present example may be advantageous over known methods. For example, known compounding methods such as twin screw extrusion may be limited in terms of the sizes of bioactive particles that can be used or the PEEK may react with the filler
25 (e.g. as in the case of Bioglass 45S5 especially under prolonged temperature or additional shear). Also materials formed may essentially have available only surface bioactivity from filler presented at the surface. The method described herein may advantageously allow parts to be made comprising PEEK and bioactive fillers, with improved potential for osseointegration as the filler particles can be substantially homogeneously arranged within the PEEK matrix, so as
30 to interconnect with one another. This is difficult to achieve using methods of compounding or compression moulding unless high levels of filler are used (eg. greater than 70%). Additionally the filler particles can be present at high loadings and/or with filler particles in contact with one another which would be difficult to obtain using methods such as extrusion which have a maximum filler particle size (before attrition due to shear forces) and where filler concentration
35 is restricted due to a reaction or high viscosity. Prior art arrangements may have limited potential for osseointegration as the distribution of bioactive particles is heterogeneous due to the methods used (eg. compounding), or filler particle size restrictions (eg. powders or whisker or fibres) or overall upper limits on the filler concentrations needed to provide

bioactivity (through frequency of occurrence at the surface) whilst still satisfying structural needs (e.g. in the region of 40wt% filler of HA in PEEK) for retaining structural integrity.

Example 6 – Mechanical Testing of Materials

5

Five strip test pieces, nominally 10mm wide, 4mm thick and 80mm in length, were tested. Prior to testing each test specimen was conditioned for a minimum period of 16 hours at $23 \pm 2^\circ\text{C}$ and $50 \pm 10\%$ relative humidity.

10 The flexural strength and modulus of each test specimen was then determined in general accordance with BS EN ISO 178:2003, at a speed of 2mm/minute. The span length of the flexural jig was set to 60mm and the radius of the support and loading nose utilised was 5mm. The displacement of each test piece was measured by an LVDT flexural jig for the determination of the flexural modulus values.

15

The results were as follows:

	<u>Flexural Strength (MPa)</u>	<u>Flexural Modulus (MPa)</u>
	<u>11.0</u>	<u>317.4</u>
	<u>13.3</u>	<u>347.6</u>
	<u>7.5</u>	<u>354.3</u>
	<u>9.7</u>	<u>262.1</u>
	<u>11.7</u>	<u>328.8</u>
<u>Mean</u>	<u>10.6</u>	<u>322.0</u>

20 Benefits associated with processes and materials described in the examples may include some or all of the following:

(a) The laying up, flow and spreading of the PEEK helps create a more open (non-compressed) structure. This can lead to benefits if it is desired to create a structure
25 where subsequent infiltration is required.

(b) The inclusion of a solid filler allows subsequent machining. Machining sintered materials which already possess porosity is more likely to smear closed the surface pores and/or fracture the material.

30

- (c) Constructs made as in the examples herein have the open porosity only obtained with e.g. 70-80wt% filler under other methods (e.g. compression moulding PEEK: NaCl blends) but achieved using only 50wt% filler. Therefore the constructs may retain more strength.
- 5
- (d) Large constructs (e.g. sheets) can be created.
- (e) The porous material can be readily deburred or cut and modified when porous (within reason), which is difficult with, for example, porous metals in the medical field (eg. Trabecular Metal from Zimmer, Regenerex from Biomet).
- 10
- (f) The porous material can be repeatedly sterilised using steam, ethylene oxide or gamma, unlike porous plastics used in the medical arena (eg. in craniomaxillofacial porous polyethylene called Medpor from Porex)
- 15
- (g) The resulting tissue ingrowth and regeneration can be monitored with the porous PEEK material since it can be visualised due to the radiolucent nature of the PEEK as opposed to porous metals, which generate artefacts under CT or MRI scans.
- 20
- (h) The reduced modulus of the porous PEEK may help transference of micromechanical stresses into the ingrowing tissue and may benefit the tissue regeneration. This is theorised under the Orthopaedic theory of Wolffs Law or soft tissue's Davis' Law.
- (i) Solid and filled regions can be formed easily in one unitary part.
- 25
- (j) The PEEK is allowed to flow (rather than sinter, melt and only bond at touch points) which merges the PEEK particles better together leading to less friability.
- (k) The laying up of layer-by-layer encourages an openness in the arrangement of the PEEK and filler and resultant openness of the end material such that removal of the filler is easier than in compressed parts and creates more readily the interconnected channels sought for tissue ingrowth. If an implant is made which is implanted in vivo with the filler left inside (e.g. using HA, TCP or Bioglass), then the facilitated contact and openness allows these channels to be formed as the filler is absorbed in situ in the
- 30
- body.
- 35
- (l) The removal of the filler (e.g. porogen or fugitive material) is made easier using this "uncompressed process" since filler particles contact more readily and loosely and the internal structure encourages more openness. This may be contrasted with prior art

routes (e.g. using compression moulding) where porogen can become surrounded and entrapped by matrix material.

- 5 (m) Compression moulded materials comprising polymers and porogens (e.g. salt crystals) form angular pores due to the crystal shapes. The sharp edges to the pores may be potential sites for crack propagation in the material when placed under load. The method of the present examples does not use solely the filler material (e.g. fugitive material) structure to solely define the pores. In addition selection of the correct filler can confer more rounded pore shapes.
- 10 (n) In compression moulding, a large mass of material is heated at once which results for some time in an uneven temperature distribution (e.g. the outside of the mass may be subjected to higher temperature for longer times compared to material centrally within the mass) with potential for uneven melting and/or degradation of the polymer matrix material. In the examples described herein, heat can be applied evenly from one
- 15 direction for a shorter time to target the area required to melt such that prolonged exposure is avoided.
- 20 (o) As an alternative to use of microgranules consisting of PEEK, compounds may be prepared in a variation of Example 1 by combining PEEK with fillers such as barium sulphate or carbon or glass fibres. In addition, Bioactive (eg. TCP, HA, bioglass, ceramics, anti-infection agents) filled PEEK, imaging (eg. BaSO₄) or reinforcing structures (e.g. nanofilaments, fibres, whiskers) can be compounded into PEEK and subsequently be made into smaller granules to be used as feedstock.
- 25 Filler (e.g. porogen or fugitive material) may be removed from constructs and parts, for example machined parts, made as described above, using purification apparatus as described in PCT/GB02/02525. The apparatus includes a pressure vessel which has a heated and thermally insulated jacket. Upstream of the vessel is a water supply line for delivering
- 30 pressurized water into the vessel and downstream of the vessel there is a water drain for removing water to waste. In use, a sample of material (e.g. machined ingot or part plaque, rod or film) is placed in the vessel and then liquid water at high pressure and temperature is caused to flow through the vessel. The water penetrates the PEEK polymer and dissolves the fugitive material. Other solvents may be used to remove other fillers partially or wholly. For
- 35 example PEEK is resistant to NaOH which can solubilise 45S5 Bioglass, or HCl which can solubilise CaCO₃.

The methods and materials described herein may have a wide range of applications. They may advantageously be used in making medial implants which may be partially or entirely

porous, having had a porogen/fugitive material removed during their preparation or an implant which incorporates a bioactive filler which is removed in vivo may be provided.

5 The methods described may be used to make a craniomaxillofacial implant. This may be designed with porous regions to prevent implant migration through tissue ingrowth and a smooth area to facilitate overlying muscle movement (e.g. jaw). The porous area may be part of all of one side or a combination of two sides. Figure 4 shows a mid-face implant with porous outer region 28. They may also be used to deliver a loaded filled implant (eg. PEEK and HA), of which the HA can be resorbed in situ and bone to grow into the remaining
10 interconnected channels.

Parts of hip implants for example acetabular cups with a porous backing (part 30 – see Figure 6) may be made using methods described herein.

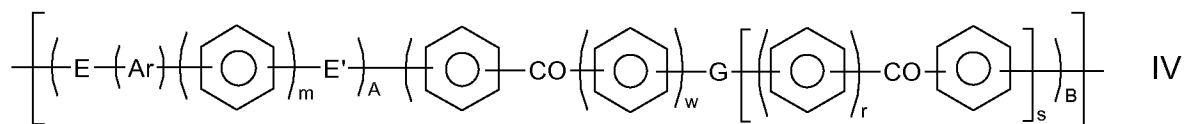
15 As shown in Figure 7, a material which includes a partially solid region 40, suitably comprising PEEK, and a partially porous region 42, suitably comprising porous PEEK, may be prepared. This may have various uses. such as for providing materials parts of spinal implants, for example of types described in United States Patent Application 20080161927.

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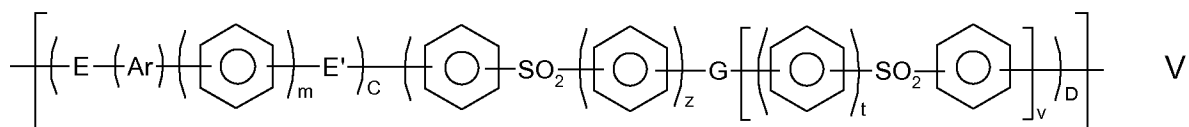
CLAIMS

1. A method of making a material comprising the steps of:
 - 5 (i) forming a layer L1 of a composition comprising a polymeric material and a filler material;
 - (ii) subjecting the layer L1 to a temperature above the melting temperature of the polymeric material in order to melt the polymeric material in layer L1;
 - 10 (iii) forming on layer L1 a layer L2 of a composition comprising a polymeric material and a filler material;
 - (iv) subjecting layer L2 to a temperature above the melting temperature of the polymeric material in order to melt the polymeric material in layer L2.
- 15 2. A method according to claim 1, which comprises selecting first particles which comprise said polymeric material and selecting second particles which comprise said filler material, wherein said composition is formed by blending said first particles and said second particles.
- 20 3. A method according to claim 2, wherein said first particles include particles having a volume in the range 0.001 to 3mm³ and said second particles have a D₅₀ in the range 1 to 20000µm.
4. A method according to claim 2 or claim 3, wherein the ratio of the average volume of the

25 first particles to the average volume of the second particles is in the range 0.2 to 5.
5. A method according to any preceding claim, wherein said composition includes at least 30 wt% and less than 65 wt% of said polymeric material.
- 30 6. A method according to any preceding claim, wherein at least 90 wt% of said composition is made up of said polymeric material and filler material.
7. A method according to any preceding claim, wherein said polymeric material includes a repeat unit of general formula

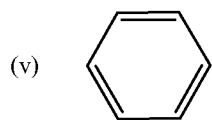
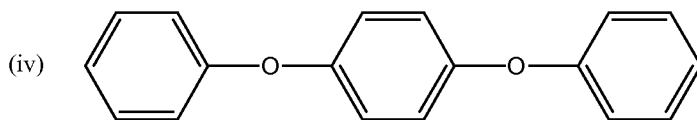
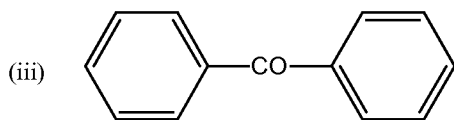
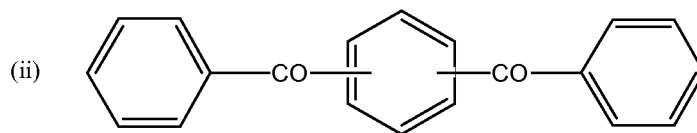
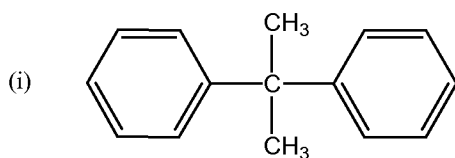


or a repeat unit of general formula

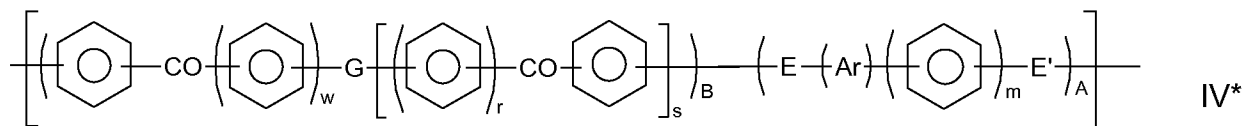


- 5 wherein A, B, C and D independently represent 0 or 1, E and E' independently represent an oxygen or a sulphur atom or a direct link, G represents an oxygen or sulphur atom, a direct link or a -O-Ph-O- moiety where Ph represents a phenyl group, m, r, s, t, v, w, and z represent zero or 1 and Ar is selected from one of the following moieties (i) to (v) which is bonded via one or more of its phenyl moieties to adjacent moieties

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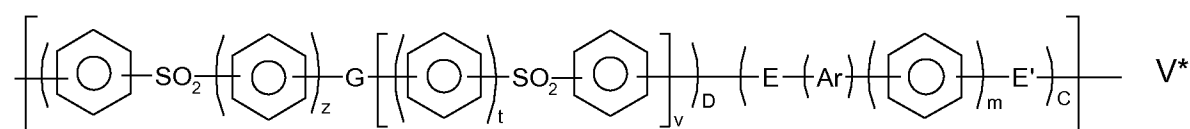


or said polymeric material includes a repeat unit of general formula



or a repeat unit of general formula

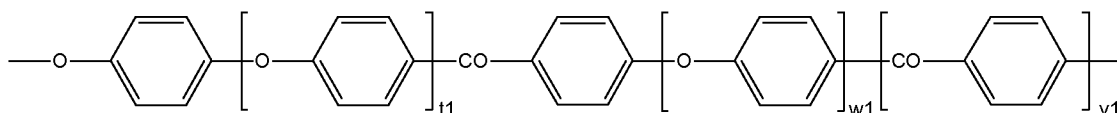
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wherein A, B, C, and D independently represent 0 or 1 and E, E', G, Ar, m, r, s, t, v, w and z are as described.

8. A method according to any preceding claim, wherein said polymeric material comprises a repeat unit of formula (XX)

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where t1, and w1 independently represent 0 or 1 and v1 represents 0, 1 or 2.

15

9. A method according to any preceding claim, wherein said polymeric material is polyetheretherketone.

10. A method according to any preceding claim, wherein said filler material has a melting point which is greater than the T_m of the polymeric material by at least 50°C.

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11. A method according to any preceding claim, wherein, in the method, a said composition comprising a said polymeric material and a filler material is selected and contacted with a surface S1 for defining layer L1, wherein layer L1 has a thickness across at least 50% of its area of less than 3mm.

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12. A method according to any preceding claim, wherein said layer L1 is heated, in step (ii), after it has been laid down so that it reaches a temperature above the T_m of the polymeric

material, provided that said temperature is less than the decomposition temperature of said polymeric material.

13. A method according to claim 12, wherein heating of said layer L1 is carried out using a heating means which comprises a radiant heat source.

14. A method according to claim 12 or claim 13, wherein after heating in step (ii) of the method, a composition comprising a said polymeric material and filler material is selected and contacted with layer L1, during step (iii) of the method.

15. A method according to claim 14, wherein said layer L1 is tacky when contacted with said composition in step (iii).

16. A method according to any preceding claim, comprising forming layers L1 to Ln wherein n is at least 10.

17. A method according to any preceding claim, wherein the volume occupied by filler material in the material made in the method is at least 10 vol% and is less than 80 vol%.

18. A method according to any preceding claim, which includes a step of altering the shape of the material after the last layer has been laid down, for example by machining or thermoforming.

19. A method according to any preceding claim, which includes forming the material into a medical implant or a part thereof.

20. A method according to any preceding claim, which includes the step of treating the material made to remove at least some of said filler material.

21. A method according to any preceding claim, wherein layer L1 is formed on a surface S1 which comprises a heat resistant surface and the method includes disengaging said layer L1 from surface S1 after formation of the material to produce a material which is separate from said surface S1.

22. A method of making a medical implant or part thereof, the method being as described in any preceding claim.

23. A material comprising a polymeric material and filler material as described in any of claims 1 to 21.

24. A material according to claim 23, which comprises a porous material comprising porous polymeric material which is polyetheretherketone which has a porous volume fraction of less than 65% and which is at least 54%; and/or a solid volume fraction of less than 50% and which is at least 50%; and/or an average connectivity of 1.5 to 2.5mm³; and/or an average pore size in the range 550 to 800µm.

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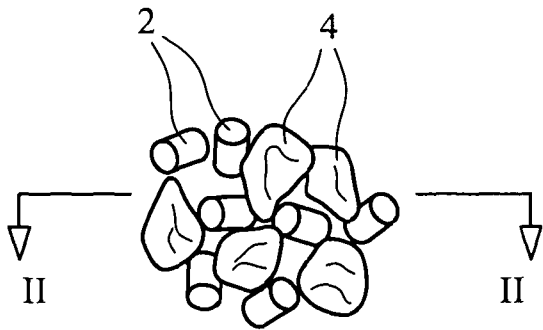


FIG. 1a

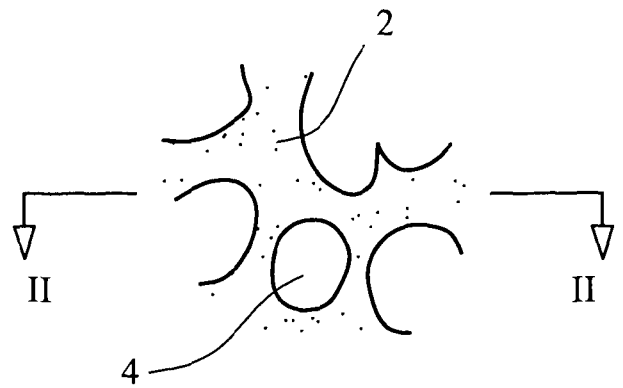


FIG. 1b



FIG. 2a



FIG. 2b

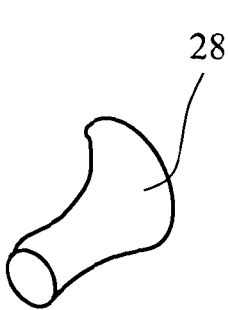


FIG. 5

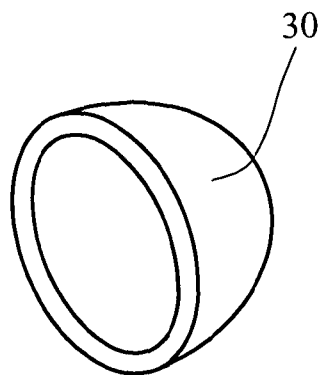


FIG. 6

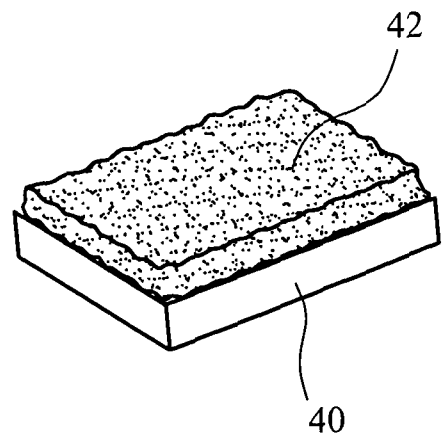


FIG. 7



Fig. 3a



Fig 3b



Fig.3c

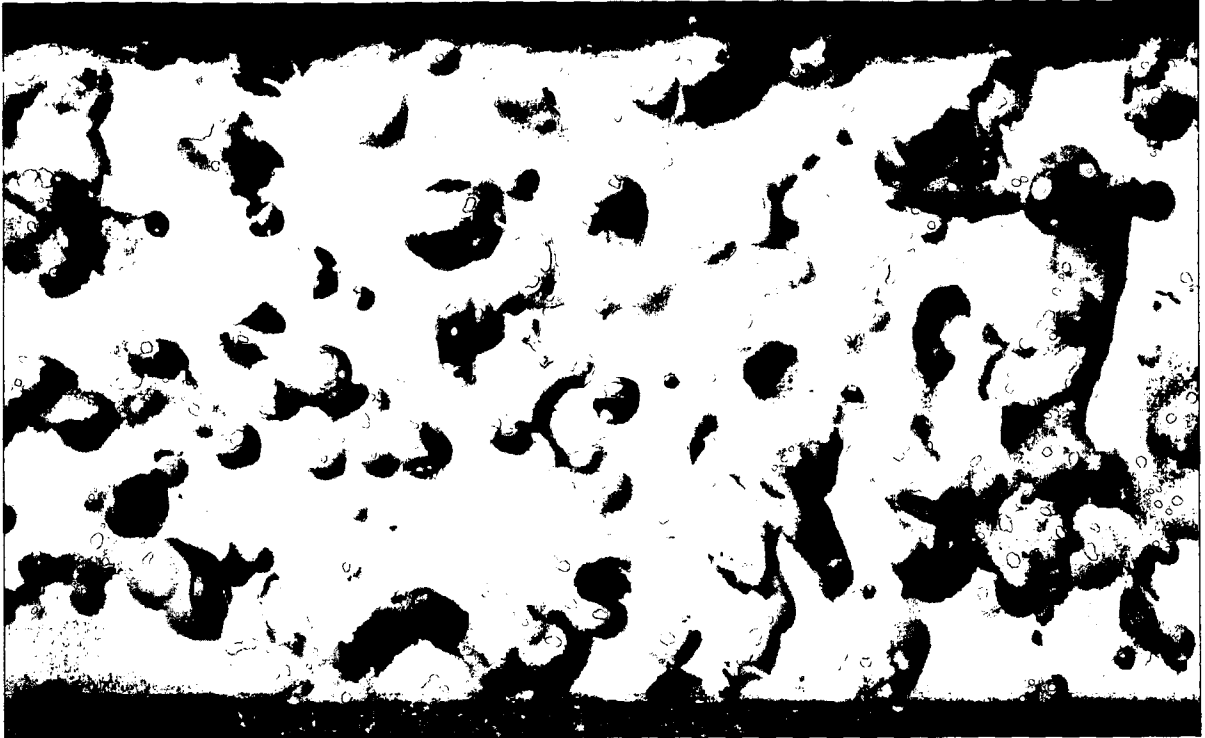


Fig. 3d



Fig. 3e

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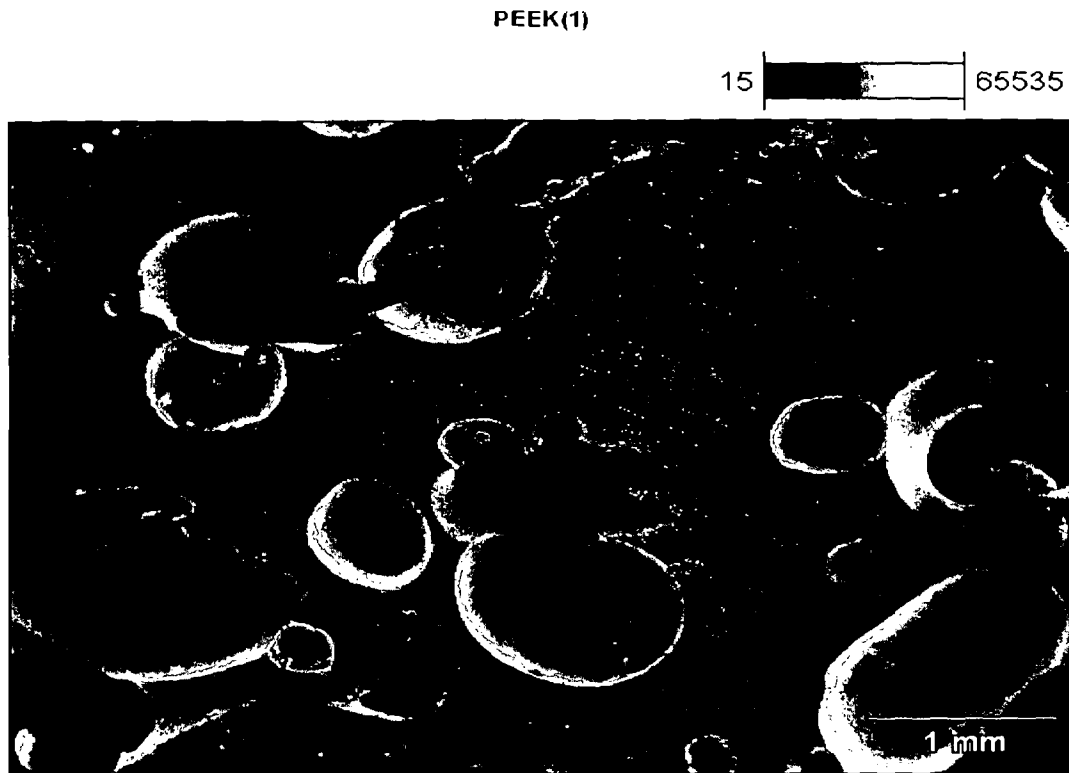


Fig 4a

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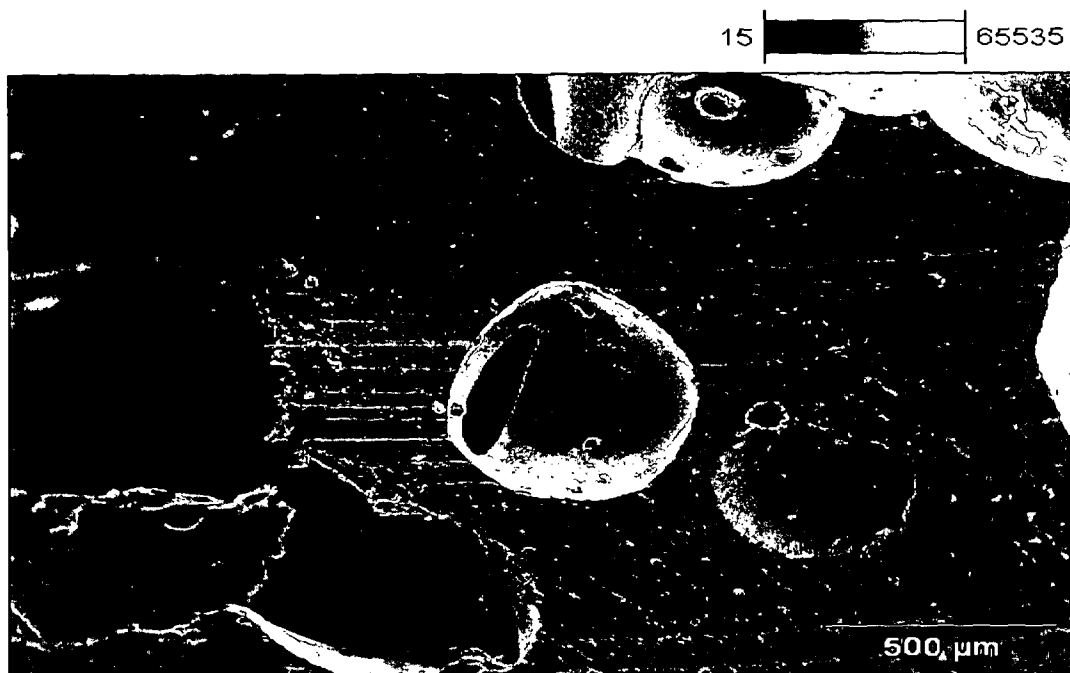


Fig. 4b

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2011/050430

A. CLASSIFICATION OF SUBJECT MATTER

INV. B29C67/00 B29C67/20 A61L27/56 A61L27/18 A61L27/48
C08J9/26 B32B37/04

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)

B29C A61L C08J B32B 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 practical, search terms used)

EP0-Internal

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Y	paragraph [0012] - paragraph [0030]; figure 3	20

X	WO 2009/014718 A1 (POREX CORP [US]; NOBLE AARON M [US]; MAO GUOQIANG [US]; HENRY SEBASTIE) 29 January 2009 (2009-01-29)	1-19, 21-24
Y	page 3, paragraph 2 - page 5, paragraph 5 page 8, paragraph 3 - paragraph 4 page 12, paragraph 1 page 14, paragraph 4 - paragraph 5 page 17, paragraph 2 - paragraph 3; example 3	20

	-/--	



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

3 May 2011

Date of mailing of the international search report

23/05/2011

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INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2011/050430

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	paragraphs [0013], [0074] - paragraph [0076]; claims 11-129; figures -----	20
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Information on patent family members

International application No

PCT/GB2011/050430

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