delivery systems where shape-memory is required. US-A-2006/0 140 999 describes the use of similar shape-memory polymers for use in drug release systems, wherein the shape-memory material comprises units, derived from monomers selected from the group consisting of caprolactone, lactide, glycolide and dioxanone. Examples include PDS—PCL and PDS—PLGA multi-block copolymers. These materials cannot exhibit any significant swelling capacity under (simulated) physiological conditions, since swelling would induce loss of mechanical properties and thus loss of the memorised shape.

Other phase-separated, segmented multi-block copolymers include polyetherester copolymers as described in US-A-5 980 948. These copolymers consist of crystalline aromatic segments and soft PEG-containing segments linked by hydrolysable ester bonds. The copolymers have the inherent drawback that low swellable compositions, *i.e.* compositions rich in hydrophobic aromatic segments, are not well-degradable, due to the high crystallinity and hydrophobicity of the aromatic segments. Highly swellable compositions, *i.e.* compositions rich in PEG, are not well-degradable either, due to the low concentration of ester bonds. In contrast, the multi-block copolymers of the current invention are degradable at each segment A/segment B ratio, due to the presence of ester bonds in segment A as well as in segment B. Further, in contrast to the multi-block copolymers of the current invention, the T_g of polyetherester copolymers cannot be varied and is always low, around the T_g of PEG, *i.e.* -30 °C.

Objective of the embodiments disclosed herein~~invention~~ is to overcome one or more of the drawbacks observed in the prior art.

In a first aspect the ~~invention~~disclosure is directed to a biodegradable, semi-crystalline phase separated, thermoplastic multi-block copolymer, the copolymer being characterised in that:

a) it comprises at least one hydrolysable pre-polymer (A) segment and at least one hydrolysable pre-polymer (B) segment;

b) said multi-block copolymer having a T_g of 37 °C or less and a T_m of 110-250 °C under physiological conditions;

c) the segments are linked by a multifunctional chain-extender;

d) the segments are randomly distributed over the polymer chain; and

~~c)~~d) at least part of pre-polymer (A) is derived from a water-soluble polymer.

The multi-block copolymer of the ~~invention~~disclosure can be composed of at least two different segments each having different physical characteristics, including degradation and swelling characteristics. Due to their unique make-up and their semi-crystalline phase separated morphology, the materials of the ~~invention~~disclosure are surprisingly versatile and extremely suited for constructing drug delivery matrices and drug eluting coatings, which are utilisable for encapsulating certain therapeutic agents and for sustained release of the encapsulated therapeutic agent either locally or into the systemic circulation. As is described herein below, the composition of the ~~invention~~disclosure is of particular interest for the controlled release of a biologically active compound, such as a biologically active polypeptide to a host.

In a second aspect, there is provided a process for preparing a biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above, comprising

i) performing a chain extension reaction of pre-polymer (A) and pre-polymer (B) in the presence of a multifunctional chain-extender, wherein pre-polymer (A) and (B) are both diol or diacid terminated and the chain-extender is di-carboxylic acid or diol terminated; or

ii) performing a chain extension reaction using a coupling agent, wherein pre-polymer (A) and (B) are both diol or diacid terminated and the coupling agent is preferably dicyclohexyl carbodiimide.

In a third aspect, there is provided the use of a biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above for drug delivery, preferably in the form of microspheres, microparticles, nanoparticles, nanospheres, rods, implants, gels, coatings, films, sheets, sprays, tubes, membranes, meshes, fibres, or plugs.

In a fourth aspect, there is provided a composition for the delivery of at least one biologically active compound to a host, comprising at least one biologically active compound encapsulated in a matrix, wherein said matrix comprises at least one biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above.

In a fifth aspect, there is provided a composition as defined above for treating rheumatoid arthritis, hepatitis, diabetes, metabolic syndromes, osteoarthritis, renal disease, inflammation, local pain processes, local infections, local skin diseases, tumours (or their sites after surgical removal as a postoperative treatment to destroy any tumour cells possibly remaining), prostate or breast cancer, agromegaly, ocular diseases such as age-related macular degeneration, local brain diseases such as Parkinson's disease, and cardiovascular diseases such as acute myocardial infarction, chronic heart failure or arthrosclerosis.

In a sixth aspect, there is provided a method of manufacturing a composition as defined above, comprising the successive steps of

a) emulsifying an aqueous solution of a water-soluble biologically active compound in a solution of a biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above in an organic solvent, such as dichloromethane or ethyl acetate;

b) subsequently emulsifying the resultant emulsion of a) in an aqueous solution comprising a surfactant such as polyvinyl alcohol, thereby yielding a water-in-oil-in-water (W/O/W) emulsion; and

c) extracting the organic solvent to solidify microspheres.

In a seventh aspect, there is provided a method of manufacturing a composition as defined above, comprising the successive steps of

a) dispersing the biologically active compound as a solid powder in a solution of a biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above in an organic solvent, such as dichloromethane or ethyl acetate;

b) emulsifying the resultant dispersion of a) in an aqueous solution comprising a surfactant such as polyvinyl alcohol, thereby yielding a solid-in-oil-in-water (S/O/W) emulsion; and

c) extracting the organic solvent to solidify the microspheres.

In an eighth aspect, there is provided a method of manufacturing a composition as defined above, comprising the successive steps of

a) emulsifying an aqueous solution of a water-soluble biologically active compound in a solution of a biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above in an organic solvent, such as dichloromethane or ethyl acetate;

b) adding a polymer precipitant, such as silicon oil, to the resultant emulsion of a) to form embryonic microparticles; and

c) extracting the polymer precipitant and the organic solvent to solidify the microspheres.

In a ninth aspect, there is provided a method of manufacturing a composition as defined above, comprising the successive steps of

a) dispersing the biologically active compound as a solid powder in a solution of a biodegradable, semi-crystalline, phase separated, thermoplastic multi-block copolymer as defined above in an organic solvent, such as dichloromethane or ethyl acetate;

b) adding a polymer precipitant, such as silicon oil, to the resultant dispersion of a) to form embryonic microparticles; and

c) extracting the polymer precipitant and the organic solvent to solidify the microspheres.