

## PolyPEG<sup>®</sup> – Enhancing Biological Therapeutics



PolyPEG<sup>®</sup> is a novel, proprietary PEGylation technology based on low viscosity polymers that are designed to enhance biological therapeutics. PolyPEG<sup>®</sup> molecules differ structurally from linear and branched PEGs in comprising a “comb-like” arrangement of short PEG chains (typically of 1-2 kDa molecular weight) attached to a polymer backbone via ester linkages.

Offering a differentiated approach to half-life extension, PolyPEG<sup>®</sup> molecules can be tailored for a particular requirement for PEGylation of a range of therapeutic molecules. They can be synthesised with a chosen molecular weight (in the range 10-80+ kDa) and conjugating group for stable and site-directed attachment to biologics using established or novel chemical techniques.

A significant advantage of PolyPEG<sup>®</sup> polymers is their low viscosity; they are at least five-fold less viscous than comparable linear and branched PEGs allowing high concentrations to be administered without difficulty.

The ‘comb-like’ nature of PolyPEG<sup>®</sup> provides a unique approach to PEGylation by exploiting the properties of a structure that degrades to small units that are readily excreted over time. This allows their use at high cumulative total doses, while avoiding potential toxicological problems associated with accumulation of larger molecular weight PEG chains in tissues.

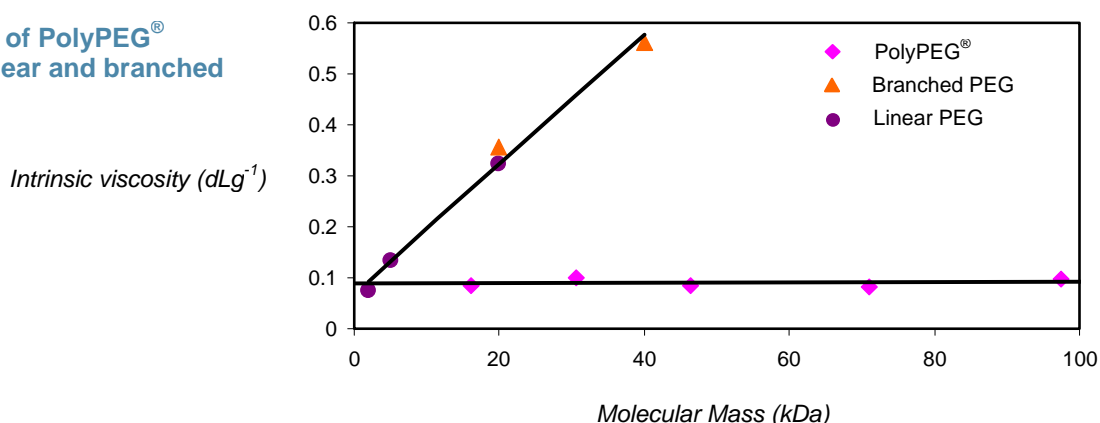
### Design Versatility

PolyPEG<sup>®</sup> can be covalently attached site-specifically to a wide range of protein, peptide and other biologically active molecules, including oligonucleotides and small molecules using conventional (eg at cysteine or lysine residues, or at the N-terminus) and novel techniques. Properties such as molecular weight (ranging up to 80+ kDa), length of PEG teeth (0.5, 1 or 2 kDa) and attachment groups can all be tailored to provide the optimal PolyPEG<sup>®</sup> for achieving a specific profile for the therapeutic product.

### Low Viscosity

The high molecular weights possible with PolyPEG<sup>®</sup> (up to 80+ kDa) allow a significant increase in the hydrodynamic volume of a biomolecule through the site-directed attachment of a single polymer. Furthermore, as PolyPEGs<sup>®</sup> are at least five-fold less viscous than comparable linear and branched PEGs (Fig 1), high concentrations of PolyPEG<sup>®</sup> biomolecule conjugates can be formulated without difficulty.

**Fig 1: Viscosity of PolyPEG<sup>®</sup> compared to linear and branched PEGs**



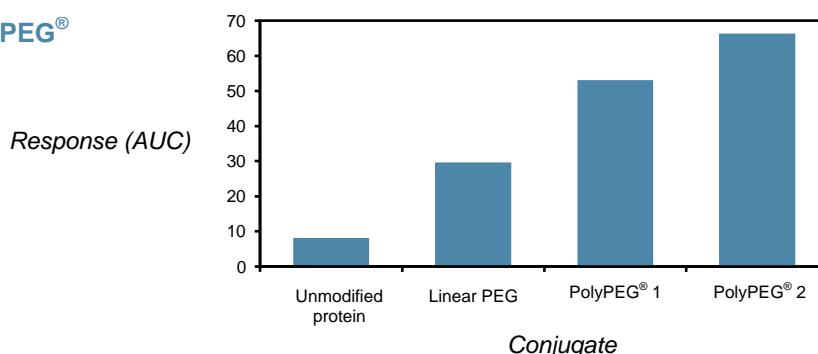
### Manufacture

Manufacturing processes to produce PolyPEG<sup>®</sup> are readily scalable with current production levels up to the 10 kg scale. These processes are straightforward and reproducible and a strategy for GMP production of material is in place.

## Efficacy

PolyPEG<sup>®</sup> protein conjugates show enhanced bioactivity *in vivo* (Fig 2), compared to standard linear PEGs and unconjugated protein controls. Proteins conjugated to PolyPEG<sup>®</sup> also show minimal loss of *in vitro* activity.

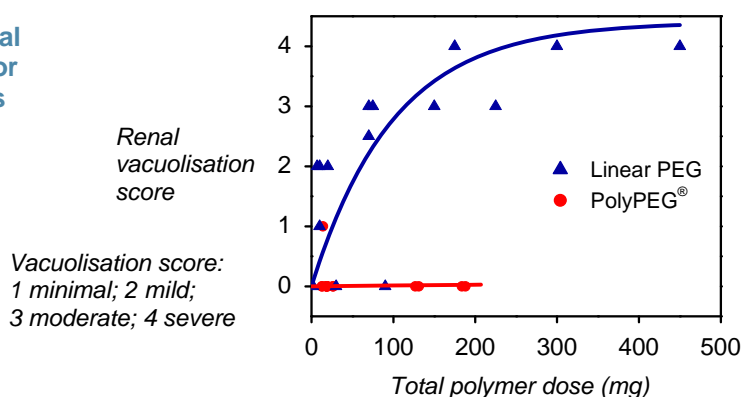
**Fig 2: Biological activity of PolyPEG<sup>®</sup> protein conjugates *in vivo***



## Safety

The PolyPEG<sup>®</sup> backbone is based on methacrylate, a polymer that is used in wide ranging medical applications, such as contact lenses and stent coatings. A major advantage of PolyPEG<sup>®</sup> is the short-chain length of PEG and the presence of ester bonds between the backbone of the comb and the PEG teeth. Slow degradation over time facilitates clearance of the smaller PEG and methacrylate molecules from the body, thereby avoiding the potential problems associated with tissue accumulation of larger PEG chains from conventional linear PEGs (Fig 3).

**Fig 3: Comparison of pre-clinical renal toxicity versus total PEG exposure for PolyPEG<sup>®</sup> and linear PEG conjugates**



## Intellectual Property

PolyPEG<sup>®</sup> is protected by a series of granted patents and patent applications. The patent coverage includes the polymer molecules and their derivatives, and the processes to produce them.

## Commercial Strategy

The unique and novel features of PolyPEG<sup>®</sup> offer a means of product differentiation in terms of ease of formulation based on the low viscosity of these polymers, as well as on safety and efficacy grounds. WEP's strategy is to establish partnerships with pharmaceutical and biotechnology companies wishing to develop novel PolyPEG<sup>®</sup> versions of molecules to enhance their therapeutic effect. A typical collaboration starts with WEP working with its partners to define and produce the optimal PolyPEG<sup>®</sup> for the purpose and to establish the optimal protein conjugation conditions.

In addition to supplying PolyPEG<sup>®</sup>, the Company's objective is to license-out the PolyPEG<sup>®</sup> technology for specific target molecules and/or applications on either an exclusive or non-exclusive basis.