

dPEG® for ADC Linker Design

Preventing low solubility, high aggregation, and low stability

dPEG®, from Vector Laboratories, are “discrete polyethylene glycol” products that can be utilized in ADC linker design. While traditional PEGs are not single compounds, each dPEG product represents a single compound with a unique, specific, single molecular weight (MW) (Figure 1). Vector Laboratories manufactures dPEG using a patented process to synthesize monodisperse linkers with longer lengths (>12 EO), orthogonal branching, greater functional group customization, and superior purity.

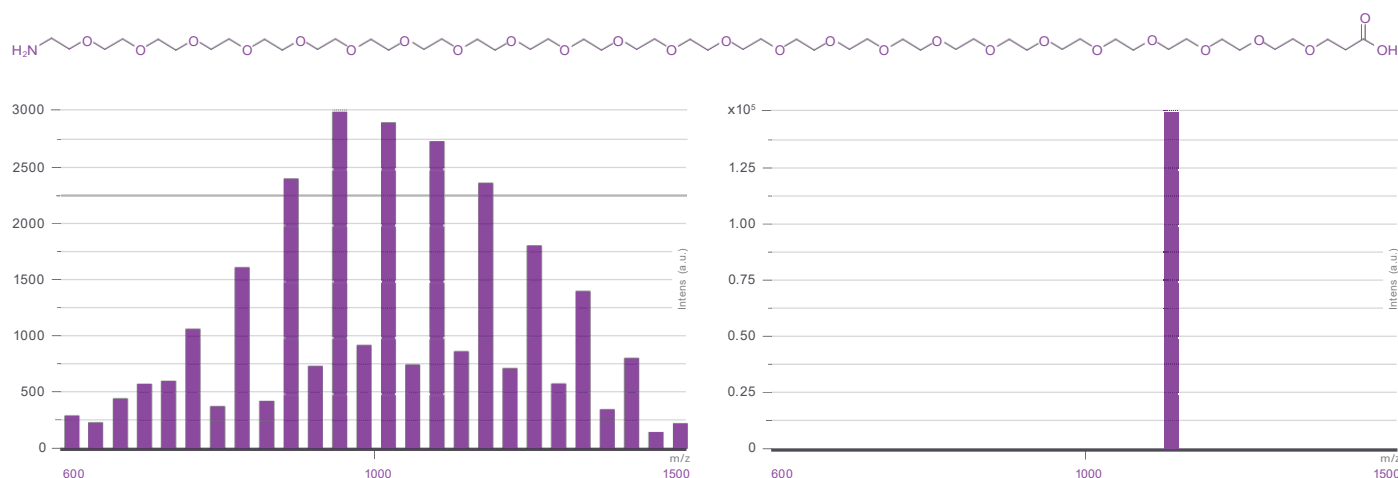
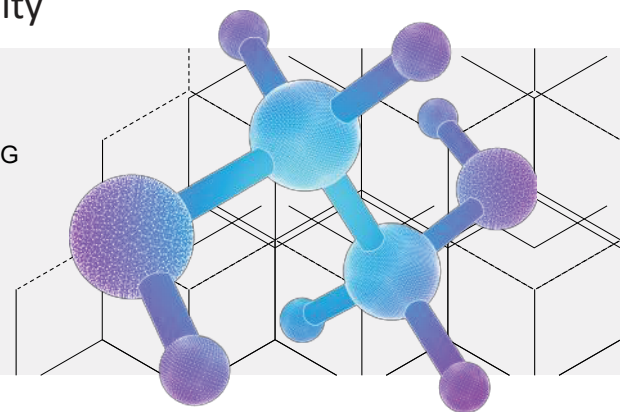


Figure 1: Side-by-side comparison of actual mass spectra from a traditional, dispersed PEG (left spectrum) and a dPEG® of equivalent mass from Vector Laboratories (right spectrum). The mass spectrum on the left is of PEG1000. It has $M_w = 1027$ Daltons; $M_n = 888$ Daltons; and $D = 1.16$. The masses in this dispersed PEG range from 600 – 1,500 Daltons. The mass spectrum on the right is of Vector Laboratories product number QBD-10317, amino-dPEG_n-acid, the structure of which is shown across the top of the two mass spectra. QBD-10317 is a single molecular weight compound with a single, discrete chain length. The molecular weight of QBD-10317 is 1146.355 Daltons. Because it has no dispersity, $D = 1$.

BioDesign™ and dPEG Linkers

BioDesign is an expert-guided, collaborative linker development service for bioconjugate therapeutic development. The portfolio provides a variety of dPEG architectures, including Sidewinder™ and BodyArmor® (Figure 2). Sidewinder products offer flexibility in controlling the distance of a payload from the antibody while optimizing hydrophilicity. The BodyArmor product architecture is like Sidewinder but includes additional orthogonal dPEG strands. These and other dPEG linkers provide significant benefits compared to traditional PEGs when used in ADC design.



Figure 2: Architecture for Sidewinder and BodyArmor dPEG linkers. Purple starburst is reactive group to attach to the antibody, green – reactive group to attach to the payload/trigger, blue – end capping.

The dPEG Advantage:

- Increased payload solubility and conjugation efficiency: dPEG linkers can reduce the overall hydrophobicity and improve ADC conjugation efficiency by offsetting payload hydrophobicity.
- Reduced aggregation of ADCs: The length and positioning of dPEG can be optimized to reduce the aggregation of specific combinations of antibodies, reactive groups, cleavable triggers, payloads, and DARs.
- Improved ADC stability of enzyme-cleavable triggers: The hydrophilicity and biocompatible properties of dPEG can be leveraged to create steric effects that modulate trigger-payload metabolism and ADC stability without the physicochemical limitations of traditional linkers.

BioDesign's comprehensive portfolio provides a wide range of linkers that can be utilized across scientific fields of study. Visit vectorlabs.com/BioDesign for more information about dPEG products and to view the full catalog of linkers.

